Risk Factors in Early Implant Failure: A Meta-Analysis

Guillermo Manzano, DDS,* Javier Montero, DDS, PhD,† Javier Martín-Vallejo, PhD,‡ Massimo Del Fabbro, BSc, PhD,§ Manuel Bravo, MD, PhD,|| and Tiziano Testori, MD, DDS¶

Background: *Clinicians should be able to weigh the role of the main risk factors associated with early implant failure.*

Purpose: *The aim of this meta-analysis was to assess the influence of different patient-related and implant-related risk factors on the occurrence of early implant failure.*

Materials and Methods: *In July, 2014 the main electronic databases were searched for studies reporting on early failures. Relevant papers were selected by 2 independent authors using predefined selection criteria. Three authors independently scored the included studies for quality assessment. The estimated odds ratios of the main risk factors from the selected papers were subjected to meta-analysis.*

Results: *Nine studies were included. A total of 18,171 implants were meta-analyzed, of which 10,921 were analyzed for smoking, 15,260 for implant diameter, 16,075 for implant length, and 16,711 for implant location (maxilla vs mandible). The main significant risk factors for early implant failures were the smoking habit (odds ratio [OR], 1.7; 95% confidence interval [CI], 1.3, 2.3), implants shorter than 10 mm (OR, 1.6; 95% CI, 1.2, 2.2) and implants placed in the maxilla (OR, 1.3; 95% CI, 1.0, 1.6).*

Conclusions: *Clinicians should be aware of the increased risk of early failure in the presence of smokers, implants with reduced length, and implant-supported maxillary rehabilitation. (Implant Dent 2016;25:1–9)*

Key Words: dental implant, early failures, systematic review, risk assessment

Unsuccessful implant surgery can be characterized by the mobility of the implant, continuous radiolucency around the implant, peri-implantitis with suppuration, or subjective complaints from the patient.[1] However, no specific criteria for unsuccessful dental implants have been defined.[2] The inability of tissue to establish and/or maintain osseointegration is thought to cause implant failures.[3] Implant failures have been frequently associated with factors such as poor bone quality, insufficient bone volume, inadequate primary implant stability, and overload.[4]

Implant failures can be subdivided into early or late failures, depending on when they occur, that is, before abutment connection (early) or after implant loading (late). This subdivision is necessary because the etiology of these 2 kinds of failures is often different.[5] Early failure of an implant results from an inability to establish an intimate bone-to-implant contact.[6] This means that bone healing after implant insertion is impaired or jeopardized. The mechanisms that normally lead to wound healing by means of bone apposition fail, and instead fibrous scar tissue is formed around the implant.[7] This can lead to epithelial downgrowth, the so-called saucerization or marsupialization of the implant, which results in mobility or even implant loss.[8] Early failures are characterized by minimal bone loss,[3] and most of them occur very soon; so, knowledge of the potential risk factors of early failure is of paramount importance for clinicians.[9] Clinical studies have identified the foll-owing factors: implant features (width, length, surface, thread design, shape, etc), the quality and quantity of the bone site, surgery-related factors (flap/flapless, submerged/nonsubmerged positioning, insertion torque [related to bone density], bone standard drilling protocol/adapted drilling in low-density bone, Piezosurgery/conventional drilling, etc), use of grafted bone, and systemic factors such as genetic predisposition, smoking, and metabolic disorders.[2,10]

*Postgraduate Student, Master in Dental Sciences, University of Salamanca (USAL), Salamanca, Spain.
†Tenured Lecturer in Prosthodontics, Department of Surgery, Faculty of Medicine, University of Salamanca (USAL), Salamanca, Spain.
‡Tenured Lecturer in Statistics, Department of Statistics, School of Nursing, University of Salamanca (USAL), Salamanca, Spain.
§Associate Professor, Head of Section of Oral Physiology, Department of Biomedical, Surgical and Dental Sciences, IRCCS Galeazzi Institute, University of Milan, Milan, Italy.
||Professor of Preventive and Community Dentistry, Faculty of Odontology, University of Granada, Granada, Spain.
¶Visiting Professor, Head of the Section of Implant Dentistry and Oral Rehabilitation, Department of Biomedical, Surgical, and Dental Sciences, Dental Clinic (Chairman: Prof. R.L. Weinstein), IRCCS Galeazzi Institute, University of Milan, Milan, Italy.

Reprint requests and correspondence to: Tiziano Testori, MD, DDS, IRCCS Istituto Ortopedico Galeazzi, Via R. Galeazzi 4, Milan, 20161, Italy, Phone: +39 02 50319950, Fax: +39 02 50319960, E-mail: tiziano.testori@unimi.it

ISSN 1056-6163/16/02502-001
Implant Dentistry
Volume 25 • Number 2

DOI: 10.1097/ID.0000000000000386

Alternatively, late failure of an implant has been associated with both plaque-induced and/or overload-induced peri-implantitis.[11] Although many studies have focused on the role of systemic and local factors in the long-term maintenance of osseointegration,[12–15] less is known about the factors affecting initial bone apposition until abutment connection.[4,16] The incidence of early implant loss has been reported in a range between 0.76% and 7.47% and late implant loss (in studies with 5–10 years follow-up) in a range between 2.1% and 11.3%.[13] Clinicians should be able to weigh the role of the main risk factors associated with early implant failure to minimize them.

The aim of this meta-analysis was to assess the influence of different patient and implant-related risk factors on the occurrence of early implant failure.

MATERIALS AND METHODS

Search Strategy

In July, 2014, 2 electronic searches were performed in the PubMed database to retrieve the pertinent literature published in English language during the last 10 years. First, we used the following search string: "dental implants [Mesh] AND early [all fields] AND failure [all fields]," obtaining 53 articles. This broad search strategy was pursued to capture as many relevant studies as possible. Later, we used a more restrictive strategy ("early failure" AND "dental implants"), resulting in 29 articles. After adding as filter the term "randomized controlled trial" to both the above search strings, we did not obtain any study addressing risk factors for early failure with this study design. Reference lists of the papers eventually included were hand-searched to identify additional relevant studies and possible false exclusions.

The full search strategy and the corresponding results obtained by each step are shown in Figure 1.

Study Selection

Two authors (G.M. and J.M.) independently selected references on the basis of titles and abstracts for risk factors in early implant failures, using predefined exclusion criteria.

Case reports, reviews, nonhuman studies, studies exclusively dealing with immediate and/or early loading, and medically compromised patient groups (eg, irradiated patients and systemic diseases such as diabetes) were excluded. Disagreements between the authors were resolved in discussion sessions, and if not resolved, a third

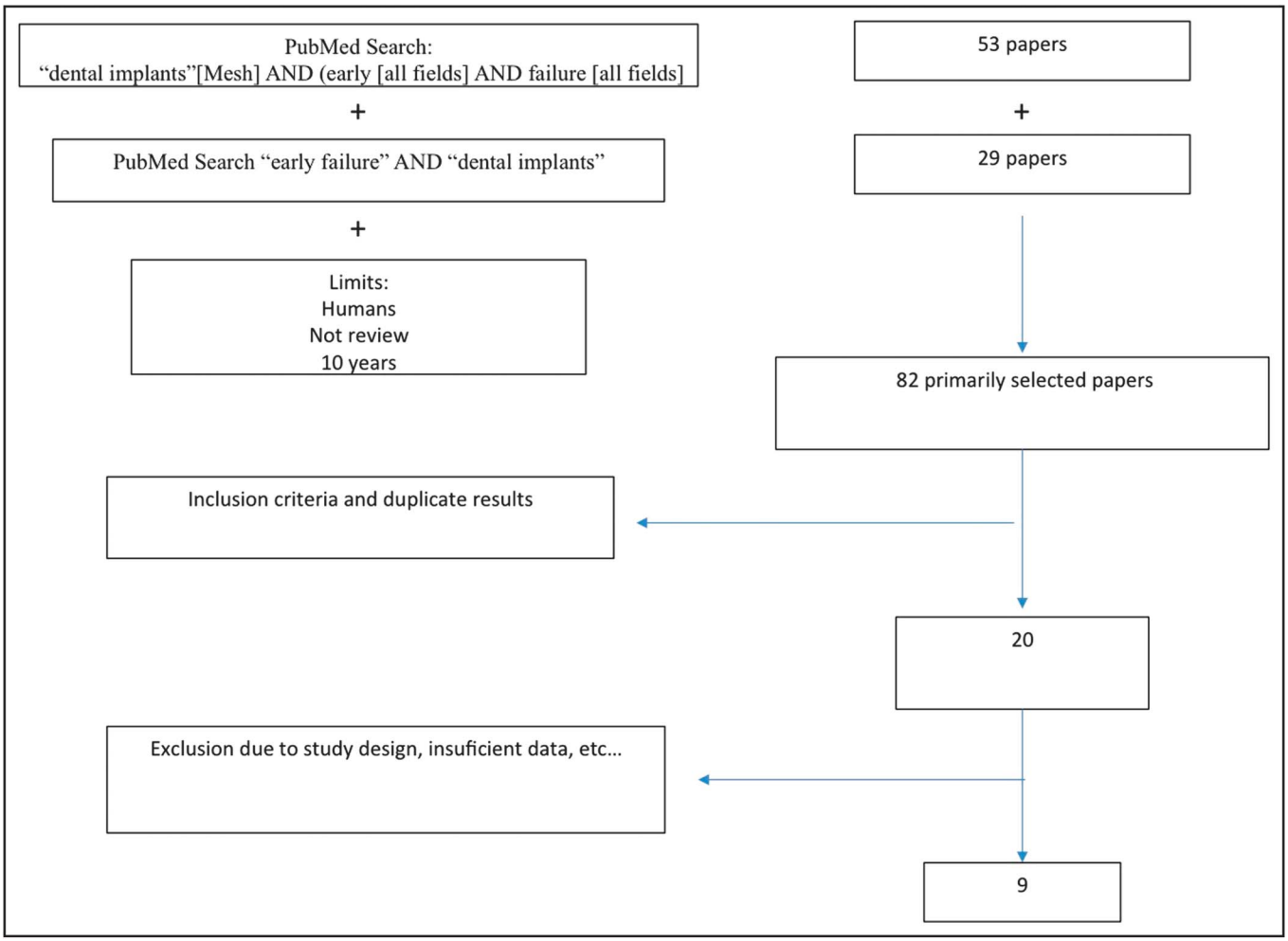

Fig. 1. Flow chart for the PubMed search process and selection for the meta-analysis.

author (M.B.) was called in who reviewed the manuscript independently.

After abstract selection, full-text copies of the selected papers were obtained. Then, 3 authors from different institutions (M.P., M.B., and F.J.M.) independently assessed these full-text papers using a pilot-tested assessment form. Each author quantified several parameters (eg, sample size and selection method, study design, follow-up period, adequacy in reporting results, and appropriateness of the statistical analysis performed, etc) on either a 5-point Likert-scale type or a 0 to 10 scale, finally giving a 0 to 10 score as global evaluation of each paper.

Of the 20 full-text articles assessed by the panel, only 9 were included in the meta-analysis. Eleven papers were excluded because of various reasons such as incomplete reporting of data dispersion, unclear criteria for early failure, no differentiation between early failure and late failure, etc (See Table 1).

The 9 studies meta-analyzed considered early failures as, any implant failed before applying load, and properly reported the risk associated with several patient-related or implant-related factors for early implant failures. The quality of these studies was above 5 in all the parameters (Table 2).

Outcome Variables Selection

In this review, we were particularly interested in assessing the risk associated with 2 implant-related factors, that is, implant length (analyzed in 6 studies) and implant diameter (4 studies) and 2 patient-related factors, that is, smoking habit (6 studies) and the location of the implant (6 studies). We looked for association between failure and other associated factors (implants placed in grafted sites, in fresh extraction sockets and characteristics of these sockets, surgeon experience, intra or postoperative complications, etc), but could not find enough data to perform a meta-analysis for most of them. In this study, we considered the implants placed in smoking patients (smoking variable), implants narrower than 4 mm (width variable), implants shorter than 10 mm (length variable), and implants placed in the maxilla (location variable) as risk factors. The unit of analysis was the implant.

Table 1. Selected and Discarded Articles in the Final Meta-Analysis Selection

Author, Year (Ref)	Status	Reason for Exclusion
Alsaadi et al, 2007[8]	Included	
Alsaadi et al, 2008[17]	Included	
Anitua et al, 2008[18]	Included	
Baqain et al, 2012[2]	Included	
Roos-Jansåker et al, 2006[19]	Included	
Shibuya et al, 2012[3]	Included	
Urban et al, 2012[20]	Excluded	Different criteria used to consider early failure
Van Steenberghe et al, 2002[5]	Included	
Vehemente et al, 2002[21]	Excluded	No differentiation between early and late failures
Zembic et al, 2010[22]	Excluded	Implants evaluated after loading
Bornstein et al, 2008[23]	Included	
Gianserra et al, 2010[24]	Excluded	Insufficient data description
Huynh-Ba et al, 2008[25]	Excluded	No relationship between early failure and the variables studied in this study
Kinsel et al, 2007[26]	Excluded	Implants evaluated after immediate loading
Koldsland et al, 2009[9]	Excluded	No differentiation between early and late failures
Kronström et al, 2001[4]	Included	
McDermott et al, 2003[27]	Excluded	No differentiation between early and late failures
Susarla et al, 2008[28]	Excluded	No differentiation between early and late failures
Sverzut et al, 2008[29]	Excluded	Different criteria used for early failure

Statistical Analyses

For the comparison of the aggregated data, the chosen effect size was the odds ratio (OR). Odds ratio can be defined simply as a measure of the association between an exposure and an outcome (in our case early implant failure). Thus, the OR represents the odds that an early implant failure will

Table 2. Summary of Judges' Qualifications of the Parameters of the Most Relevant Papers Evaluated

Study Author, Year (Ref)	Sample Size	Study Design	Follow-up	Results	Statistical Quality*	Global Evaluation*
Alsaadi et al, 2007[8]	†	†		†	8	7.7
Alsaadi et al, 2008[17]	‡	‡		‡	6.7	6.3
Anitua et al, 2008[18]	†	†	†	†	6.7	6.7
Baqain et al, 2012[2]	§	†		†	6.4	6.7
Roos-Jansåker et al, 2006[19]	§	†	†	†	7.3	7.3
Shibuya et al, 2012[3]	§	‡	†	‡	6	5.7
Van Steenberghe et al, 2002[5]	§	‡		‡	4.3	5
Bornstein et al, 2008[23]	‡	†	‡	†	5.6	6
Kronström et al, 2001[4]	‡	†		‡	6.3	7.3

*Average judges' clarification over a 0 to 10 range.
†Three judges rated the parameter as correct.
‡Two judges rated the parameter as correct.
§Only one judge rated the parameter as correct.

occur given a particular exposure, compared to the odds of failure occurring in the absence of that exposure. This means that for a given risk factor, an OR greater than 1 implies a higher risk of failure compared with nonexposed implants. The Mantel-Haenzsel method was used to integrate the OR under the assumption of a fixed effects model. The test of homogeneity, Q, was performed to test the assumption of a fixed effect model that the true effect size was the same in all the primary studies. Because the power of statistical tests of homogeneity is robust, and the Q tests would only find significant results when the OR discrepancy was large,[30] we decided to explore the heterogeneity between studies by the contributions to the Q test to validate the Q results when the resulting *P*-value was below 0.15.[31] The I^2 statistics was also used to evaluate heterogeneity.[32] The meta-analysis was performed using the software MIX 2.0 (Biostat XL, 2011).

RESULTS

A total of 18,171 implants were meta-analyzed, of which 10,921 were analyzed for smoking, 15,260 for implant diameter, 16,075 for implant length, and 16,711 for implant location (maxilla vs mandible) (Table 3).

Smoking and Early Failure

For the meta-analytic technique, a total of 6 studies were included, with a total of 10,921 implants distributed in each article as reported in Table 3. In absolute terms, in these 6 items selected to study the smoking variable, we found that 16.8% of the implants had been placed in smokers. The results of the Q homogeneity test were not significant, but the *P*-value was below 0.15 ($Q = 8.31$; $P = 0.14$), because much of the variability ($I^2 = 30.8\%$) came from the paper by van Steenberghe et al.[5] The contribution of this study to the Q test was 5.06; that is, 60.8% of the heterogeneity found was because of that study.

Table 3. Frequency Distribution of the Risk Exposure of Implants and Outcomes Among the Different Studies

Study Author, Year (Ref)	Risk Factor	Implants Exposed (n)	Nonexposed Implants (n)	Exposed Implants Failed (n)	Nonexposed Implants Failed (n)
Alsaadi et al, 2007[8]	Smoking	916	6030	54	198
	Implant width	5991	945	213	39
	Implant length	456	6490	29	223
	Implant location	3625	3306	143	109
Alsaadi et al, 2008[17]	Smoking	95	623	5	7
	Implant width	499	221	10	4
	Implant length	248	472	5	9
	Implant location	388	332	8	6
Anitua et al, 2008[18]	Smoking	—	—	—	—
	Implant width	2547	3222	18	10
	Implant length	697	5090	4	24
	Implant location	3101	2686	21	7
Baqain et al, 2012[2]	Smoking	29	140	4	10
	Implant width	—	—	—	—
	Implant length	80	319	4	11
	Implant location	200	199	9	6
Roos-Jansåker et al, 2006[19]	Smoking	—	—	—	—
	Implant width	—	—	—	—
	Implant length	—	—	—	—
	Implant location	524	533	17	12
Shibuya et al, 2012[3]	Smoking	276	343	5	3
	Implant width	—	—	—	—
	Implant length	—	—	—	—
	Implant location	—	—	—	—
Van Steenberghe et al, 2002[5]	Smoking	281	982	3	24
	Implant width	—	—	—	—
	Implant length	—	—	—	—
	Implant location	—	—	—	—
Bornstein et al, 2008[23]	Smoking	24	965	3	7
	Implant width	169	1647	1	12
	Implant length	179	1638	0	13
	Implant location	1077	740	6	7
Kronström et al, 2001[4]	Smoking	—	—	—	—
	Implant width	—	—	—	—
	Implant length	2	404	1	78
	Implant location	—	—	—	—

Figure 2 shows the OR for early failure of implants placed in smokers as compared with nonsmokers for each of the studies analyzed. Considering each study individually, it may be seen that the OR is greater than 1, except in the study performed by van Steenberghe et al (OR = 0.43).[5] Nevertheless, these OR values were only significant in the studies of Alsaadi et al.[8,17] The study with the highest weight was that of Alsaadi et al, 2007,[8] with a weight of 70.39%, which influenced the integrated OR. The aggregated OR was 1.72 (95% CI, 1.3–2.3; $P < 0.01$), so smoking should be considered an important risk factor for early failure of dental implants. However, since a large amount of the variability was influenced by the data from van Steenberghe et al[5] (Table 2), we decided to perform a sensitivity analysis of the variable after excluding that study from the analysis. Then, the test of homogeneity Q was performed again, showing no heterogeneity (Q = 2.55; $P = 0.64$), and the resulting OR from the aggregated results was 1.95 (95% CI, 1.48–2.58; $P < 0.01$), confirming that smoking is indeed an important risk factor for early failure of dental implants.

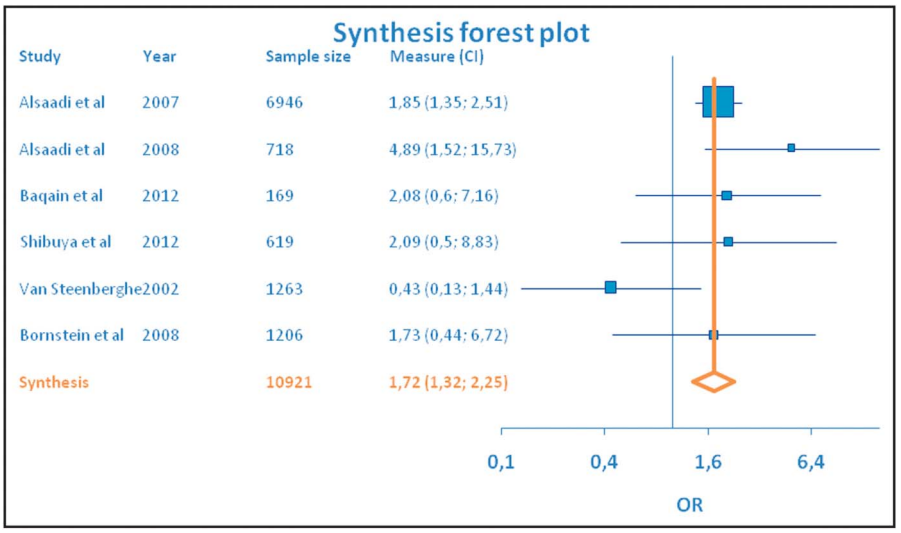

Fig. 2. Forest plot representing the risk of early failures (OR) for implants placed in smokers/nonsmokers.

Implant Width and Early Failure

Regarding implant width, 4 studies were included for the meta-analysis with a total of 15,260 implants, as shown in Table 3. 60.5% of the implants had a diameter less than 4 mm. The Q test supported the assumption of homogeneity between the OR of the papers (Q = 5.13; $P = 0.16$).

Considering each study individually, Figure 3 shows that the OR was close to 1 and nonsignificant, except in Anitua's study (OR = 2.27; $P = 0.04$; CI = 95%).[21] We also found that the cumulative meta-analysis OR was very close to 1 (OR = 1.02; $P = 0.88$; CI = 95%), indicating that implants narrower than 4 mm were not a relevant risk factor for early implant failure. For this variable too, the study carried out by Alsaadi et al[8] was the one that provided the greatest weight to the meta-analysis (79.8%).

Implant Length and Early Failure

For this association, 6 studies involving 16,075 implants were included (Table 3). Overall, only 10.3% of the implants were shorter than 10 mm. The Q test found data homogeneity (Q = 3.12; $P = 0.68$). Figure 4 shows the OR of failures for implants shorter than 10 mm in the studies included. Considering each study separately, Figure 4 shows that the OR was greater than 1, except in the study by Bornstein et al (OR = 0.34).[22] The OR value was highly significant only in the study of Alsaadi et al.[8] The cumulative meta-analysis OR was 1.6 ($P < 0.01$; CI = 95%), indicating that implants shorter than 10 mm were at a significantly higher risk of early failure. Again, the strong influence on the data of the study of Alsaadi et al[8] (59% of weight) should be noted.

Anatomical Location and Early Implant Failure

To study the influence of the anatomical location (maxilla or mandible) in early failure, 16,711 implants

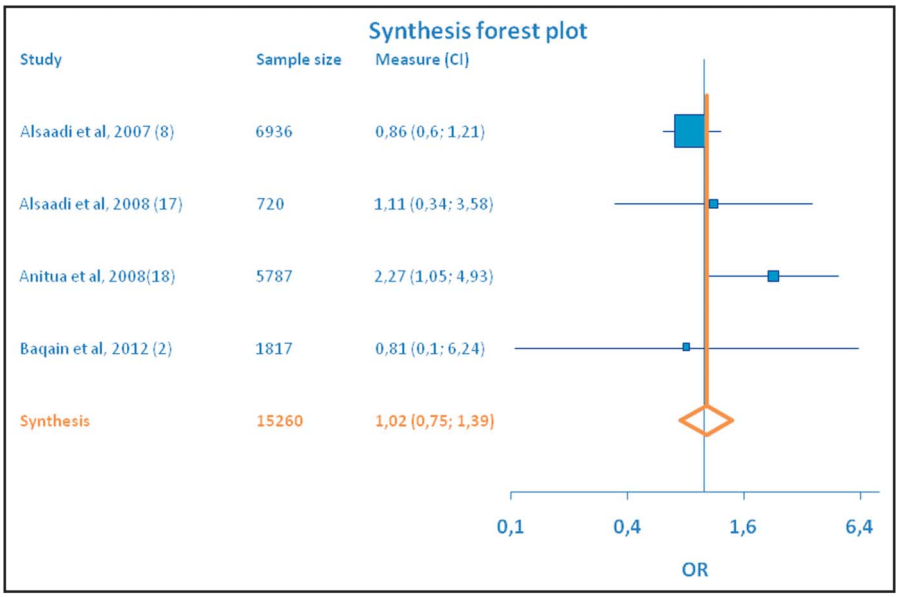

Fig. 3. Forest plot representing the risk of early failures (OR) for narrow implants (diameter <4 mm) versus wider implants.

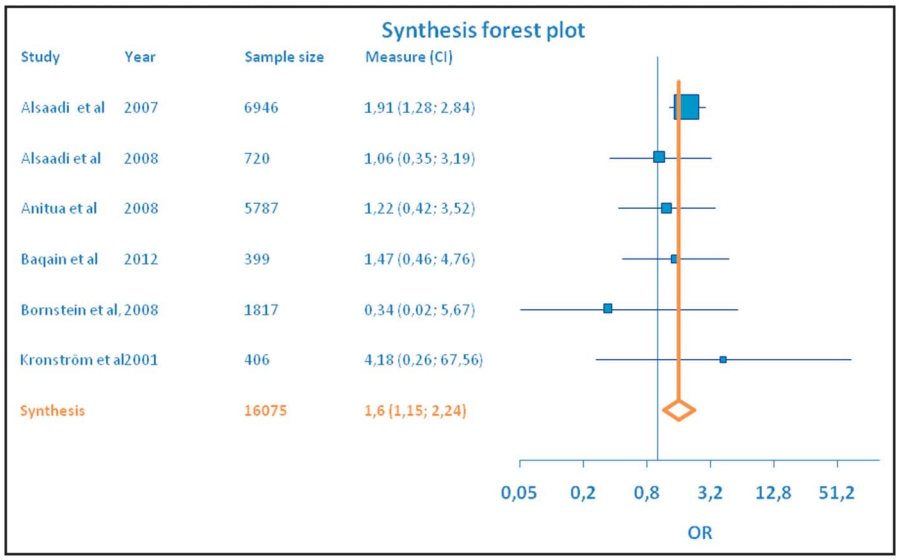

Fig. 4. Forest plot representing the risk of early failures (OR) for implants shorter than 10 mm versus counterparts.

from 6 studies were meta-analyzed (Table 3). 53.3% of the 16,711 implants had been placed in the maxilla. The results of the Q homogeneity test were not significant, and hence it could be assumed that the trends observed in the data from the different studies were homogeneous ($Q = 5.06$; $P = 0.40$).

Figure 5 depicts the OR of implant failure for implants placed in the maxilla as compared with mandible. Considering each study individually, the OR was greater than 1, except in the study by Bornstein et al[23] (OR = 0.59). The only significant OR ($P < 0.05$) was observed in the study performed by Anitua et al.[18] Again, the study by Alsaadi[8] weighed 73.6% for this analysis. The integrated OR = 1.27 ($P < 0.05$; CI = 95%) revealed that the maxilla location was a significant risk factor for early failure of dental implants.

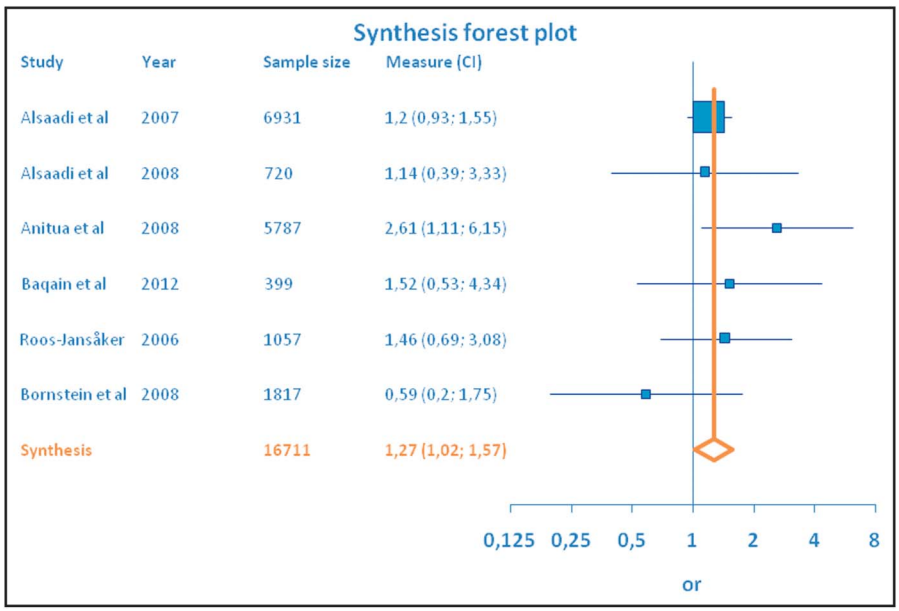

Fig. 5. Forest plot representing the risk of early failures (OR) for implants placed in maxilla versus mandible.

DISCUSSION

This meta-analysis has identified significant risk factors of early implant failure. Nevertheless, it should be noted that although significant and homogeneous, our results are not conclusive because of the small number of studies available for our analysis, and the preponderance of Alsaadi's work[8] in most of the calculations. Although randomized control trial design provides the highest level of evidence, the lack of this design obliged us to include only data from both prospective and retrospective clinical studies, which are more appropriate for risk factor assessment.

In our study, we focused on the most commonly reported risk factors in longitudinal clinical studies to pool data with a larger effective sample size than each single study. This allows for a more precise estimation of OR. Half of these predictors of early failures were patient-related (smoking and jaw bone), and the other half was implant-related (length and width). However, we are aware that there are further local and systemic risk factors that should be addressed in well-designed studies for future meta-analysis. As local risk factors, it is possible to cite the patient's history of periodontitis or peri-implantitis of implants previously placed, humoral immunity, the quantity of keratinized gingiva, drilling procedures, surgical procedures, the endodontic condition of neighboring teeth, and concomitant graft procedures, etc, whereas general risk factors radiotherapy, chemotherapy, Crohn disease, and osteoporosis have been previously reported.[5]

It is clear that a large variety of local and systemic causes can interfere with normal bone wound healing around implants after insertion. The healing of surrounding tissues starts with a blood clot that forms between the remaining bone and the implant surface, and depending on the environment and the relative immobility of the bone-to-implant interface, pluripotent mesenchymal cells will differentiate either into fibroblasts or osteoblasts,

respectively, leading to the formation of scar tissue or new bone.[8] Conditions of poor vascularity or low oxygen tension may lead the mesenchymal cells to chondrogenic differentiation.[8] The mechanical stress to which the tissues are subjected may also influence this cellular differentiation.[8] Distortional stresses may deform cells, altering their genetic expression and synthetic activity, which explains why micromovements of implants during the healing phase can affect a correct bone-to-implant bond, forming fibrous scar tissue instead.[33,34] The role of endogenous factors in cellular turnover and differentiation is less documented.[8]

Patient-Related Factors

To date, in terms of sociodemographic factors, it seems that the gender and age of patients do not directly influence the occurrence of early failures,[5] but this simple trait could not be meta-analyzed because the original distribution of the published data prevented us from doing so. However, regarding the smoking habit, it was found that smoking is a significant predictor of early failures. It should be taken into account that the effects of inhaled tobacco smoke can be divided into 2 phases: a volatile and a particulate phase. The volatile phase, accounting for 95% of cigarette smoke, provides nearly 500 different components, including nitrogen, carbon monoxide, and carbon dioxide. The roughly 3500 different chemicals released in the particulate phase include nicotine, nornicotine, anatabine, and anabasine.[35] Nicotine has been shown to increase platelet aggregation, decrease microvascular prostacyclin levels, and inhibit the function of fibroblasts, erythrocytes, and macrophages.[8,36,37] Carbon monoxide binds to hemoglobin considerably more easily than oxygen, thus displacing oxygen from the molecule and lowering the oxygen tension in the tissues.[38] Smoking alters the dynamics of bone and wound healing.[39]

The literature supports the evidence that smoking interferes with the prognosis of dental implants in a dose-dependent manner,[40] and the results of this meta-analysis concluded that this factor significantly increased the risk of early implant failure 1.3- to 2.3-fold, in agreement with other systematic reviews and meta-analyses.[41]

However, Sverzut et al[29] suggested that tobacco alone cannot be considered a risk factor for early failures. Despite this, there is evidence to suggest that smoking may have a dose-related effect on osseointegration,[8] but those authors did not take into account the number of cigarettes that patients smoked each day. The lack of statistical significance for smoking in other studies such as those performed by Anitua et al[18] or Roos-Jansåker et al,[19] may be related to the small number of individuals with implant loss, thereby reducing the power of the statistical analysis. Other studies have reported a deleterious effect of smoking on implant loss.[40,42–45] Wilson and Nunn[43] reported an increased risk of implant loss among smokers by a factor of almost 2.5 compared with nonsmokers, and Wallace[45] described failure rates of 16.6% in smokers as compared with 6.9% in nonsmokers.

In a study with a large sample size, the performance of 2066 implants placed in 310 patients was assessed, and cigarette smoking was found to be the primary factor for implant failure reported at second-stage surgery.[46]

Moreover, regarding the type of bone, and according to our meta-analysis, we estimate that implants placed in the maxilla are at a slightly higher risk than implants placed in the lower jaw, this difference being statistically significant (OR = 1.27). This finding is in agreement with the literature. Anitua et al[18] considered that placing implants in the maxilla was not a risk factor for implant loss *per se*. However, the survival estimates were significantly lower in maxillary implants than those for implants placed in the mandible. Nevertheless, these unfavorable results were explained as being a consequence of the greater anatomical difficulties found in the upper jaw in that study.

In fact, the number of implants inserted according to a two-stage protocol (1139 in the upper vs 190 in the lower jaws) and special techniques (904 in the upper vs 354 in the lower jaws) performed in the maxilla was significantly higher than in the mandible.[18] In the same line, Moy et al[47] evaluated 4680 implants in 1140 patients, and reported that implants placed in the maxilla were subject to an almost two-fold higher failure rate than those inserted in the mandible. Other studies have also shown similar trends, suggesting a higher failure for implants inserted in the maxilla.[48,49]

Implant-Related Factors

Regarding the implant-related factors assessed here (implant length and width), in a review paper, Renouard and Nisand[50] reported that there was a tendency towards an increased failure rate with short and wide-diameter machined-surface implants. However, Alsaadi et al[8] reported that the increased risk of short and wide-diameter implants may be associated with the learning curve for the site preparation, poor bone density, implant design, and the fact that these types of implant were usually used as "rescue" implants. These implants were systematically installed in compromised sites, characterized by poor bone quality and quantity. Thus, these confounding factors may explain the higher failure rate.[8] By contrast, a recent study found that the greatest risk for early failure of implants occurred when short and narrow implants were inserted.[51] Similarly, Baqain et al[2] found that implant failures were significantly more common for narrow implants (<3.5 mm) but not for shorter implants (<10 mm), which also tended to be at higher risk, although this was not significant. Our results pointed in the opposite direction, that is, narrow implants seem to perform similarly to wider implants, but implants shorter than 10 mm are at significant risk of early failure (Fig. 4). According to this meta-analysis, the greatest controversy was observed regarding the influence of width (Fig. 3), with a Q test *P*-value = 0.16, as compared with the influence of length (Fig. 4), with a Q-Test *P*-value = 0.68. It should be taken into account that as narrow implants, we considered those thinner than 4 mm instead of 3.5 mm, as is usually done, but the data of the studies analyzed did not allow us to set any other limit.

Regarding implant length, our results are in agreement with many

studies reporting that a short length is associated with implant failure. Misch et al[52] observed a low success rate (85.3%) for implants less than 10 mm in length. Olate et al[51] concluded that there was a significant relationship between early implant failure and short implant length (6–9 mm).

It is noteworthy that since narrow and short implants are placed in areas where there is limited space or insufficient volume of bone, either buccallingually or axially, both factors will impinge on clinical performance, because the total surface in contact with the bone tissue is restricted. Nevertheless, because we were unable to evaluate the patient data directly and the OR originally reported was not adjusted for such confounding variables, we were unable to meta-analyze the effect of both variables altogether. Likewise, it would be recommendable to analyze the influence of bone quality, although bone quality was rarely recorded in the articles reviewed. Bone quality has been classified into 4 categories (Lekholm and Zarb, 1985), depending on the degree of corticalization.[5] High percentages of implant failures mainly occur in type four bone (little cortical bone combined with less mineralized cancellous bone and larger trabecular spaces).[5,53,54] In fact, because of its low biomechanical properties this kind of bone often fails to provide adequate primary stability for implants, which is indispensable for the formation of efficient bone-to-implant contact.[33]

Limitations of the Study

The main limitation of this study derives from the fact that we did not include a large number of studies in the meta-analysis. We discarded many studies because they did not provide concrete data distributions for meta-analysis then, although methodologically they were valid. Moreover, other biomedical databases such as Embase and (the) Cochrane Library database could be searched for a more exhaustive approach.

Future research should focus on the effect of immediate loading as a risk factor for implant failure, because there is increasing data on this issue and it would address a relevant clinical situation for both patients and dentists, which merits independent analysis. However, the conventional loading protocol is still one of the most widely used by clinicians, and hence the information provided in this study might help the majority of clinicians to support their decision making with current evidence to enhance implant prognosis. Besides, other factors that could influence the early implant failure like implant surface, healing sites or postextraction sockets implant placement should be studied, but we did not find enough data to include these variables in the meta-analysis.

CONCLUSIONS

According to this meta-analysis, the main significant risk factors for early implant failure were smoking habit (CI = 95%, OR = 1.3–2.3), implants shorter than 10 mm (CI = 95%, OR = 1.2–2.2) and implants placed in the maxilla (CI = 95%, OR = 1.0–1.6).

DISCLOSURES

The authors claim to have no financial interest, either directly or indirectly, in the products or information listed in the paper. There has been no financial support for this work.

APPROVAL

No ethical committee approval is required.

REFERENCES

1. Albrektsson T, Lekholm U. Osseointegration: Current state of the art. *Dent Clin North Am.* 1989;33:537–554.

2. Baqain ZH, Moqbel WY, Sawair FA. Early dental implant failure: Risk factors. *Br J Oral Maxillofac Surg.* 2012;50:239–243.

3. Shibuya Y, Takata N, Takeuchi J, et al. Analysis of the 619 Brånemark System TiUnite implants: A retrospective study. *Kobe J Med Sci.* 2012;58:E19–E28.

4. Kronström M, Svenson B, Hellman M, et al. Early implant failures in patients treated with Brånemark System titanium dental implants: A retrospective study. *Int J Oral Maxillofac Implants.* 2001;16: 201–207.

5. Van Steenberghe D, Jacobs R, Desnyder M, et al. The relative impact of local and endogenous patient-related factors on implant failure up to the abutment stage. *Clin Oral Implants Res.* 2002; 13:617–622.

6. Esposito M, Hirsch JM, Lekholm U, et al. Biological factors contributing to failures of osseointegrated oral implants. (I). Success criteria and epidemiology. *Eur J Oral Sci.* 1998;106:527–551.

7. Esposito M, Thomsen P, Ericson LE, et al. Histopathologic observations on early oral implant failures. *Int J Oral Maxillofac Implants.* 1999;14:798–810.

8. Alsaadi G, Quirynen M, Komárek A, et al. Impact of local and systemic factors on the incidence of oral implant failures, up to abutment connection. *J Clin Periodontol.* 2007;34:610–617.

9. Koldsland OC, Scheie AA, Aass AM. Prevalence of implant loss and the influence of associated factors. *J Periodontol.* 2009;80:1069–1075.

10. Klokkevold PR, Han TJ. How do smoking, diabetes, and periodontitis affect outcomes of implant treatment? *Int J Oral Maxillofac Implants.* 2007;22:s173–s202.

11. Van Steenberghe D, Lekholm U, Bolender C, et al. Applicability of osseointegrated oral implants in the rehabilitation of partial edentulism: A prospective multicenter study on 558 fixtures. *Int J Oral Maxillofac Implants.* 1990;5:272–281.

12. Alsaadi G, Quirynen M, Komárek A, et al. Impact of local and systemic factors on the incidence of late oral implant loss. *Clin Oral Implants Res.* 2008;19:670–676.

13. Berglundh T, Persson L, Klinge B. A systematic review of the incidence of biological and technical complications in implant dentistry reported in prospective longitudinal studies of at least 5 years. *J Clin Periodontol.* 2002;29:s197–212.

14. Charyeva O, Altynbekov K, Zhartybaev R, et al. Long-term dental implant success and survival–a clinical study after an observation period up to 6 years. *Swed Dent J.* 2012;36:1–6.

15. Bryant SR, Zarb GA. Osseointegration of oral implants in older and younger adults. *Int J Oral Maxillofac Implants.* 1998;13:492–499.

16. Kronström M, Svensson B, Erickson E, et al. Humoral immunity host factors in subjects with failing or successful titanium dental implants. *J Clin Periodontol.* 2000;27:875–882.

17. Alsaadi G, Quirynen M, Michiles K, et al. Impact of local and systemic factors on the incidence of failures up to abutment connection with modified surface oral implants. *J Clin Periodontol.* 2008;35:51–57.

18. Anitua E, Orive G, Aguirre JJ, et al. 5-year clinical experience with BTI dental implants: Risk factors for implant failure. *J Clin Periodontol.* 2008;35:724–732.

19. Roos-Jansåker AM, Lindahl C, Renvert H, et al. Nine to fourteen-year

follow- up of implant treatment. Part I: Implant loss and associations to various factors. *J Clin Periodontol.* 2006;33: 283–289.

20. Urban T, Kostopoulos L, Wenzel A. Immediate implant placement in molar regions: Risk factors for early failure. *Clin Oral Implants Res.* 2012;23:220–227.

21. Vehemente VA, Chuang SK, Daher S, et al. Risk factors affecting dental implant survival. *J Oral Implantol.* 2002;28:74–81.

22. Zembić A, Glauser R, Khraisat A, et al. Immediate vs. early loading of dental implants: 3-year results of a randomized controlled clinical trial. *Clin Oral Implants Res.* 2010;21:481–489.

23. Bornstein MM, Halbritter S, Harnisch H, et al. A retrospective analysis of patients referred for implant placement to a specialty clinic: Indications, surgical procedures, and early failures. *Int J Oral Maxillofac Implants.* 2008;23:1109–1116.

24. Gianserra R, Cavalcanti R, Oreglia F, et al. Outcome of dental implants in patients with and without a history of periodontitis: A 5-year pragmatic multicentre retrospective cohort study of 1727 patients. *Eur J Oral Implantol.* 2010;3:307–314.

25. Huynh-Ba G, Friedberg JR, Vogiatzi D, et al. Implant failure predictors in the posterior maxilla: A retrospective study of 273 consecutive implants. *J Periodontol.* 2008;79:2256–2261.

26. Kinsel RP, Liss M. Retrospective analysis of 56 edentulous dental arches restored with 344 single-stage implants using an immediate loading fixed provisional protocol: Statistical predictors of implant failure. *Int J Oral Maxillofac Implants.* 2007;22:823–830.

27. McDermott NE, Chuang SK, Woo VV, et al. Complications of dental implants: Identification, frequency, and associated risk factors. *Int J Oral Maxillofac Implants.* 2003;18:848–855.

28. Susarla SM, Chuang SK, Dodson TB. Delayed versus immediate loading of implants: Survival analysis and risk factors for dental implant failure. *J Oral Maxillofac Surg.* 2008;66:251–255.

29. Sverzut AT, Stabile GAV, de Moraes M, et al. The influence of tobacco on early dental implant failure. *J Oral Maxillofac Surg.* 2008;66:1004–1009.

30. Boissel JP, Blanchard J, Panak E, et al. Considerations for the meta- analysis of randomized clinical trials. Summary of a panel discussion. *Control Clin Trials.* 1989;10:254–281.

31. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;21:1539–1558.

32. Galbraith RF. The radial plot: Graphical assessment of spread in ages. *Int J Radiat Appl Instrum.* 1990;17: 207–214.

33. Ivanoff CJ, Sennerby L, Lekholm U. Influence of initial implant mobility on the integration of titanium implants. An experimental study in rabbits. *Clin Oral Implants Res.* 1996;7:120–127.

34. Szmukler-Moncler S, Piattelli A, Favero GA, et al. Considerations preliminary to the application of early and immediate loading protocols in dental implantology. *Clin Oral Implants Res.* 2000;11:12–25.

35. Hoffmann D, Hoffmann I. The changing cigarette, 1950-1995. *J Toxicol Environ Health.* 1997;50:307–364.

36. Jorgensen LN, Kallehave F, Christensen E, et al. Less collagen production in smokers. *Surgery*. 1998;123: 450–455.

37. Zevin S, Gourlay SG, Benowitz NL. Clinical pharmacology of nicotine. *Clin Dermatol.* 1998;16:557–564.

38. Leow YH, Maibach HI. Cigarette smoking, cutaneous vasculature, and tissue oxygen. *Clin Dermatol.* 1998;16:579–584.

39. Porter SE, Hanley EN. The musculoskeletal effects of smoking. *J Am Acad Orthop Surg.* 2001;9:9–17.

40. Bain CA. Smoking and implant failure–benefits of a smoking cessation protocol. *Int J Oral Maxillofac Implants.* 1996; 11:756–759.

41. Strietzel FP, Reichart PA, Kale A, et al. Smoking interferes with the prognosis of dental implant treatment: A systematic review and meta-analysis. *J Clin Periodontol.* 2007;34:523–544.

42. Bain CA, Moy PK. The association between the failure of dental implants and cigarette smoking. *Int J Oral Maxillofac Implants.* 1993;8:609–615.

43. Wilson TG, Nunn M. The relationship between the interleukin-1 periodontal genotype and implant loss. Initial data. *J Periodontol.* 1999;70:724–729.

44. Lambert PM, Morris HF, Ochi S. The influence of smoking on 3-year clinical success of osseointegrated dental implants. *Ann Periodontol Am Acad Periodontol.* 2000;5:79–89.

45. Wallace RH. The relationship between cigarette smoking and dental implant failure. *Eur J Prosthodont Restor Dent.* 2000;8:103–106.

46. Gorman LM, Lambert PM, Morris HF, et al. The effect of smoking on implant survival at second-stage surgery: DICRG Interim report No. 5. Dental implant clinical research group. *Implant Dent.* 1994;3: 165–168.

47. Moy PK, Medina D, Shetty V, et al. Dental implant failure rates and associated risk factors. *Int J Oral Maxillofac Implants.* 2005;20:569–577.

48. Eckert SE, Choi Y-G, Sánchez AR, et al. Comparison of dental implant systems: Quality of clinical evidence and prediction of 5-year survival. *Int J Oral Maxillofac Implants.* 2005;20:406–415.

49. Davarpanah M, Martinez H, Etienne D, et al. A prospective multicenter evaluation of 1,583 3i implants: 1- to 5-year data. *Int J Oral Maxillofac Implants.* 2002;17:820–828.

50. Renouard F, Nisand D. Impact of implant length and diameter on survival rates. *Clin Oral Implants Res.* 2006;17: s35–s51.

51. Olate S, Lyrio MCN, de Moraes M, et al. Influence of diameter and length of implant on early dental implant failure. *J Oral Maxillofac Surg.* 2010;68:414–419.

52. Misch CE, Steignga J, Barboza E, et al. Short dental implants in posterior partial edentulism: A multicenter retrospective 6-year case series study. *J Periodontol.* 2006;77:1340–1347.

53. Friberg B, Jemt T, Lekholm U. Early failures in 4,641 consecutively placed Brånemark dental implants: A study from stage 1 surgery to the connection of completed prostheses. *Int J Oral Maxillofac Implants.* 1991;6:142–146.

54. Jaffin RA, Berman CL. The excessive loss of Brånemark fixtures in type IV bone: A 5- year analysis. *J Periodontol.* 1991;62:2–4.