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Review

Monte Carlo simulation of reasons for early failure of implants: effects of two risk factors

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Abstract

We have estimated the joint effects of two important risk factors on early failure of implants and then ranked all quoted risks by importance. We made a systematic search of published papers listed in PubMed, Web of Knowledge, Scopus, and Cochrane Central up to March 2018, and identified a total of 437 records. Eight studies met the inclusion criteria, in which seven significant risk factors for early failure were selected and used to build a conceptual simulation model. Selected risk factors were: "male sex", "smoking", "quality of bone", "short implants", "wide implants", "adjacent teeth", and "periodontitis". Based on these risk factors, all two-factor combinations that accounted for a total of 21 areas of greatest risk were created. We made a Monte Carlo simulation with 10 000 iterations and a sensitivity analysis to evaluate the estimates of these risks and to identify those that had the most influence on the model of early failure. The outcomes of the Monte Carlo simulation model showed that the SRS values of the combinations of these risks had different ranges of effects and probabilities of the early risk of failure. As a result, the most sensitive areas of greatest risk were "smoking and periodontitis", the second "short implants and periodontitis", and the third "smoking and short implants". The least sensitive combination of risks for early failure was "wide implants and male sex". This is to our knowledge the first study that has illustrated the contributions of various combinations of risk factors to early failure of implants. "Smoking and periodontitis" was thought to be associated with the greatest risk of early failure.
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Keywords: Dental Implants; Treatment Failure; Risk Factors; Monte Carlo Method; Risk Assessment

Introduction

Early failure is now a well-recognised complication of treatment with dental implants, and failure is regarded as "early" when it occurs before the implant has been loaded.[1] The risk factors for early failure are thought to interfere with the process of osseointegration,[2] they have long been the subject of research, as the causes are accepted as being multifactorial.[3] Estimation of an individual patient's risk of early failure by recognising the risk factors, therefore, would be important for the clinician.

As a number of factors have been found to have a considerable impact on early failure, a question arises about the joint effects of certain risk factors when they are present at the same time. Although many studies have assessed the importance of various risk factors on early failure, none have, to our knowledge, examined the combined effect of multiple risk factors, possibly because of the difficulty in collecting sufficient numbers of implants that share the same combination of risk factors. Another problem would be that some risk factors might correlate with each other, which would lead to a synergistic effect that would make it difficult to compare their individual impact accurately. Because such evidence is lacking, the focus is on the individual factors that have previously been identified as factors that are important in early failure.

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Given that various different risk factors have been identified as being associated with early failure, it seems more reasonable to focus on more common factors among papers in which an effort has been to assess the importance of those risk factors.

Several authors have emphasised the need for studies that evaluate the effects of multiple risk factors on failure of dental implants. It was proposed by Liddelow and Klineberg that analysis of the risk of combined factors must be made case-by-case, taking known risks into consideration.[4] Chen et al emphasised that the compound effect of multiple risk factors should be examined in future studies.[5] As the general expectation is that the impact of two independent risk factors will be greater than either one of them alone, it raises the intriguing question of which combinations of these risk factors are the most influential on early failure. The aim of this study was therefore to estimate the joint effects of two important risk factors associated with early failure and rank all the combinations in order of their importance using Monte Carlo simulation.

Material and methods

Search of publications and extraction of data

We made a systematic search of PubMed, the ISI Web of Knowledge, Scopus and the Cochrane Central Register of Controlled Trials (CENTRAL) to retrieve all studies published in English before March 2018 that dealt with the relations between early failure of dental implants and associated risk factors. No restrictions were applied about the type of study to identify more potentially relevant papers from the references of those reviewed. Initially, the titles of all studies identified were screened to exclude obviously irrelevant records and retain potentially relevant ones. Next, the abstracts of the retained studies were reviewed to select the ones that were suitable for assessment of the full text. Full texts of possibly eligible articles were read and assessed against the inclusion and exclusion criteria. Finally, the studies that fulfilled the eligibility criteria were selected for simulation. The focused PICO (Participants, Intervention, Comparisons, Outcomes) question was: "What are the significant risk factors (C) associated with the early failure (O) of dental implants (I) in partially or completely edentulous patients (P)"?

The following complete set of MeSH terms and free text-words were used: ((("Risk Factors"[Mesh] OR "risk factors"[All Fields] OR "predictors"[All Fields] OR("predisposing"[All Fields] AND "factors"[All Fields]) OR "predisposing factors"[All Fields])) AND ("Dental Implants"[Mesh] OR "dental implants"[All Fields] OR ("dental"[All Fields] AND implant*[All Fields]))) AND (fail[All Fields] OR failed[All Fields] OR failure[All Fields] OR loss[All Fields] OR lost[All Fields] OR success[All Fields] OR survival[All Fields] OR "survival"[MeSH Terms])) AND early[All Fields).

Inclusion criteria were:

Studies that reported on risk factors for early failure of dental implants; studies that accepted early failures of dental implants as implants that fail during the period of osseointegration, or at the second-stage operation, or before prosthetic loading; studies that reported at least one risk factor to be identified as significant for early implant failure; studies that included frequency distributions of significant risk factors as well as data on their failure at implant level; and studies that used multilevel regression analyses to test the independence of significant risk factors and their correlation with other confounding factors.

Exclusion criteria were:

Risk factors that reported sample sizes of less than 20 implants; studies that did not report sample sizes for risk factors; and studies that provided only patient level data.

Finally, a significant risk factor was included in the simulation process only if it was found in at least two or more studies. Other significant risk factors identified in single articles were regarded as individual risk factors and not selected for further analysis.

The titles, abstracts and full texts were independently screened and reviewed for selection by the authors (OB and SP), and disagreements resolved by discussion. Inter-reviewer reliability in the selection process was assessed using the Kappa test. Papers that met the inclusion criteria were then hand-searched to extract the frequency of the risk factors and their failure rates in the study sample.

The authors (OB and SP) independently assessed the methods used in the included studies using The Newcastle-Ottawa Scale, which was applied by evaluating the studies for a total of nine items under three categories; selection, comparability, and outcome. Each study selected could receive a maximum of nine stars (points), as each item brought only one star. Studies with 8–9 points were regarded as being of high quality, 6–7 points indicated medium quality, and <6 points suggested poor quality. Inter-rater agreement on assessment of quality was assessed with a Kappa statistic. Differences of opinion were resolved by discussion.

Monte Carlo simulation modelling

Monte Carlo simulation involves random sampling of probability distributions within a predictive model to produce hundreds or even thousands of different options. The distribution of values is calculated for the outcome of the model, and therefore reflects the probability that certain values can occur.[6] For this purpose, a stochastic Monte Carlo simulation was applied using MS Excel add-in @Risk (version 7, Palisade Corp. Ithaca). The main advantage of this type of

simulation is to include the variability of input values by estimating the range of outputs as distributions. The probable range of values of the output of the model can also be examined by analysing how the output value would behave if some other, fixed variable values were changed within their reasonable range or assigned a probability distribution.[7] A sensitivity analysis can be used to characterise how model outputs respond to changes in input, with an emphasis on finding the input variables to which outputs are most sensitive.[8]

Data about common risk factors in the selected papers were combined to form the data pool. Collected data were processed using the Monte Carlo method to simulate the influence of risk events; 10,000 iterations were used in the simulation model.

Initially, Failure Rate of the Risk Factor *i* (FRR) was calculated as;

$$\boldsymbol{FRR_{ia} = NFR_{ia} \div SR_{ia}, \quad i = 1..n \quad a = 1..x} \tag{1}$$

where $\boldsymbol{NFR_i}$ represents the number of implant failures for risk factor *i* for article $\boldsymbol{a}$ and $\boldsymbol{SR_i}$ represents the total sample size of risk factor *i* in the related studies.

To calculate the weight of the frequency for each risk factor in each study Ratio of Risk Factor Frequency (RRF) was used as follows,

$$\boldsymbol{RRF_{ia}} = \frac{\boldsymbol{FR_{ia}}}{\boldsymbol{N_i}}, \quad \boldsymbol{i = 1..n \quad a = 1..x} \tag{2}$$

where $\boldsymbol{FR_{ia}}$ represents frequency of risk factor $\boldsymbol{i}$ for article $\boldsymbol{a}$, and N_i represents total number of all implants including risk factor *i* in the related studies.

Weighted Failure Rate (WFR_i) multiplies previously calculated values in Equation (1) and Equation (2) for each article related to risk factor *i* as follows,

$$\boldsymbol{WFR_i} = \sum_{a=1}^{N} [(FRR)]_{ia} \times \boldsymbol{RRF_{ia}}), \quad \boldsymbol{i = 1..n \quad a = 1..x} \tag{3}$$

Weight of the papers is calculated to find the expected impact of the risk factors. This enables us to have all components necessary to calculate the fitting density of triangular distribution. Probability distribution shows how the probability density of a risk factor may vary over a permitted range of values.[9] Assuming the risk factors are independent, Monte Carlo analysis can be used to estimate the distribution of multiple risk factors when combined.[10] By using the probability distributions constructed, Simulated Risk of Scenarios (SRS_{ij}) were generated to integrate two different risk factors in a combination model as follows;

$$\begin{aligned} \boldsymbol{SRS_{ijs}} &= \boldsymbol{RiskTriang(Min, WFR, Max)_i} \\ &+ \boldsymbol{RiskTriang(Min, WFR, Max)_j}, \\ &\boldsymbol{i = 1..n \quad j = 1..m \quad s = 1..y \quad i \neq j} \end{aligned} \tag{4}$$

where *n*,*m* represents the risk factors and *y* indicates the number of iterations, respectively.

Uncertainty and variability of the simulated model were taken into account by using probability density functions with 95% prediction intervals, which is the middle 95% of the iteration values. The middle 95% of the simulated data values corresponds to the 2.5th percentile to the 97.5th percentile, which can be found directly with the RiskPtoX function in @Risk. Finally, a sensitivity analysis was applied to the developed model to test the strength of the overall SRS_{ijs} value. Results of the sensitivity analysis were obtained during the Monte Carlo simulation by using Spearman's rank order correlation, which is automatically calculated by @Risk software.

Results

Search of publications

Systematic search of the four databases resulted in 437 hits. Hand searching of the reference lists led to identification of four additional records, and 247 remained after duplicates had been removed. Screening of titles excluded 84 studies that were not related to dental implants, and 163 studies were subjected to screening of the abstract, which resulted in the elimination of 51 papers that were not studies about the survival of implants. The remaining 112 papers were assessed by reading the full texts. Thirty-three studies that either did not state the exact timing of failure of the implant or did not distinguish early from late failures, together with 16 studies that did not evaluate risk factors, were removed. Review papers, meta-analyses, and case reports were also excluded. For two otherwise eligible articles, the full texts could not be retrieved. The eligibility criteria were then applied to the remaining 34 papers, which resulted in the exclusion of 26, because 13 reported no significant risk factors for early failure, five presented only individual risk factors, five did not provide data about failures, and three did not satisfy the statistical criteria for inclusion. A total of eight observational studies completely fulfilled the inclusion criteria, from which seven significant risk factors were selected for the simulation process. The level of inter-reviewer agreement on study selection was substantial (κ: 0.78, 95% CI 0.70 to 0.86). The details of search and selection are shown in Fig. 1.

Seven risk factors were selected: "smoking" (SM), "bone quality" (BQ), "short implants" (SH), "wide implants" (WD), "adjacent teeth" (AT), "periodontitis" (P) and "male sex" (M). Table 1 shows the studies selected and the distribution of significant risk factors for early failure of implants. "Adjacent teeth" as a risk factor referred to the natural teeth next to the implant. "Wide implants" were those implants that had a diameter of more than 4 mm, and "short implants" were <10 mm long. Selected types of bone quality for the simulation were types 1 and 4 based on the results of the corresponding studies. Frequency data including the sample studied and the number of implants for each risk factor were extracted (Table 2), together with their failure rates (Table 3).

According to the results of the quality assessment, two studies scored 9 points and five scored 8 points, indicated

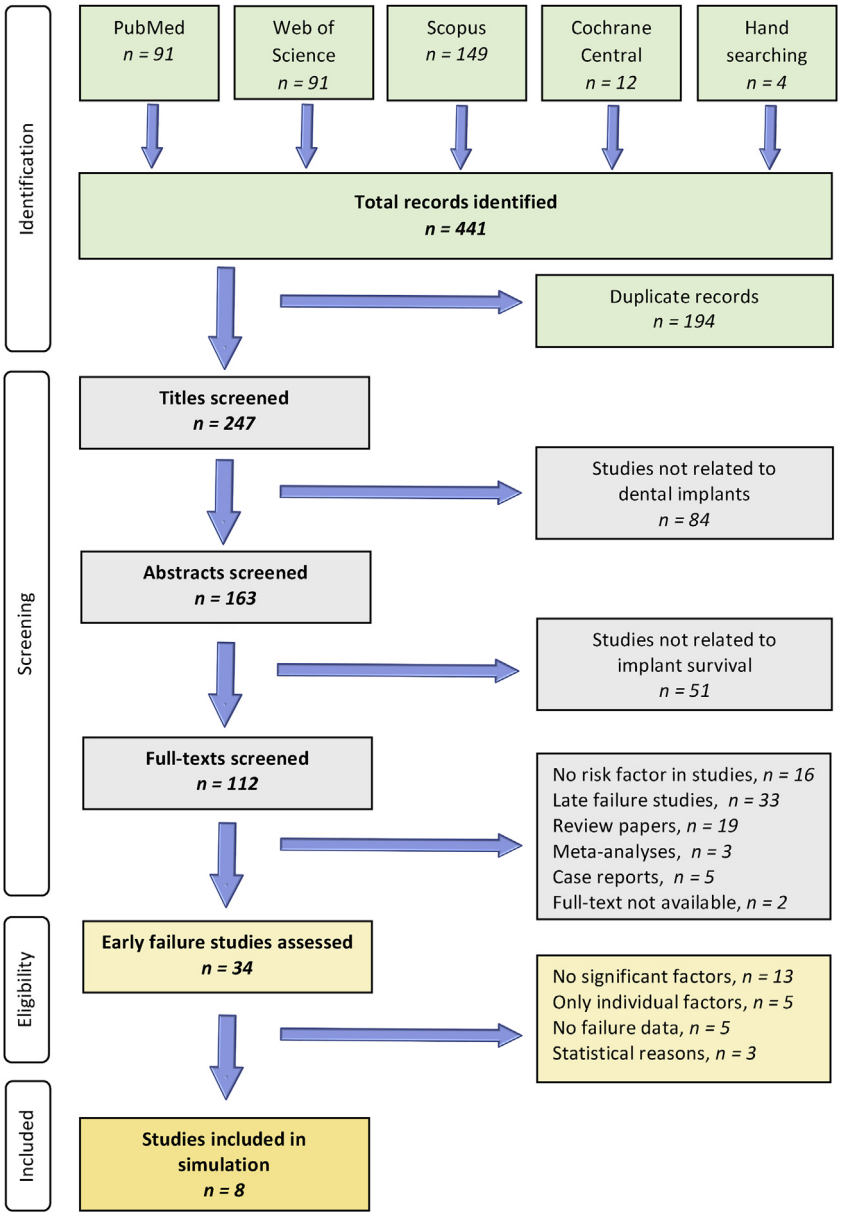

Fig. 1. Algorithm showing the search and selection strategy.

Table 1
Distribution of the selected risk factors in the studies.

First author and year	Risk factors						
	Smoking	Bone quality	Short implants	Wide implants	Adjacent teeth	Periodontitis	Male sex
Grisar 2017	+						+
Alsaadi 2008	+				+		
Alsaadi 2007	+	+	+	+	+		
Chrcanovic 2016	+						
Derks 2015	+		+			+	
Noguerol 2006	+	+		+			
Olate 2010			+				
Olmedo-Gaya 2016						+	+

Table 2
Frequency data extracted from the selected studies.

First author and year	Total No. of implants (factor No.)						
	Smoking	Bone quality	Short implants	Wide implants	Adjacent teeth	Periodontitis	Male sex
Grisar 2017	1139 (255)	–	–	–	–	–	1139 (550)
Alsaadi 2008	720 (95)	–	–	–	720 (289)	–	–
Alsaadi 2007	6946 (916)	5782 (1188)	6946 (456)	6936 (142)	2448 (812)	–	–
Chrcanovic 2016	6575 (2018)	–	–	–	–	–	–
Derks 2015	11311 (4015)	–	11311 (1015)	–	–	11311 (3145)	–
Noguerol 2006	1084 (592)	1084 (137)	–	1084 (297)	–	–	–
Olate 2010	–	–	1649 (131)	–	–	–	–
Olmedo-Gaya 2016	–	–	–	–	–	276 (63)	276 (103)

Table 3
Early failure rates of the risk factors.

First author and year	No. (%) early failures						
	Smoking	Bone quality	Short implants	Wide implants	Adjacent teeth	Periodontitis	Male sex
Grisar 2017	24 (9.4)	–	–	–	–	–	36 (6.5)
Alsaadi 2008	5 (5.3)	–	–	–	12 (4.2)	–	–
Alsaadi 2007	54 (5.9)	76 (6.4)	29 (6.4)	12 (8.5)	63 (7.8)	–	–
Chrcanovic 2016	180 (8.9)	–	–	–	–	–	–
Derks 2015	88 (2.2)	–	30 (3.0)	–	–	72 (2.3)	–
Noguerol 2006	65 (11.0)	11 (8.0)	–	24 (8.1)	–	–	–
Olate 2010	–	–	13 (9.9)	–	–	–	–
Olmedo-Gaya 2016	–	–	–	–	–	11 (17.5)	8 (7.8)

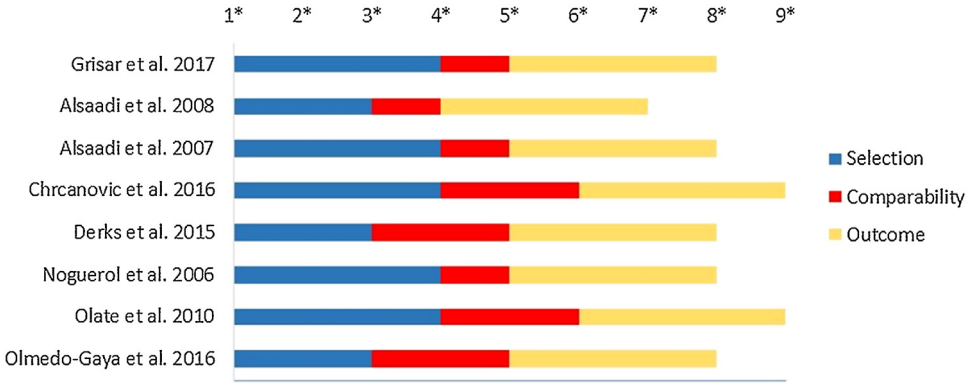

Fig. 2. Quality of methods used in observational studies included.

that the quality of the methods used was high. Only one study received a score of 7 points, indicating medium quality (Fig. 2). The inter-rater agreement during the quality assessment was also substantial with a kappa value of 0.72 (95% CI 0.45 to 0.99).

Monte Carlo simulation

Based on the selected seven significant risk factors, all two-factor combinations that account for the total of 21 areas of greatest risk were created: "smoking and periodontitis" (SM + P), "smoking and short implants" (SM + SH), "smoking and adjacent teeth" (SM + AT), "smoking and bone quality" (SM + BQ), "smoking and male sex" (SM + M), "smoking and wide implants" (SM + WD), "short implants and periodontitis" (SH + P), "short implants and adjacent teeth" (SH + AT), "short implants and male sex" (SH + M), "short implants and wide implants" (SH + WD), "adjacent teeth and periodontitis" (AT + P), "adjacent teeth and male sex" (AT + M), "bone quality and periodontitis" (BQ + P), "bone quality and short implants" (BQ + SH), "bone quality and adjacent teeth" (BQ + AT), "bone quality and male sex" (BQ + M), "bone quality and wide implants" (BQ + WD), "periodontitis and male sex" (P + M), "wide implants and periodontitis" (WD + P), "wide implants and adjacent teeth" (WD + AT), "wide implants and male sex" (WD + M).

The outcomes of the Monte Carlo simulation model show that the SRS values of the risk factors had different ranges of effect and probability on the early failure risk. Estimated effects of the top 10 ranked areas of greatest risk of early failure of an implant were compiled in a single graph (Fig. 3).

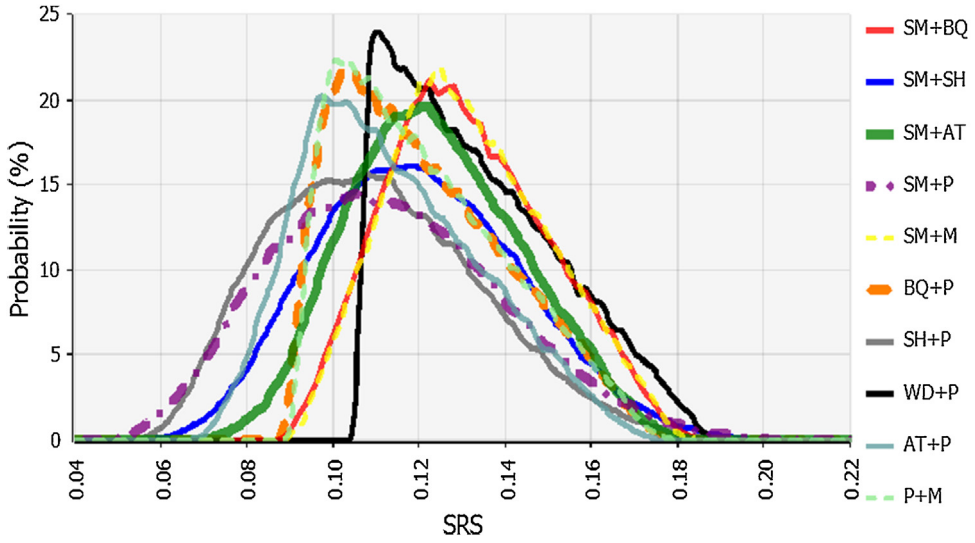

Fig. 3. Probability density function of the top 10 areas of greatest risk. SM = smoking, BQ=bone quality, SH = short implants, WD = wide implants, AT = adjacent teeth, P = periodontitis, and M = male sex.

The graph was prepared to illustrate the probability density distribution of areas of greatest risk based on the SRS values.

As a result of the simulation and sensitivity analysis, the most sensitive area of greatest risk was "smoking and periodontitis" with the highest Spearman rank coefficient of 0.333. "Short implants and periodontitis" was ranked the second, followed by "smoking and short implants," which was ranked third. Other areas in the top 10, in descending order, were "adjacent teeth and periodontitis", "smoking and adjacent teeth", "bone quality and periodontitis", "periodontitis and male sex", "smoking and bone quality", "wide implants and periodontitis", and "smoking and male sex". Least sensitive ones for early failure were "bone quality and male sex", "bone quality and wide implants", and "wide implants and male sex", which were ranked 19th – 21st, respectively. Ranking of the top 10 high-risk areas is shown in a tornado graph that indicates more sensitive to less sensitive from top to bottom, as shown in Fig. 4. Spearman rank coefficient values for all areas of risk are shown in Fig. 5.

The outcomes of the simulation are summarised in Table 4 as range, mean (SD), and 95% prediction interval.

Discussion

Early failure of implants has been attributed by previous authors to many risk factors including systemic conditions, design of the implant and its characteristics, local factors related to bone and dentition, and the patient's habits. Individual factors also identified as significantly associated with early failure were: Crohn's disease, osteoporosis, implantation in a posterior region;[11] brand of implant;[12] narrow keratinised gingiva, use of polyglactin sutures, and narrow implants;[13] radiotherapy and chemotherapy, claustrophobia and limited volume of bone; [2] techniques of bony expansion;[14] taking antidepressants;[15] apical lesions, hormone replacement, gastric problems, type I diabetes, and radical hysterectomy;[16] age <60, and Periotest® values;[1] use of bisphosphonates and haemorrhagic disease;[17] MMP-8 promoter polymorphism;[18] dehiscence of the buccal bone;[19]; *B forsythus* avidity and *S aureus* antibody titre;[20] shape of the jaw;[21] bone augmentation surgery and total edentulism;[22] surgeon, number of placed implants, and one or two jaws treated;[23] year at operation, surgical technique, and immediate grafting technique;[24] and maxillary implants.[25] As the number of significant risk factors increases, it becomes of interest to find out how multiple risk factors affect the risk of early failure of an implant.

Smoking was the most commonly encountered significant risk factor for early failure and was mentioned in 10 studies, only six of which fulfilled the inclusion criteria and selected for the simulation. We also did not include a study that reported the significant influence of "short implants" on early failure, because the sample size was less than 20 implants.[14] The bone resorption score was also identified in two different studies,[20,23] but this was not included in the simulation process as no frequency data were given. Three studies were statistically too weak to show independent effects of the risk factors analysed despite the suggestion that they significantly affected the success of early implants.[26–28]

Grisar et al reported that the diameter of the implant was a significant risk factor for their study group, but they did not make it clear whether this was linked to wide, regular, or narrow implants.[22] A meta-analysis of risk factors for early failure reported that smoking, short implants, and those placed in the maxilla were the main significant risk factors.[29] On the other hand, 13 studies reported that none of the risk factors that were assessed in their studies had an impact on early failure.

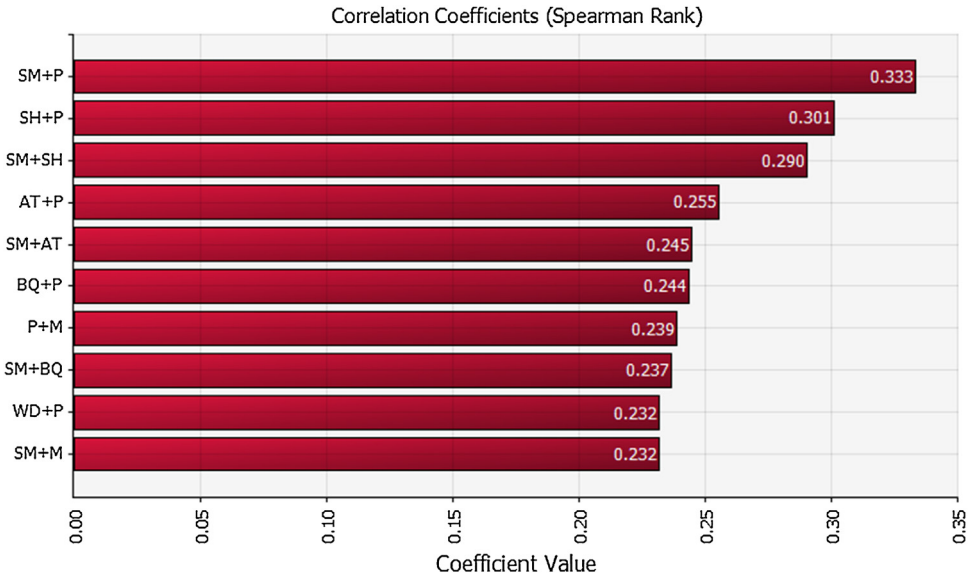

Fig. 4. Ranked sensitivity of the top 10 areas of greatest risk on overall SRS. SM = smoking, BQ = bone quality, SH = short implants, WD = wide implants, AT = adjacent teeth, P = periodontitis, and M = male sex.

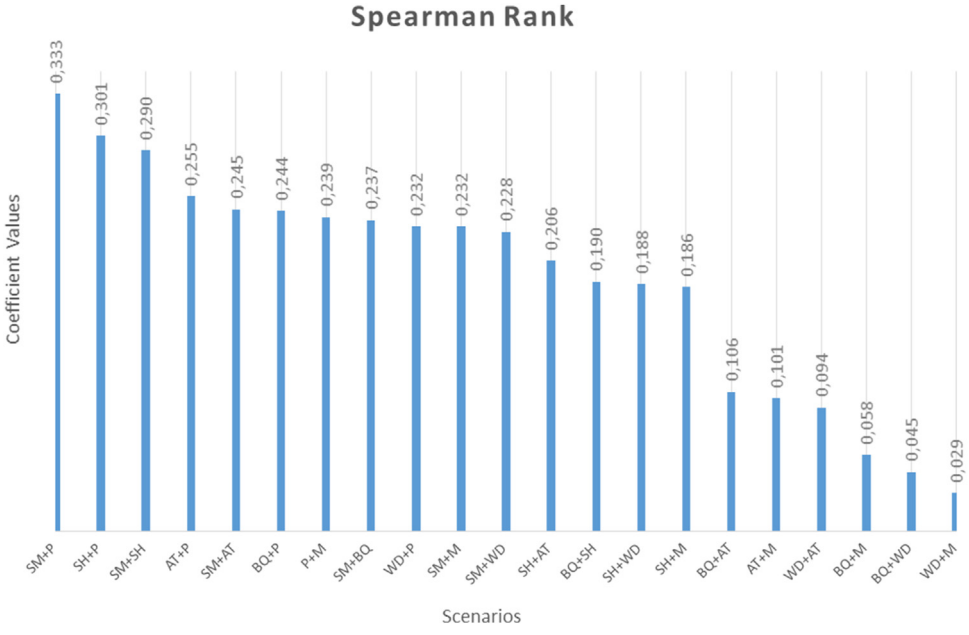

Fig. 5. Spearman rank coefficient values of the areas of greatest risk.

The focus of this study was to model the common factors that were found to be statistically relevant to early failure of implants, and to test them in different conditions. The same risk factors that were present in at least two or more papers, therefore, were chosen to create these conditions,which makes the risk factors selected more reliable in relation to early failure of implants, while individual risk factors could still raise more doubt.[7] Smoking has been identified as a significant risk factor in more studies than any other risk factor. The fact that a relatively large number of studies evaluated a particular risk factor does not necessarily indicate the importance of that factor, as it may be the result of the degree of interest that the authors had in that factor.

The statistical methods used in the selected papers for evaluation of the significance of risk factors were all multivariate analyses. Because univariate analyses do not account for possible interactions between risk factors, it was stipulated that risk factors could be included into the simulation only if they remained significant after multivariate regression, which confirms the independence of the risk factors. Cosyn et al and Vervaeke et al stressed the need for multivariate analyses in identifying genuinely significant risk factors.[30,31] On the other hand, interactions of these risk factors in relation to

early failure are not within the scope of this study, because of the lack of information about their correlations.

To our knowledge, this is the first study that has evaluated the effects of multiple risk factors on early failure. So far, only two studies have mentioned the use of the Monte Carlo method for the assessment of early failure of implants, but no explanation was provided as to how the simulation and analysis were conducted.[12,32] Monte Carlo simulation has been widely used in many different fields, including manufacturing, engineering, finance, and medical sciences to estimate the probabilistic effect of any given factor on the outcome.[6] Limited studies and small samples are the main difficulties when comparing the strength of various risk factors, and they hamper the ability to draw reasonable conclusions. Monte Carlo simulations can overcome these problems using repeated sampling to assess the properties and behaviour of a variable.[33] A strong advantage of the Monte Carlo simulation for problems with missing data is its ability to evaluate effects relative to the true population being described.[34,35]

Evaluation of risk for multiple factors might be challenging. Although the significance of the effects of single risk factors on early failure has been studied intensively, existing studies do not help to understand the collective effects of integrated risk factors. In a search for a solution to this problem, a simulation model was proposed to estimate the risks of different areas of risk that were created by combining significant risk factors. The simulation model has allowed us to illustrate the impact of paired factors with the assigned probability distributions. Models of two risk factors were selected for assessment. All pairwise combinations of significant risk factors were generated to develop the simulation model.

Considering the sensitivity analysis of all the simulated conditions, "smoking and periodontitis" was by far the most influential combination, and the second area of greatest risk that was strongly associated with early failure was "short implants and periodontitis". The third was "smoking and short implants". These top three, with their remarkably high sensitivities, can be considered to be of major importance for early failure of implants. An interesting observation was the small differences in estimated coefficient values between the fifth and sixth, seventh and eighth, and also the ninth and 10th ranked areas of greatest risk, which implies that these had similar impacts on early failure. "Wide implants and male sex" was ranked last, and seemed to have the weakest influence on early failure because it had the lowest Spearman rank coefficient (0.029). Overall, those areas that included "periodontitis" and "smoking" were ranked much higher than the other areas of greatest risk, whereas those with "adjacent teeth" and "male sex" were ranked notably lower. After "smoking and periodontitis" in the top 10, there were four combinations of "periodontitis" as well as four of "smoking". It is also important to note that these two risk factors are potentially modifiable factors.

Because we could find no research that has reported a ranking of multiple risk factors in terms of their importance for early failure, there were no data with which we could compare our results. There are several shortcomings and weaknesses that should be considered when the results of this study are applied to clinical practice. Shortcomings include the few common risk factors among the papers compared with individual ones, and the unknown interactions between the risk factors that could not have been taken into account in the simulation. In the model, the areas of greatest risk were generated by using the data in a deterministic manner, but the estimates were obtained by using probabilistic sensitivity analysis. Stochastic models may, therefore, lead to results that differ from the deterministic ones. The probability densities of the created areas were also calculated with the assumption of a triangular distribution of input data, which may indicate a potential selection bias.

Table 4
Output values of the simulation.

	Range	Mean (SD)	95% PI
WD + AT	0.1230–0.1616	0.1448 (0.0077)	0.1308–0.156
SM + BQ	0.0870–0.1879	0.1314 (0.0186)	0.1027–0.1644
SM + SH	0.0552–0.2028	0.1202 (0.0235)	0.0837–0.1607
SM + WD	0.1039–0.1926	0.1439 (0.0182)	0.1159–0.1765
SM + AT	0.0666–0.1840	0.1239 (0.0198)	0.0933–0.1584
SM + P	0.0472–0.2063	0.1127 (0.0263)	0.0725–0.1589
SM + M	0.0882–0.1860	0.1317 (0.0184)	0.1034–0.1643
BQ + SH	0.0950–0.1774	0.1288 (0.0152)	0.1066–0.1564
BQ + WD	0.1451–0.1643	0.1524 (0.0037)	0.1473–0.1593
BQ + AT	0.1067–0.1560	0.1324 (0.0084)	0.1175–0.1454
BQ + P	0.0876–0.1825	0.1213 (0.0194)	0.0952–0.1574
BQ + M	0.1297–0.1575	0.1401 (0.0045)	0.1334–0.1482
SH + WD	0.1110–0.1826	0.1412 (0.0148)	0.1198–0.1682
SH + AT	0.0729–0.1746	0.1211 (0.0166)	0.0956–0.1506
SH + P	0.0540–0.1988	0.1100 (0.0241)	0.0741–0.1528
SH + M	0.0958–0.1749	0.1290 (0.0150)	0.1072–0.1564
WD + P	0.1041–0.1879	0.1337 (0.0190)	0.1089–0.1694
WD + M	0.1464–0.1616	0.1526 (0.0028)	0.1487–0.1577
AT + P	0.0663–0.1788	0.1136 (0.0205)	0.0841–0.1511
AT + M	0.1080–0.1544	0.1326 (0.0081)	0.1181–0.1446
P + M	0.0887–0.1802	0.1214 (0.0192)	0.096–0.1573

PI = Prediction interval.
SM = smoking, BQ = bone quality, SH = short implants, WD = wide implants, AT = adjacent teeth, P = periodontitis, and M = male sex.

Conclusions

In this simulation study, we made an estimate about the strength of simulated areas of greatest risk for early failure of implants. In this assessment, the most important that had the strongest impacts on early failure were "smoking and periodontitis", "short implants and periodontitis", and "smoking and short implants". The least important were "bone quality and male sex", "bone quality and wide implants", and "wide implants and male sex". The ranking of the areas of greatest risk by importance based on the risk estimates derived from the Monte Carlo simulation is expected to help in understanding the contribution of various combinations of risk factors to the early failure of implants. When we evaluate the risk of

early failure, we should make efforts not only to target single risk factors, but also multiple combinations of these factors.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patients' permission

Not applicable, as no patients were involved.

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