Risk Factors for Postoperative Infections After Dental Implant Placement:
A Case-Control Study

Rui Figueiredo, DDS, MS, PhD, 1 Octavi Camps-Font, DDS, 1
Eduard Valmaseda-Castellón, DDS, MS, PbD, 1 and Cosme Gay-Escoda, MD, DDS, MS, PbD 5

Purpose: To determine possible risk factors for postoperative infections after implant surgery, explain their effects on the occurrence of such infections, and assess the relation between postoperative infections and early implant failure.

Patients and Methods: A case-and-control study was performed. Postoperative infections were defined as purulent drainage or fistula in the operated region with pain or tenderness, localized swelling, redness, and heat or fever before prosthetic loading. Bivariate and multivariate analyses of the data were performed.

Results: Eighty-eight outpatients (22 patients in the infection group and 66 controls) were selected. Male gender and submerged healing were meaningfully associated to the development of postoperative infections (bivariate analysis). Healing type and location were the independent variables included in the final logistic regression model. Postoperative infections during the osseointegration period considerably increased the risk of early failure (odds ratio = 78.0; 95% confidence interval, 9.12 to 666.90).

Conclusions: Patients undergoing dental implant placement in the mandible with submerged healing are more prone to postoperative infections. This complication is relevant because it is associated with a considerable and almost 80-fold increase in the risk of early implant failure.

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Since Brånemark defined osseointegration in the mid-1960s, 1 oral rehabilitation has changed as a result of the introduction of dental implants. Although the survival rates of osseointegrated implants are high, 2 short- and long-term complications can occur. 3

Early failures in implant dentistry are an uncommon finding, with incidences ranging from 1 to 2%, according to most studies. 4 Bone quality, local and systemic conditions, severe surgical trauma, infections, and occlusal overload have been suggested as critical factors influencing osseointegration. 5,6

Postoperative infections are rare complications that usually occur within the first month after dental implant placement. The reported prevalence varies across published studies, with figures reaching 11.5%. 7-11 As with any biomaterial infection, the treatment of such complications can be quite complex, and infection can persist until the implanted device is removed. 12

1 Professor, Master Degree Program in Oral Surgery and Implantology; Associate Professor, Department of Oral Surgery; Faculty of Dentistry, University of Barcelona; Researcher, IDIBELL Institute, Barcelona, Spain.
1 Fellow, Master Degree Program in Oral Surgery and Implantology, Faculty of Dentistry, University of Barcelona, Barcelona, Spain.
1 Professor, Department of Oral Surgery; Director, Master Degree Program of Oral Surgery and Implantology, Faculty of Dentistry, University of Barcelona; Researcher, IDIBELL Institute, Barcelona, Spain.
2 Chair and Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Barcelona; Coordinating Investigator, IDIBELL Institute; Head, Department of Oral and Maxillofacial Surgery, Teknon Medical Center, Barcelona, Spain.

Dr Figueiredo is a consultant for Inibsa Dental and Biohorizons.

Address correspondence and reprint requests to Dr Figueiredo:
Facility of Dentistry, University of Barcelona, Campus de Bellvitge UB; Facultad d’Odontologia, C/Feixa Llarga, s/n, Pavelló Govern, 2 plantas, Despatx 2.9, 08907 L’Hospitalet de Llobregat, Barcelona, Spain; e-mail: rui@ruibf.com

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In this regard, several studies have reported considerably higher early implant failure rates when postoperative infections occur during the osseointegration period.\(^8\)\(^-\)\(^10\) Therefore, the identification of risk factors is essential. Considering the low prevalence of this complication, a case-and-control study would be an adequate design for identifying the main risk factors.\(^13\)\(^-\)\(^15\)

Accordingly, the main objectives of the present study were to determine possible risk factors for postoperative infections after dental implant placement, to explain the effects of these risk factors on the occurrence of such infections in an outpatient clinic, and to assess the relation between these infections and early implant failure.

**Patients and Methods**

A retrospective case-and-control study was performed of patients selected from a list of 474 patients (1,625 implants) consecutively treated from February 2009 through October 2012 at the Master Degree Program in Oral Surgery and Implantology of the University of Barcelona (Barcelona, Spain). The study design followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for case-and-control studies.\(^14\) The protocol complied with Declaration of Helsinki guidelines and was approved by the clinical research ethics committee of the Dental Hospital of the University of Barcelona.

Patients were given full information about the surgical procedures and treatment alternatives, and informed consent was obtained in all cases. Preoperative analysis included complete medical histories and clinical and radiographic examinations (with panoramic radiographs or computed tomograms).

Exclusion criteria were general contraindications to implant surgery, radiotherapy in the head and neck area, uncontrolled diabetes, current pregnancy or lactation, and current substance abuse.

Patients with active periodontal disease were previously treated according to the American Academy of Periodontology guidelines.\(^15\)

The infected group (IG) included those patients with purulent drainage (pus) or fistula in the operated region with pain or tenderness, localized swelling, redness, and heat or fever (\(>38^\circ\)C) before prosthetic loading.\(^16\) If the postoperative infection involved several implants, then 1 was randomly selected by a random-numbers table based on the position of the implant according to the double-digit FDI classification.

Three controls were selected for each patient in the IG. Because the IG was small (owing to the low incidence of immediate postoperative infection in oral implants), 3 controls were selected to increase statistical power. Thus, for each patient in the IG, the next 3 surgical patients were selected as controls. Accordingly, the control group (CG) included those patients who underwent the same surgical procedure within the above-mentioned time frame but did not develop infection during the postoperative period. Only 1 implant was selected for each control using the same selection method as for the IG.

Cases with incomplete clinical records or with dental implants placed in previous failure sites were excluded from the analysis. The authors also excluded patients who required guided bone regeneration procedures or procedures involving nonconventional prosthetic loading (\(\geq 3\) months in the mandible and 4 months in the maxilla after implant placement were required).

Implant mobility or impaired osseointegration before prosthetic abutment connection was regarded as early failure.\(^17\) Patients were recalled for a follow-up visit to determine the implant survival rate, defined as an implant in its original position without mobility.

**SURGICAL PROCEDURE**

The implants were placed according the protocol of the oral implantology unit. Articaine in a 4\% solution with epinephrine 1:100,000 (Artinibsa; Inibsa Dental, Llíça de Vell, Spain) was used as the local anesthetic, and all procedures were performed by third-year residents of the Master Degree Program in Oral Surgery and Implantology. A mid-crestal incision was made and full-thickness flaps were elevated to expose the alveolar ridge. Implant sites were prepared using drills of increasing diameter, under constant irrigation with sterile saline, according to the recommendations of the manufacturer. Functional and esthetic requirements were taken into account to determine the inclination of the implants in the mesiodistal and buccolingual directions. The flaps were usually reposited with 4-0 polyamide sutures (Supramid; Aragó, Barcelona, Spain). The sutures were removed 7 to 15 days after surgery. Owing to the retrospective nature of this study, small variations in surgical technique could have occurred.

Postoperative instructions were provided, and use of the prescribed drugs was explained in a paper sheet given to the patient. Patient compliance was not specifically assessed.

**DATA SAMPLING**

One trained researcher examined all clinical records. The following data were retrieved: age; gender; patient health status based on the American Society of Anesthesiologists (ASA) Physical Status Classification System (ASA score 1 or >1);\(^18\) smoking habit (nonsmoker, 1 to 10 cigarettes/day, or >10
cigarettes/day); periodontal disease (healthy or periodontal compromise); implant manufacturer; location (maxilla or mandible); position (anterior or posterior); protocol for implant placement according to the classification of Hämmerle et al; number of implants placed in the same surgical procedure (1, 2 to 4, or >4); primary stability (insertion torque >15 N-cm²); submerged or non-submerged healing; surgeon performing the operation; postoperative follow-up appointments; and use of antibiotics or antibacterial mouth rinses after surgery. The dates of implant placement, infection diagnosis, infection resolution, and last follow-up also were recorded.

STATISTICAL ANALYSIS

Sample size calculation was based on the assumptions that postoperative infections affect 5.9% of the patients and that the development of infection increases the risk of early implant failure at least 10-fold. Considering an α risk of 0.05, a power of 90%, and a 10% exclusion rate, 22 patients with infection were required. Three controls were included for each patient with infection (66 controls were analyzed) to increase statistical power without recruiting more cases.

Statistical analysis was carried out with SPSS 22.0 (IBM Corp, Armonk, NY). Normality of scale variables (patient age, time elapsed from implant placement to infection onset, and follow-up period) was explored using the Shapiro-Wilk test. Where normality was rejected, the median and interquartile range (IQR) were calculated. Where distribution was compatible with normality, the mean and standard deviation (SD) were used. Parametric and nonparametric tests (Pearson χ² test, Fisher exact test, and Mann-Whitney U test) were used to compare the groups. The odds ratio (OR) with 95% confidence interval (95% CI) was calculated for each categorical variable. The level of significance was set at a P value less than .05.

A multivariate analysis was performed using a non-conditional logistic regression model. The binary dependent variable was group (0 for CG and 1 for IG), representing the occurrence of infection. Independent variables were added to the model using a forward stepwise procedure based on the likelihood ratio. To avoid overfitting of the model, the number of variables included in the final binary logistic regression model for the adjusted OR estimation was limited to 2 by selecting those that most altered the lower limit of the 95% CI of the OR (by ≥10%). Goodness of fit of the data was tested with the Hosmer-Lemeshow test. The logistic regression equation was used to calculate the adjusted OR of the included predictive variables with 95% CI. The cutoff point was set using a receiver operating characteristic (ROC) curve.

Results

The IG was comprised of 22 patients and the CG consisted of 66 patients; they were selected from a list of 474 patients (1,625 implants) consecutively treated from February 2009 through October 2012 at the Master Degree Program in Oral Surgery and Implantology of the University of Barcelona.

After the procedure, all patients in the IG and CG were prescribed amoxicillin 750 mg orally every 8 hours for 7 days (Clamoxyl; GlaxoSmithKline, Madrid, Spain), ibuprofen 600 mg orally every 8 hours for 4 to 5 days (Algàsdis; Esteve, Barcelona, Spain), paracetamol 1 g orally every 8 hours for 3 to 4 days (Gelocatil; Gelos, Barcelona, Spain), and a mouth rinse (0.12% chlorhexidine digluconate 15 mL every 12 hours for 15 days; Clorhexidina Lacer; Lacer, Barcelona, Spain).

The mean patient age was 56.8 years (SD, 11.2 yr) and 51.2 years (SD, 11.8 yr) for the IG and CG, respectively (t = −1.937; df = 86; P = .06).

The median time from implant placement to the onset of postoperative infection was 28 days (IQR, 38.3). The earliest infection appeared 12 days after the operation, and the latest was diagnosed 139 days after implant placement. This variable did not seem to be related to an increased risk of early implant failure (U = 52.5; P = .65).

Table 1 presents the associations between the binary variables, and Table 2 presents the results of the remaining variables.

The final logistic regression model included submerged healing and mandible location as independent variables. The results of the model are presented in Table 3.

The change in the likelihood ratio of the logistic regression model was statistically significant (χ² = 19.92; df = 1; P < .001). The Nagelkerke R² value was 19.2% and thus explained slightly less than one fifth of the observed variation. Despite the small number of cases, the Hosmer-Lemeshow test showed a good data fit (P = .98), and there was no collinearity (tolerances ~ 1.00; variance inflation factors ~ 1.00). The assumptions of the model were fulfilled.

The adjusted ORs are listed in Table 4. The ROC had an area under the curve of 0.73 (95% CI, 0.61 to 0.85; P = .001). With a prevalence of 0.0653 and a probability of infection cutoff point of .20, the sensitivity was 81.8%, the specificity was 53.0%, the positive predictive value was 10.8%, and the negative predictive value was 97.7%.

Twelve patients in the IG (54.6%) and 1 in the CG (1.5%) developed an early failure (OR = 78.0; 95% CI, 9.12 to 666.90; P < .001). The implants that were loaded had a survival rate of 80.0% for the IG and a rate of 95.2% for the CG (OR = 0.24; 95% CI,
Patients in the IG were followed for 42.9 months (SD, 10.2 months; range, 23 to 74 months) and those in the CG were followed for 35.9 months (SD, 13.3 months; range, 18 to 77 months; \( t = 1.593; df = 76; P = .115 \)).

### Discussion

To the authors’ knowledge, this is the first published case-and-control study on postoperative infections after dental implant placement. The main limitations of the present study are its retrospective nature and the criteria used to define infection, based mostly on clinical observations. This could be improved in future research by using objective diagnostic methods, such as the measurement of acute-phase protein levels.\(^{21}\)

The authors decided not to include patients who required simultaneous bone augmentation procedures because this can be an important confounding variable and such procedures can increase the risk of infection, especially when membranes are exposed, owing to inadequate wound closure.

Some reports have addressed the prevalence and described some of the clinical features of postoperative infections after dental implant placement. The results of binary variables and variables with more than 2 categories are presented in Tables 1 and 2, respectively.

### Table 1. RESULTS OF BINARY VARIABLES

<table>
<thead>
<tr>
<th>Variable</th>
<th>IG, Odds (%)</th>
<th>CG, Odds (%)</th>
<th>OR (95% CI)</th>
<th>Bivariate (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>14/8 (63.6)</td>
<td>22/44 (33.3)</td>
<td>3.50 (1.28-9.59)</td>
<td>.01*</td>
</tr>
<tr>
<td>ASA score ( &gt;1 )</td>
<td>16/6 (72.7)</td>
<td>35/31 (53.0)</td>
<td>2.36 (0.82-6.79)</td>
<td>.11</td>
</tr>
<tr>
<td>Mandible location</td>
<td>14/8 (63.6)</td>
<td>31/35 (47.0)</td>
<td>1.98 (0.73-5.34)</td>
<td>.18</td>
</tr>
<tr>
<td>Posterior position</td>
<td>12/10 (54.5)</td>
<td>36/30 (54.5)</td>
<td>1.00 (0.38-2.64)</td>
<td>1.00</td>
</tr>
<tr>
<td>Periodontal compromise</td>
<td>17/5 (77.3)</td>
<td>46/20 (73)</td>
<td>1.48 (0.48-4.56)</td>
<td>.50</td>
</tr>
<tr>
<td>Submerged healing</td>
<td>18/4 (81.8)</td>
<td>31/35 (47.0)</td>
<td>5.09 (1.55-16.64)</td>
<td>&lt;.01*</td>
</tr>
<tr>
<td>Primary stability</td>
<td>19/3 (86.4)</td>
<td>61/5 (92.4)</td>
<td>1.93 (0.42-8.82)</td>
<td>.39</td>
</tr>
<tr>
<td>Postoperative antibiotic</td>
<td>22/0 (100)</td>
<td>66/0 (100)</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Postoperative antiseptic</td>
<td>22/0 (100)</td>
<td>66/0 (100)</td>
<td>—</td>
<td>1</td>
</tr>
</tbody>
</table>

Abbreviations: ASA, American Society of Anesthesiologists; CG, control group; CI, confidence interval; IG, infected group; OR, odds ratio.

* In the bivariate analysis, male gender and unsubmerged healing were significantly associated to infection (\( P < .05 \)).

### Table 2. RESULTS OF VARIABLES WITH MORE THAN 2 CATEGORIES

<table>
<thead>
<tr>
<th>Variable</th>
<th>IG, n (%)</th>
<th>CG, n (%)</th>
<th>OR (95% CI)</th>
<th>Bivariate (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking habit (cigarettes/day)</td>
<td></td>
<td></td>
<td></td>
<td>.35</td>
</tr>
<tr>
<td>0</td>
<td>15 (68.2)</td>
<td>33 (50.0)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1-10</td>
<td>2 (9.1)</td>
<td>10 (15.2)</td>
<td>0.56 (0.11-2.78)</td>
<td></td>
</tr>
<tr>
<td>&gt;10</td>
<td>5 (22.7)</td>
<td>23 (34.8)</td>
<td>0.59 (0.19-1.80)</td>
<td></td>
</tr>
<tr>
<td>Implant manufacturer</td>
<td></td>
<td></td>
<td>.83</td>
<td></td>
</tr>
<tr>
<td>Nobel Biocare</td>
<td>11 (50.0)</td>
<td>35 (53.0)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Phibo</td>
<td>7 (31.8)</td>
<td>19 (28.8)</td>
<td>1.15 (0.41-3.28)</td>
<td></td>
</tr>
<tr>
<td>Astra Tech</td>
<td>3 (13.6)</td>
<td>10 (15.2)</td>
<td>0.89 (0.22-3.55)</td>
<td></td>
</tr>
<tr>
<td>Straumann</td>
<td>1 (4.5)</td>
<td>2 (3.0)</td>
<td>1.52 (0.13-17.67)</td>
<td></td>
</tr>
<tr>
<td>Implant placement protocol</td>
<td></td>
<td></td>
<td>.61</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0 (0.0)</td>
<td>1 (1.5)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>1 (4.5)</td>
<td>1 (1.5)</td>
<td>3.10 (0.19-51.68)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>2 (9.1)</td>
<td>3 (4.5)</td>
<td>2.10 (0.33-13.47)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>19 (86.4)</td>
<td>61 (92.4)</td>
<td>0.52 (0.11-2.38)</td>
<td></td>
</tr>
<tr>
<td>Number of implants</td>
<td></td>
<td></td>
<td>.14</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4 (18.2)</td>
<td>19 (28.8)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2-4</td>
<td>15 (68.2)</td>
<td>44 (66.7)</td>
<td>1.07 (0.38-3.01)</td>
<td></td>
</tr>
<tr>
<td>&gt;4</td>
<td>3 (13.6)</td>
<td>3 (4.5)</td>
<td>3.32 (0.62-17.80)</td>
<td></td>
</tr>
</tbody>
</table>

Note: None of the variables were statistically significant (\( P > .05 \)).

Abbreviations: CG, control group; CI, confidence interval; IG, infected group; OR, odds ratio.

infections, but there are no clearly identified risk factors. Thus, a case-and-control design was considered efficient. The authors decided not to match controls by age or gender, because this would prevent assessing the effect of these variables on the occurrence of infection. Furthermore, the logistic regression model allowed an analysis of the data by taking into account the effect of potential confounders.

Although the prevalence per patient of postoperative infections when systemic antibiotics are administered varies considerably across published studies, Esposito et al. reported a weighted rate of 5.9% (95% CI, 3.8 to 7.9). This variation could be explained in part by the small number of participants in some reports, the lack of standardized diagnostic criteria, the different research designs, and the demographic characteristics of the samples. Because of this low rate, the OR is a reasonable estimate of the relative risk and indeed can be interpreted as relative risk.

Although the bivariate analysis identified a statistically meaningful association between male gender and the development of postoperative infection, this variable was not included in the final logistic regression model. A possible explanation for this could be that other variables, such as smoking, could act as confounders. Indeed, a significant relation was found between male gender and smoking (χ² = 2.80; df = 1; P = .04).

The impact of systemic diseases on the outcome of implant therapy remains unclear. Although some investigators have reported higher complication rates in medically compromised patients, others, in accord with the present observations, have suggested that some concrete conditions do not seem to influence treatment outcomes. Nevertheless, it seems reasonable to assume that the severity of these systemic diseases can be far more critical than the disorder itself. Therefore, a strict preoperative assessment allowing adequate diagnosis and management of any systemic disorder is mandatory before implant therapy, because this can lower the complication rates of such treatment.

The effect of smoking has been considered a risk factor for infections and peri-implant bone loss. In the authors’ opinion, such unsubmerged healing can favor a more aerobic environment and can promote the drainage of any infectious or inflammatory substances. In contrast, when soft tissue integrity is not maintained during the healing phase of a submerged implant, considerably more bone loss occurs owing to insufficient biological width or bacterial infection. Therefore, unintentional exposure of the cover screw during the healing period could be a risk factor for infections and peri-implant bone loss. In the present study, this particular issue could not be assessed owing to a lack of data in the clinical records. In the future, prospective studies should be performed to confirm this relation.

The lack of primary stability has been considered to have a negative impact on implant survival. However, the present results do not seem to support this notion, because only 1 of the 13 reported failures occurring before prosthetic loading (7.7%) had an implant insertion torque less than 15 N-cm². In the authors’ opinion, to confirm these results, future studies should use more objective methods to measure primary stability, such as resonance frequency analysis.

### Table 4. Adjusted OR of Variables Included in the Logistic Regression Model

<table>
<thead>
<tr>
<th>Submerged Healing</th>
<th>Mandible Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted OR (95% CI)</td>
<td>Logistic Regression (P)</td>
</tr>
<tr>
<td>6.21 (1.81-21.32)</td>
<td>.004</td>
</tr>
<tr>
<td>2.73 (0.93-7.99)</td>
<td>.076</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio.
Previous research carried out in the authors’ department found smoking to be a probable risk factor for implant failure, postoperative complications, and peri-implant disease.\textsuperscript{28,29} Surprisingly, this association was not found in the present study.

Placing several implants in the same patient requires larger mucoperiosteal flaps, increased operating time, and more contamination of the wound, which can contribute to an increased risk of postoperative complications. In this report, the proportion of patients in the IG who received more than 4 fixtures was approximately 3-fold greater than in the CG. However, the difference was not important, probably owing to the small number of cases with these characteristics.

A recent meta-analysis has reported a weighted postoperative infection rate of 5.9% when patients are under prophylactic systemic antibiotics. A slightly higher prevalence was observed when antibiotics were not administered (7.0%).\textsuperscript{20} In the present sample, no comparison could be made regarding this variable, because all patients received the same postoperative drugs.

The fact that infection has a delayed onset (generally occurring 1 month after the surgical procedure) stresses the importance of establishing a strict patient follow-up protocol during the first postoperative weeks to ensure early treatment. This late onset could be related to withdrawal of the antibiotic (generally prescribed for 7 days) and of the chlorhexidine mouth rinse (used for 15 days). Changes in the oral flora caused by postoperative short-duration systemic and topical antibacterial therapy also could favor the development of opportunistic infections.\textsuperscript{20}

The logistic regression model could explain only slightly less than one fifth of the observed variation and had a low positive predictive value, probably because these infections have a multifactorial etiology. However, the model allows a profile of high-risk cases to be defined and could be a useful tool for identifying such patients before the surgical procedure.

The presence of bacteria can interfere with the healing processes of a biomaterial.\textsuperscript{3} Indeed, several studies have reported considerably higher early implant failure rates when postoperative infections occur during the osseointegration period.\textsuperscript{8,10} The present results confirm these findings, because patients diagnosed with postoperative infections before prosthetic loading had a far higher (almost 80-fold) risk of early failure.

The proportion of the loaded implants that survived in the CG was approximately 15% larger than in the IG. However, probably owing to the small number of participants in the IG who developed postoperative infection, the difference was not statistically meaningful.

In conclusion, patients with dental implant placement in the mandible and submerged healing are more prone to postoperative infections. This complication is relevant, because it is associated with a considerable and almost 80-fold increase in the risk of early implant failure.

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