Novel and Accurate Predictive Model of Peri-implantitis for Implant Prosthesis in Managing Patients With Chronic Periodontitis

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Abstract

The aim of this study was to identify the influencing factors of peri-implantitis for implant prosthesis and to establish a predictive model of occurrence in managing patients with chronic periodontitis. 430 patients (a total of 686 implants) with 5 years follow-up were included in the study. The demographic and clinical characteristics independent variables were including patient related factors (age, gender, duration of symptoms, smoking, diabetes, severity of periodontitis, bone mineral density, oral hygiene) and implants related factors (position, implant diameter, implant length, additional operations, probing depth, gingival index, plaque index, load-bearing time). Univariate analysis identified the influencing factors, the statistically significant factors were further analyzed by multivariate logistic regression, and the predictive model was established. After 5 years of follow-up, peri-implantitis occurred in 95 of 686 implants (13.8%). Multiple linear regression indicated that smoking (p = 0.011), diabetes (p < 0.001), severe periodontitis (p = 0.023), larger implant diameter (p < 0.001) and poor oral hygiene (p < 0.001) increased the odds of occurrence of peri-implantitis. There were no significant differences in other factors. (p > 0.05) Logistic regression drew the equation: occurrence of peri-implantitis = \[1 + e^{(16.172 + 5.395 \times \text{smoking} + 4.807 \times \text{diabetes} + 8.109 \times \text{severe periodontitis} + 5.569 \times \text{larger implant diameter} + 11.138 \times \text{poor oral hygiene})}\] \(^{-1}\). The sensitivity of predictive factors was 91.77%, 88.43%, 82.64%, 85.21% and 92.02%, respectively. The specificity was 45.65%, 49.17%, 66.23%, 42.39% and 65.41%, respectively. The AUC was 0.721, 0.620, 0.453, 0.651 and 0.826, respectively. Hosmer-Lemeshow test showed a good fitting of the predictive model with an overall accuracy of 87.2%. Smoking, diabetes, severe periodontitis, larger implant diameter and poor oral hygiene are important risk factors of peri-implantitis. We also established a novel and accurate predictive model for the occurrence of peri-implantitis in managing patients with chronic periodontitis. The use of these parameters, in the form of a predictive model, has the potential to improve decision-making in the application of the treatment plan.

Background

Dental implants were considered as the "third set of teeth" of human beings because of their aesthetic comfort, good retention and no damage to adjacent teeth. Implant prosthesis was widely used in the replacement of removable denture and fixed denture, and was the preferred method for clinical restoration of dental loss and dentition loss at present. Despite the continuous development and improvement of dental biomaterials, implant surface treatment technology and dental implant technology, implant prosthesis had achieved a high success rate and survival rate, but there were still many failure cases and complications in implant prosthesis.\(^1,2\)

Peri-implant disease was an infectious disease that was one of the most common biological complications.\(^3,4\) However, peri-implantitis was an irreversible lesion with not only soft tissue inflammation but also marginal bone loss. Patients with history of periodontitis would have residual periodontal microbiota around the remaining teeth in the oral cavity, and these microbiotas would generate bacterial banks, leading to microbial aggregation around the implants. Gram-negative bacteria,
streptococcus, campylobacter and other bacterial colonies could form a complex microflora around the implant, and eventually lead to peri-implantitis.

Reports on the incidence of peri-implantitis have been mixed. Dreyer published a systematic review showing that the overall prevalence of peri-implantitis was 1.1%-85.0%, 0.4% within 3 years and 43.9% within 5 years.\(^5\) Studies by Schwarz et suggested that the prevalence was 8.9%-56% for patients and 4.7%-43% for implants.\(^6\),\(^7\) This difference may be attributed to different study designs and sample sizes among different studies, and more importantly, there was no consensus standards for epidemiological studies of peri-implantitis. Usually, Bleeding On Probing (BOP) (+), Probing Depth (PD) ≥ 5mm and Marginal Bone Loss (MBL) > 2mm were used as the diagnostic criterion for peri-implantitis.\(^8\)

Therefore, this study aimed to analyze the independent influencing factors of peri-implantitis by logistic regression, constructed visual prediction model and to provide a decision-making tool for dental implant physician. With the help of predictive model, dental implants can not only get a nice doctor-patient communication, but also make personalized diagnosis and treatment plan for each patient, so as to prevent peri-implantitis to the greatest extent, and then provide long-term survival and success rate of implants.

**Materials And Methods**

1.1 Patient Selection

A retrospective analysis was performed in our hospital from January 2012 to July 2014. The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the ethics committee of Xuhui District Dental Center. All the participants signed informed consents prior to the study. All patients were treated with single crown repair with adhesive retention (Active System).

Inclusion criteria: (1) at least one year of implant restoration function load; (2) met the diagnostic criteria for peri-implantitis; (3) complete clinical data and imaging information; (4) chronic periodontitis was treated with implants. Exclusion criteria: (1) the restoration is not completed after implantation; (2) the functional load of implant restoration is less than one year; (3) loss of follow-up; (4) incomplete clinical or imaging data; (5) trauma or tumor.

1.2 Operation Procedure

There are generally three procedures for tooth implantation. The first procedure involved local anesthesia, incision of the gums, preparation with a bone drill, preparation of the implant socket with a fractional drill, implantation of the implant, and suturing. Second, the healing platform is placed on the implant and the gums are sutured. This will create a better gum cuff. The third stage is performed after three weeks to one month. The mold is taken like a common denture, and a suitable crown is made. After the crown is made, the patient can wear it.
1.3 Outcomes

All patients were followed up for at least 5 years after operation. Data were collected preoperatively and at 3, 6, 12, 36, 60 months and final follow-up after operation. The variables collected in this study included patient related factors (age, gender, duration of symptoms, smoking, diabetes, severity of periodontitis, bone mineral density, oral hygiene) and implants related factors (position, implant diameter, implant length, additional operations, probing depth, gingival index, plaque index, load-bearing time).

1.4 Statistical analysis

SPSS 20.0 statistical software (SPSS Inc., Chicago, Illinois) was used for the statistical analysis. Mann-Whitney U test was performed for continuous variable as appropriate. Categorical variables were evaluated with Fisher's exact test or Chi-square test as appropriate. The difference was statistically significant if p<0.05. Multiple stepwise logistic regression analysis was used to choose the significant variables and model the effect of variables on the likelihood of getting the peri-implantitis at follow-up. 80% of patients in our study cohort were also randomly selected, so that their data could be used as the training set for the creation of a predictive regression model. Once the regression model was built, it was validated using the remaining 20% of enrolled patients. Hosmer-Lemeshow test was used to test the goodness of fit. Receiver-operator characteristic (ROC) curve analysis was used to quantify the predictive performance of the regression model.

Results

2.1 Patient demographic and clinical characteristics

According to the inclusion criteria, 430 patients with a total of 686 implants were included in the study. Among these patients were 201 males and 229 females, with a mean age of 44.0±5.3 years. Of these patients, 166 (38.6%) had BMI index under 26, 227 (52.8%) range 26-30 and 37 (8.6%) above 30. The mean duration of symptoms was 5.8 years (range, 3-12). 109 (25.3%) patients had history of smoking. 90 (20.9%) patients had diabetes. The location of implants, 170 (24.8%) were at after maxillary teeth, 181 (26.4%) were at anterior maxillary teeth, 283 (41.3%) were at after mandibular teeth and 52 (7.6%) were at anterior mandibular teeth. For the severity of periodontitis, 79 (18.4%) patients were for mild, 178 (41.4%) patients were for moderate and 173 (40.2%) patients were for severe, respectively. For the bone mineral density, 416 (60.6%) patients were type II, 245 (35.8%) patients were type III and 25 (3.6%) patients were type IV, respectively. The baseline scores at presentation were mean of 2.6±0.2mm for Probing Depth, mean of 1.2±0.1 points for Gingival Index and mean of 1.8±0.2 points for plaque index, respectively. The mean diameter of implants was a mean of 4.4±0.2mm. The mean length of implants was a mean of 11.5±0.5mm. The mean load-bearing time was 3.2±0.3 years. 218 (31.8%) patients received additional operations. 325 (47.4%) patients were with poor oral hygiene. Table 1 summarizes the demographic and clinical characteristics.

2.2 Multiple stepwise logistic regression model analysis
Peri-implantitis occurred in 95 of 686 implants (13.8%). We used univariate analysis to evaluate the all the independent factors, including patient related factors (age, gender, duration of symptoms, smoking, diabetes, severity of periodontitis, bone mineral density, oral hygiene) and implants related factors (position, implant diameter, implant length, additional operations, probing depth, gingival index, plaque index, load-bearing time). Among all the characteristics, implant diameter, severity of periodontitis, plaque index, oral hygiene, smoking and diabetes were associated with a high incidence of peri-implantitis. (p<0.05) Table 1 demonstrates the univariate analysis of the risk factors affecting the peri-implantitis.

These six risk factors enter the logistic regression. The result indicated that implant diameter, severity of periodontitis, oral hygiene, smoking and diabetes were associated with a high incidence of peri-implantitis were also significantly associated with the occurrence of peri-implantitis. (p<0.05) However, plaque index was not significantly associated with peri-implantitis in the multivariate model.

Smoking (p=0.011), diabetes (p<0.001), severe periodontitis (p=0.023), lager implant diameter (p<0.001) and poor oral hygiene (p<0.001) increased the odds of occurrence of peri-implantitis. For the Exp (B) of the five characteristics and constant, this was calculated to be 5.395, 4.807, 8.109, 5.569, 11.138 and 16.172, respectively. Table 2 demonstrates the coefficient and p-value of the predictive model regression analysis. The occurrence of peri-implantitis could be calculated based on the predictive model equation as follows: peri-implantitis = [1+e^{(16.172+5.395*smoking+4.807*diabetes +8.109*severe periodontitis+5.569*lager implant diameter+11.138*poor oral hygiene)}]-1

### 2.3 Accuracy of the model

The area under the receiver operating characteristic curve was used to estimate the accuracy of the model. AUC under ROC curve was 0.721, 0.620, 0.453, 0.651 and 0.826 for smoking, diabetes, severe periodontitis, lager implant diameter and poor oral hygiene, respectively, which demonstrated good discrimination. The diagnosis sensitivity of the three characteristics was 91.77%, 88.43%, 82.64%, 85.21% and 92.02%, respectively, which demonstrated high accuracy. The diagnosis specificity of the three characteristics was 45.65%, 49.17%, 66.23%, 42.39% and 65.41%, respectively, also demonstrating high accuracy. The predictive model had a good fitting, as assessed by a Hosmer–Lemeshow statistic with an overall accuracy of 87.2%. (Table 3) Table 4 shows the diagnosis capability in in occurrence of peri-implantitis.

### Discussion

As the most common complication of oral implants, peri-implantitis may affect the success rate of oral implants. So, correct and deep understanding of peri-implantitis is particularly important. In order to avoid the occurrence of peri-implantitis, it is very important to predict the probability of peri-implantitis preoperatively based on patient case data, so as to make personalized diagnosis and treatment plan for each patient, and ensure the long-term survival rate and success rate of implantation.
Smoking, diabetes, severe periodontitis, larger implant diameter and poor oral hygiene are important risk factors of peri-implantitis. We also established a novel and accurate predictive model for the occurrence of peri-implantitis in managing patients with chronic periodontitis. The use of these parameters, in the form of a predictive model, has the potential to improve decision-making in the application of the treatment plan.

Some research compared both showed there was no statistical difference about the soft tissue around implant and alveolar bone absorption between smokers and non-smokers, and the implant success and survival rate can amount to 100%. But the overwhelming consensus was that smokers have a higher rate of implant failure than nonsmokers. Vervaeke reported that implant bone loss in smokers was 1.18 mm higher than that in non-smokers. A meta-analysis including 13 studies (478 smokers vs 1207 non-smokers) showed that smoking increased implant bone loss by 0.164 mm per year. Smoking not only increases the risk of post-implant infection and marginal bone loss, but also changes in peri-implant tissue and flora, which in turn increases the risk of peri-implant inflammation and implant failure, resulting in reduced survival. Some authors suggest that the controversy between smoking and peri-implantitis may be related to differences in the definition of how much smokers smoke in the study. In this study, smokers were defined as having more than 10 cigarettes a day. The incidence of peri-implantitis was 42.1% (40/95) in smokers and 9.3% (55/591) in nonsmokers. Although smoking is not an absolute contraindication to dental implant treatment, some studies have shown that smoking can increase the activity of argininase in saliva, thereby reducing the production of nitric oxide and causing local blood circulation disturbance, thus increasing the susceptibility to bacterial infection. In addition, smoking can inhibit the gene expression of bone salivary protein and osteocalcin, reduce the number of osteoblasts on titanium implants, down-regulate osteoblasts, and affect the implant-bone interface binding, resulting in implant failure. So, we suggested that patients with chronic periodontitis should try to quit smoking or strictly control the amount of smoking.

Ting showed that diabetes patients with poor control were considered to be at high risk of peri-implantitis. Similarly, Monje found that the risk of peri-implantitis in diabetes patients was about 50% higher than that in non-diabetes patients. And, even among non-smokers, the risk of peri-implantitis was 3.39 times higher in those with high blood sugar than in those with normal blood sugar. Continuously unstable hyperglycemia delayed wound healing and increased peri-implant soft tissue inflammation by reducing the expression of growth factors in wound fluid and epithelial reformation. It has been widely recognized that diabetes is a relative contraindication to dental implant therapy. Therefore, strict control and maintenance of blood glucose level can maintain aesthetic and functional stability of implants.

Roccuzzo reported a study including 112 patients and divided them into periodontal health group, moderate and severe periodontitis group. After 10 years, they returned to the three groups and measured the implant marginal bone loss of, which were 0.75±0.88mm, 1.14±1.11mm and 0.98±1.2mm, respectively, and the difference was statistically significant. The results of this study showed that there were statistical differences in peri-implantitis among patients with different severity degrees of
periodontitis. Occurrence of peri-implantitis in the severe group and moderate group was significantly greater than that in the mild group, indicating that patients in the severe group and moderate group were more prone to get peri-implantitis than those in the mild group.

Currently, there is no standard definition for the classification of implant diameter size. Rodrigo should the incidence of peri-implantitis in narrow implants (>3.5mm) was as high as 95.1%, with a statistically significant difference. An animal study by Morelli confirmed that narrow implants (3.3 mm and 4.1 mm) showed a tendency to induce peri-implantitis more easily than standard implants (3.8 mm and 4.1mm). In addition, with regard to wide-diameter implants, Flanagan believed that the diameter of implants should be controlled within 4.7mm. Diameters larger than 5mm are more likely to increase the risk of peri-implantitis, because larger diameters may lead to poor blood supply around implants and further affect osseointegration. Moreover, the risk of peri-implantitis increased significantly with implant diameter increasing (RR=1.6/ mm, P<0.01). However, Shi evaluated 98 narrow implants (3.3mm), of which only 8 were diagnosed with peri-implantitis, showing no statistical difference, suggesting that narrow implants can be a predictable clinical treatment option. Hattingh reported a prospective study of 51 wider-diameter (>6mm) implants with a mean follow-up of 23 months, showing almost no marginal bone loss. We suggest that there is controversy regarding the relationship between implant diameter and peri-implantitis. The risk of peri-implantitis is increased by the relative thinness of labial-bucolic bone after wide-diameter implants and the resorption of alveolar bone during implant union healing. However, wide diameter implants have advantages in stress distribution, which can improve the stress distribution in the cortical bone region, while narrow implants tend to be more prone to stress concentration. In conclusion, bone stress should be kept within the physiological range in order to prevent pathological implant overload.

Patients do not pay attention to plaque control will lead to plaque accumulation around the implant, plaque, calculus and other long-term retention without timely cleaning, oral pathogenic bacteria will act on the gum around the implant, accelerate the secretion of inflammatory mediators. Make gum cannot t closely, the impact of biology closed, eventually lead to peri-implantitis. The results show that good oral hygiene is beneficial to the stability of the implant, may improve the success rate of implant prosthesis.

The oral health status of patients with periodontitis were generally poor. There were a large number of subgingival free plaque and attached plaque under the periodontal pocket, which was difficult to completely eradicate. Especially, the number of bacteria in the oral cavity of patients with poor oral health self-maintenance ability was several times higher than that of healthy individuals. Therefore, clinicians should strengthen oral hygiene education for patients, especially those with a history of periodontitis, guide patients to develop the habit of brushing and gargle.

We determined the factors that can predict the occurrence of peri-implantitis in managing patients with chronic periodontitis. This model can be useful to guide dentists to improve decision-making and anticipating the outcome based on patient characteristics. Smoking, diabetes, severe periodontitis, lager
implant diameter and poor oral hygiene are important risk factors increasing the odds. The predictive model was reasonable and accurate and need to be verified in a prospective study.

Our study should be considered in the context of several notable strengths. First, this study is the first, to our knowledge, that provides a predictive model analyzing the independent influencing factors of peri-implantitis by logistic regression, and also offers a framework to select patients suitable for implant prosthesis. Dentists can assess these factors to get a nice doctor-patient communication and a personalized treatment plan for each patient. Second, we conducted a rigorous and precise statistical analysis to guarantee the comprehensiveness. Our multiple stepwise logistic regression model analysis was reasonable, and the model was accurate (the overall accuracy was 87.2%) in predicting the likelihood of occurrence of peri-implantitis, according to the strict diagnostic criteria at 5 years follow-up, high AUC for ROC. Third, because of its intuitionism, visualization and simplicity, this model may become one of the important auxiliary tools for clinical decision-making in the future.

There were also shortcomings in this study. First, the sample size of this study is limited, which may affect the study results to some extent. Second, the selection of cases in this study was limited, whether to perform bone augmentation and maxillary sinus lift had not been collected, and further analysis is needed in the later studies. Thirdly, this was a retrospective study mainly based on clinical case data and oral imaging data. The prediction model obtained in this study has only been tested in only one center, and larger multi-center studies and prospective studies are needed to support and optimize our prediction model in the later stage.

Conclusions

Smoking, diabetes, severe periodontitis, larger implant diameter and poor oral hygiene are important risk factors for occurrence of peri-implantitis. The occurrence of peri-implantitis could be calculated based on the predictive model equation as follows: \[ \text{peri-implantitis} = \left[ 1 + e^{(16.172 + 5.395 \times \text{smoking} + 4.807 \times \text{diabetes} + 8.109 \times \text{severe periodontitis} + 5.569 \times \text{lager implant diameter} + 11.138 \times \text{poor oral hygiene})} \right]^{-1}. \] The predictive model was reliable and accurate in predicting the likelihood of occurrence of peri-implantitis. The use of these parameters, in the form of a predictive model, has the potential to improve decision-making about the treatment plan. Dentists can use the model to improve patient selection and the success rate of implant prosthesis in managing patients with chronic periodontitis.

Declarations

Ethics approval and consent to participate

The study was reviewed by the Department of Stomatology, Xuhui District Dental Center and ethical approval was waived as written consent was obtained from the patient.

Consent for publication
Written patient consent was obtained for publication of all aspects of the case including personal and clinical details and images, which may compromise anonymity.

**Availability of data and material**

All supporting data can be provided upon request to the authors.

**Competing interests**

All authors read and approved the final manuscript and declare that they have no competing interests.

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### Tables

#### Table 1. Demographic and clinical characteristics (430 patients with 686 implants)

| Characteristic                                      | Value                  |
|-----------------------------------------------------|------------------------|
| Age (mean ± SD), years                              | 44.0±5.3               |
| Gender: male (n, %)                                 | 201 (46.7%)            |
| BMI (n, %)                                          |                        |
| <26                                                 | 166 (38.6%)            |
| 26-30                                               | 227 (52.8%)            |
| ≥30                                                 | 37 (8.6%)              |
| Duration of symptoms (mean, range), years           | 5.8 (3,12)             |
| Smoking (n, %)                                      | 109 (25.3%)*           |
| Diabetes (n, %)                                     | 90 (20.9%)*            |
| Implant Dental Position (n, %)                      |                        |
| after maxillary teeth                               | 170 (24.8%)            |
| anterior maxillary teeth                            | 181 (26.4%)            |
| after mandibular teeth                              | 283 (41.3%)            |
| anterior mandibular teeth                           | 52 (7.6%)              |
| Severity of Periodontitis (n, %)                    |                        |
| mild                                                 | 79 (18.4%)*            |
| moderate                                             | 178 (41.4%)*           |
| severe                                               | 173 (40.2%)*           |
| Bone mineral density (n, %)                          |                        |
| type II                                              | 416 (60.6%)            |
| type III                                             | 245 (35.8%)            |
| type IV                                              | 25 (3.6%)              |
| Implant Diameter (mean ± SD), mm                    | 4.4±0.2*               |
| Implant Length (mean ± SD), mm                      | 11.5±0.5               |
| Additional Operations (n, %)                         | 218 (31.8%)            |
| Probing Depth (mean ± SD), mm                       | 2.6±0.2                |
| Gingival Index (mean ± SD)                           | 1.2±0.1                |
| Plaque Index (mean ± SD)                             | 1.8±0.2*               |
| The load-bearing time (mean ± SD), years             | 3.2±0.3                |
| Poor oral hygiene (n, %)                             | 325 (47.4%)*           |

Note: SD: standard deviation, *: variables compared with 2 groups, p-Value <0.05

#### Table 2. Univariate analysis of the factors affecting the success rate of ESWT

|          | B      | S.E.  | p-Value | Exp (B) |
|----------|--------|-------|---------|---------|
| Smoking  | 1.531  | 0.011 | <0.001* | 5.395   |
| Diabetes | 3.467  | <0.001| 4.807   |
| Severity of Periodontitis | 3.216  | 0.023 | 8.109   |
| Implant Diameter            | 4.436  | <0.001| 5.569   |
| Plaque Index                | 7.131  | 0.084 | 5.163   |
| Poor oral hygiene           | 4.206  | <0.001| 11.138  |
| Constant                     | 4      | .805  | <0.001  | 16.172  |

Note: *: variables compared with 2 groups, p-Value <0.05
Table 3. Predictive model established by logistic regression analysis

| Observed          | Peri-implantitis | No-Peri-implantitis | Percentage Correct (%) |
|-------------------|------------------|---------------------|------------------------|
| Peri-implantitis   | 76               | 19                  | 80                     |
| No Peri-implantitis| 33               | 558                 | 94.4                   |
| Overall Percentage | /                | /                   | 87.2                   |

Table 4. Diagnosis capability of risk factors in occurrence of peri-implantitis

| Characteristics       | Sensitivity (%) | Specificity (%) | Area under ROC curve (95%CI)       | Youden index |
|-----------------------|-----------------|-----------------|------------------------------------|--------------|
| Smoking               | 91.77           | 45.65           | 0.721 (0.696-0.800)                 | 0.4141       |
| Diabetes              | 88.43           | 49.17           | 0.620 (0.513-0.726)                 | 0.5631       |
| Severity of Periodontitis | 82.64         | 66.23           | 0.453 (0.611-0.746)                 | 0.6135       |
| Implant Diameter      | 85.21           | 42.39           | 0.651 (0.491-0.706)                 | 0.3823       |
| Poor oral hygiene     | 92.02           | 65.41           | 0.826 (0.711-0.838)                 | 0.6589       |