

## **Protocol**

**The prediction of failure rate of dental implants**

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During the past decades, dental implant therapy has developed into a successful treatment option for patients confronted with both partial and complete edentulism. Based on the literature, the survival rate of dental implants, which is defined that the dental implants are still in the mouth after insertion, is around 95% in the 5-year follow-up and around 90% in the 10-year follow-up [1-3]. The success rate of dental implants, which is defined as dental implants in function, with good hard and soft tissue physiology and user satisfaction ranges from 85.2% to 88.7% in the follow-up of up to 20 years [4-6]. This indicates that both the success rate and survival rate of dental implants is high. However, both survival rates and success rates vary across patients with different profiles. The expense of dental implant treatment is high and implant placement is a surgical procedure which is invasive and thus risky for the patients' health. Once the failure of dental implants occurs, it may cause some severe negative consequences for patients. For example, the failure will cause a financial loss for patients and a possible shock concerning both mental and physical aspects. To reduce these risks it is important and necessary for clinicians to be able to predict the risk of the failure of dental implants of individual patients before they undergo dental implant treatment.

### **Aim:**

The aim of the project is to identify important risk factors for failure of dental implants and to develop a prediction model for the failure rate of dental implants at follow-up as a tool for clinicians to establish patients individual risk profile.

### **Methods:**

#### *Study design*

The study is a retrospective design. The clinical data of all the adult patients who were referred to the Department of Oral Implantology and Prosthetic Dentistry, Academic Centre for Dentistry Amsterdam (ACTA) at their first intake for placement of dental implant(s) from September 2009 to September 2013 are collected retrospectively from the clinical data management system of ACTA in the study.

#### *Predictors*

The initial list of potential predictors for the failure of implants is first determined based on previous literature and the Dutch Clinical Practice Guideline (KPR). Then, the list of the predictors is sent to the international experts from the International Team for Implantology (ITI) for further screening. Finally, the short list of the potential predictors is determined based on the experts' opinions and the availability of the predictors in the clinical data management system of ACTA. The potential predictors include five domains: patients' demographic characteristics, lifestyle habits, general health, dental health, and implant characteristics.

#### *Outcomes*

The outcomes include the follow-up time of implants and whether the failure of the implants is observed at the follow-up. The follow-up time is defined as a period in days starting from the date at the placement of suprastructure (baseline) to the date at the last follow up time or the

date when the failure is observed. The failure of implants is defined as the presence of peri-implantitis, presence of mobility of implants, or removal of the implants for any reasons, for instance, unacceptable performance in aspects of function, tissue physiology, esthetics, and patients' satisfaction after placement of suprastructure.

### *Statistical analysis*

The univariate and multivariate Cox regression analysis is used to identify important risk factors for the failure of dental implants and to develop the model. Then, the performance of the models, in aspects of calibration and discrimination, is assessed. Calibration is defined as the agreement between predicted outcomes and observed outcomes. For assessment of calibration, the included implants are separately grouped into deciles based on their predicted risk of failure. The calibration of the model is assessed by plotting the predicted risk of failure against 1 minus the individual Kaplan-Meier estimate for each decile in the follow-up. Discrimination is defined as the ability of the model to differentiate between those with and without outcome events. The discrimination of the model in the follow-up is assessed with the concordance index (C-index). Then, the model is converted to a score chart and line chart in order to facilitate the calculation of the failure rate of implants. The score of each included predictor is produced by the regression coefficients being divided by the smallest regression coefficient among the predictors and subsequently rounded. Finally, the clinical values of the model are assessed, using prevalence, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the model at the optimal cutoff score.

All the statistical procedures are performed with SPSS software 25.0 (IBM, New York, the USA) and R software 3.2.3 (R Development Core Team, Vienna, Austria).

### **What is already known:**

Recently, there are many studies focusing on the evaluation of survival rate of implants based on longitudinal cohorts. However, they mainly reported the values of the failure rate of implants in the follow-up (like 5-year survival rate) or compared the failure rate of different types of implants. These types of studies are beneficial for the groups of patients but not for the individual patients. Also, there are several studies focusing on the prognostic factors that may be associated with the survival rate of dental implants. But these studies belonged to prediction factor studies instead of prediction modeling studies. The findings in these studies are difficult to directly apply to clinical practice.

However, there is a very limited number of studies focusing on the prediction of survival rate (or failure rate) of implants in the follow-ups. For example, Chuang et al. (1) used a clustered marginal approach to predict the survival rate in 2002 and found that among those who had a delayed procedure, did not smoke, and underwent a two-stage implant procedure, the predicted 1- and 5-year survival rates were 97.2% and 93.4%, respectively. For those who had an immediate implant placed, smoked, and underwent a one-stage procedure, the predicted survival rates were 58.5% and 27.6%, respectively. In 2006, Chuang and Cai (2) used Cox proportional hazards frailty model to predict the future implant survival based on some predictors including smoking status, the timing of placement of the implant and implant staging.

In this study, they predicted that for a non-smoking individual with 2 implants placed, an immediate implant and in one stage, the probability that 1 implant would survive 12 months was 85.8% and the joint probability of surviving for 12 months was 75.1%. If 1 implant was placed earlier and had survived for 12 months, then the second implant had an 87.5% chance of surviving 12 months. However, in these two studies, the authors only included a small number of predictors and did not develop a score chart for the individual patients. Also, the performance of the models was not assessed.

### **What is the project will add:**

The project can provide clinicians with the predicted probability of the failure rate of dental implants of each individual patient preoperatively. The model may be helpful for clinicians to make decisions about the postoperative care for the patients. Also, the model can help shape the patients' expectations about the survival of dental implants.

### **What is new:**

In the project, we will use some more predictors to predict the survival rate of dental implants to make the prediction model more accurate. Also, we will develop a score chart for clinicians. In this score chart, clinicians can easily calculate the sum score of each patient and find out the corresponding predicted probability of the failure rate of dental implants of each individual patient. The score chart is very easy-to-use in the clinical practice. Besides, in this project, the methodology (the prediction model developed with Cox regression analysis) is novel in dentistry.

### **References:**

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6. Ostman PO, Hellman M, Sennerby L. Ten years later. Results from a prospective single-centre clinical study on 121 oxidized (TiUnite™) Branemark implants in 46 patients. Clin Implant Dent Relat Res 2012;14:852-860.

## **Informed consent**

In this project, we retrospectively collect the existing clinical data of patients (notably baseline, treatment, and outcome data) from a digital patient care registration system (Axiom) . These data will be de-identified, coded and handled confidentially to preclude the possibility of re-identification before being analyzed. The researchers involved will handle the data in a secure, coded, and privacy-protected manner and guarantee that no traceable personal data will be published. Each patient in the Department of Implantology, ACTA has been informed about the use of their data for scientific research in the future at patients' first intake. Patients that refused to consent as such will of course not be included in this project. We only include the patients who provided their consent to the use of the data. **So, in this case, a new informed consent is not applicable in the project.**