Survival Analysis of Dental Implants

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Abstracts

The purpose of this paper is to evaluate the clinical outcome of dental implants through a survival analysis of placed implants. A retrospective cohort study comprises 213 patients who received a total of 785 implants from May 2006 to April 2012 by a single surgeon. We adopt Kaplan-Meier method to analyze the survival pattern of the placed implants during this 6-year period. The method calculates the probability of an implant survival or failure after a given period of time. The estimated survival probability is called the product-limit estimate or sometimes the Kaplan-Meier estimate of the survival probability. The analyses include the influences of demographics and health status of patient, tooth position, implant brand, implant dimension, type of implant tooth, type of implant site, and pre-loading status. In this cohort, the first 24-month cumulative survival rate of all dental implants was 96.1% and the 60-month rate reduced to 94.4%. Therefore, the dental implant cumulative failure within 2 years after placement was only 3.9% that further implant failure probability for the next 3 years was trivial at 1.8%. Hence, this could institute a practical surveillance protocol for such a long-term dental rehabilitation.

Keywords: implant failure, censored time, cumulative survival rate, Kaplan-Meier method, hazard function, Cox proportional hazards regression model

1. Introduction

The purpose of this paper is to evaluate the clinical outcome of dental implants through a survival study of placed implants. We employed Kaplan-Meier (KM) method to estimate the survival function of implant data and conducted statistical tests to evaluate whether the survival functions of different groups are statistical equivalent. We also examined several covariates which may be associated with survival time. Finally, we built statistical models of survival time (or more accurately, the hazard function) by means of Cox (1972)'s methodology.

2. Methods

2.1 Study design and sample

The present study was designed as a retrospective cohort study. The cohort comprises 213 patients who received implant treatment by a single oral and maxillofacial surgical specialist during the 6-year period from May 2006 to April 2012. All patients who received implant placement by this specialist during the said period were included in the sample.

2.2 Survival duration of a dental implant

The long term success of dental implant treatment had already been well established. In this study, we wish to evaluate a single surgeon's treatment outcome by reviewing the 5-year survival rate to benchmark with the international standard. Additionally, we would like to establish a practical surveillance protocol as at the first 2-year period to see whether there is any significant difference in treatment outcome.

In this study, the survival duration (in month) of a dental implant starts at implant surgery date and ends when it fails before the cut-off of the observation period (i.e. in April 2013), or when the observation period ends. We compiled two sets of survival durations, one was capped with a maximum period of 24 months and the other was capped with a maximum period of 60 months, for all dental implants.

2.3 Kaplan-Meier method

The KM estimator was adopted in our study in estimating cumulative survival rate of dental implants. It is the most widely used method for estimating survivor functions from lifetime data in biostatistics research. The KM estimator, also known as the product-limit estimator, was well-recognized for many years since Kaplan and Meier (1958) showed that it was in fact a nonparametric maximum likelihood estimator for estimating survival function. Suppose there are k distinct event times, $t_1 < t_2 < \ldots < t_k$. At each event time t_i, there are n_i individuals who are said to be at risk of an event. At risk means they have not experienced an event nor have been censored[1] prior to time t_i. If any cases are censored at exactly t_i, they are considered to be at risk at t_i. Let d_i be the number of individuals who die (in our case implant fail) at t_i. The KM estimator of the survivor function $S(t)$ is defined as:

$$\hat{S}(t) = \prod_{i:t_i \le t} \left(1 - \frac{d_i}{n_i}\right) \quad \text{for} \quad t_1 \le t \le t_k \tag{1}$$

Equation (1) says that for a given time t, take all the event times that are less than or equal to t. For each of those event times, compute the quantity in brackets, which can be interpreted as an estimate of the conditional probability of surviving to time t_{i+1}, given that one has survived to time t_i. Then multiply all of these conditional probabilities together.

2.4 Testing for differences in survival functions

After estimating the survival function of all dental implants, we next evaluate whether the survival functions are statistically equivalent (i.e. identical survival experience) among different groups. The log-rank test and Wilcoxon test will be used for testing the differences in survival functions among different groups, with the null hypothesis that all groups have the same survivor function.

2.5 Testing for effects of covariates

We also examine whether there are any quantitative covariates which are associated with the survival time of dental implants. The log-rank test and Wilcoxon test will be used for testing significance of the association of each covariate with the survival time, with the null hypothesis that all these covariates are jointly unrelated to survival time.

2.6 Cox proportional hazards regression model

The Cox proportional hazards regression model (named Cox's model) is a well-recognized statistical technique for analyzing survival data. The regression method introduced by Cox (1972) is used to simultaneously investigate the effects of several explanatory variables on survival time. Cox proposed a new estimation method in his 1972 paper that later named partial likelihood. Cox's model is considered a semi-parametric procedure because the baseline hazard function and the probability distribution of the survival times do not have to be specified. Briefly, the Cox's model regresses survival time (or more accurately, the hazard function, $\lambda_i(t)$) on several explanatory variables (so-called covariates), x_{ij}. The basic model is usually written as

[1] If the dental implant has not failed by the end of the observation period or if the patient has withdrawn from follow-up, this implant is considered a censored case.

$$\lambda_i(t) = \lambda_0(t)\exp\left(\sum_{j=1}^{k}\beta_j x_{ij}\right) \tag{2}$$

Equation (2) says that the hazard for individual implant *i* at time *t* is the product of two factors: a function $\lambda_0(t)$ and an exponential function of a linear combination of a set of *k* fixed covariates. The function $\lambda_0(t)$ can be regarded as the hazard function for an individual whose covariates all have values of 0. It is often called the baseline hazard function. Equation (2) is called the proportional hazards model because the hazard for any individual is a fixed proportion of the hazard for any other individual.

3. The Data

A retrieval of records from a computerized medical record system (namely, Clinic Solution™) for all patients who received dental implants by the same specialist from May 2006 to April 2012 was undertaken to identify 785 placed implants. The study variables are described in Table 1. All patients were recalled to follow-up at 1 month, 6 months, 12 months and 24 months after implant placement. Clinical and radiographic assessments were performed at the follow-up visits. Per-implant gingival stability and crestal bone level maintenance are the key monitoring parameters.

Table 1. Description of Study Variables

Variable	**Descriptions**
Demographics	The patient's gender and age at implant placement and smoking history (whether a smoker or non-smoker).
Health status	General health status of patient was classified according to the American Society of Anesthesiology (ASA) physical status classification system. Patients were categorized as normal healthy patient (ASA I), as having mild systemic disease (ASA II) or as having serve systemic disease (ASA III).
Tooth position	The tooth position is classified according to the FDI World Dental Federation notation. Based on this notation, the category included implant position (maxilla, mandible, anterior, posterior) and tooth type (incisor, canine, premolar, molar).
Details of implant placed	First implant surgery date, implant crown cementation date, last recall date.
Reason of tooth loss	Crown and bridge failures, crown fracture, advanced periodontal disease, cross caries tooth, non-salvable root canal treatment tooth, non-salvable crack tooth, and ankylosed tooth.
Implant brand	Bicon and Nobel.
Dimension of implant placed	Diameter (in mm) × length (in mm)
Type of implant tooth	Single, splinted and bridge.
Type of implant site	Normal edentulous, immediate extract, immediate extract + graft, graft regenerated, immediate extract + sinus lift, normal edentulous + sinus lift, and edentulous + bone graft.
Pre-loading status	Two-stage technique, one-stage technique, immediate single and immediate multiple.
Insertion torque of implant placed	35, 40, 45, 50, 55, 60, 65 and 70 (in Ncm).
Bone quality	Soft, medium and hard.

4. Results

4.1 Descriptive statistics

The descriptive statistics for the study variables are presented in Table 2.

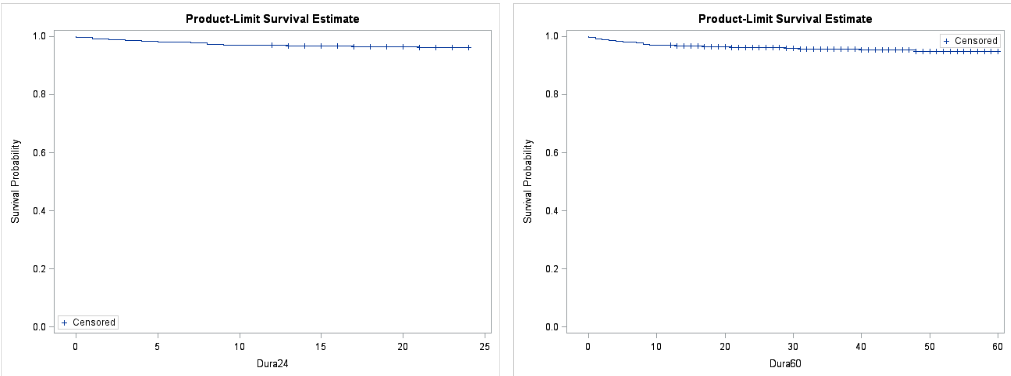
4.2 Survival curves

As shown in Figure 1, the 24-month cumulative survival rate of all implants, determined by a Kaplan-Meier curve, was 96.1% (corresponding to 30 failures) and the 60-month rate reduced to 94.9% (corresponding to 35 failures).

Table 2. Univariate Statistical Analysis of Study Variables

Variable	n	%
Demographic variables		
Gender		
Women	119	55.9%
Men	94	44.1%
Mean age at implant placement	53.0 y (sd = 12.5 y)	
Health status variables		
ASA status		
ASA I	140	65.7%
ASA II	57	26.8%
ASA III	16	7.5%
Smoker		
Yes	14	6.6%
No	199	93.4%
Anatomic variables		
Jaw		
Maxilla	440	56.1%
Mandible	345	43.9%
Anterior/ Posterior		
Anterior	203	25.9%
Posterior	582	74.1%
Tooth type		
Incisor	137	17.5%
Canine	66	8.4%
Premolar	208	26.5%
Molar	374	47.6%

Variable	n	%
Implant brand		
Bicon	646	82.3%
Nobel	139	17.7%
Type of implant tooth		
Single	268	34.1%
Splinted	209	26.6%
Bridge	308	39.2%
Type of implant site		
Normal edentulous	457	58.2%
Immediate extract	94	12.0%
Immediate extract + Graft	90	11.5%
Graft regenerated	34	4.3%
Immediate extract + Sinus lift	0	0.0%
Normal edentulous + Sinus lift	50	6.4%
Edentulous + Bone graft	60	7.6%
Pre-loading status		
Two-stage technique	679	86.5%
One-stage technique	50	6.4%
Immediate single	28	3.6%
Immediate multiple	28	3.6%



(a) 24 months' obervation period (b) 60 months' observation period

Figure 1. KM Estimate of Survival Curves

4.3 Testing for differences in survival functions

Table 3 shows that 'pre-loading status' has significant impact on equality of survival functions for the dataset with an observation period of 24 months, while 'type of implant site' and 'pre-loading status' have significant impacts on equality of survival functions for the dataset with an observation period of 60 months. In addition, 'length of implant placed' has significant impact on equality of survival functions for the Bicon data with an observation period of 60 months.

4.4 Testing for effects of covariates

Table 4 shows that 'pre-loading status' has highly significant association with survival time for the dataset with an observation period of 24 months, while 'type of implant site', 'pre-loading status' and 'diameter of implant placed' have highly significant associations with survival time for the dataset with an observation period of 60 months.

Table 3. Homogeneity Tests of Equality over Strata

Variable	24 months Log-rank (*p*)	24 months Wilcoxon (*p*)	60 months Log-rank (*p*)	60 months Wilcoxon (*p*)
Demographic variables				
Gender	0.210	0.232	0.304	0.321
Age group at implant placement	0.624	0.588	0.397	0.424
Health status variables				
ASA status	0.816	0.854	0.966	0.946
Smoker	0.658	0.694	0.780	0.771
Anatomic variables				
Jaw	0.932	0.921	0.595	0.784
Tooth type	0.776	0.805	0.473	0.651
Anterior/posterior	0.753	0.808	0.691	0.805
Implant brand	0.700	0.677	0.964	0.862
(for immediate-single only)	0.527	0.527	0.527	0.527
(for immediate-multiple only)	0.072	0.072	0.072	0.072
(for immediate-single + immediate-multiple)	0.141	0.148	0.141	0.148
Type of implant tooth	0.058	0.066	0.105	0.095
Type of implant site	0.089	0.092	*0.006*	*0.028*
Pre-loading status	*0.014*	*0.013*	*0.045*	*0.023*
(for Bicon only)	*0.003*	*0.003*	*0.026*	*0.006*
(for Nobel only)	*0.039*	*0.042*	*0.039*	*0.042*
Diameter of implant placed	0.426	0.453	0.176	0.349
(for Bicon only)	0.569	0.620	0.153	0.374
(for Nobel only)	0.685	0.692	0.685	0.692
Length of implant placed	0.803	0.809	0.931	0.895
(for Bicon only)	0.100	0.103	*0.014*	*0.038*
(for Nobel only)	0.895	0.902	0.895	0.902

Note: Significant differences (with *p*-value at 0.05 or less) in survival functions over strata are set in italics.

Table 4. Covariate Tests for the Implant Data

Variable	24 months Log-rank (*p*)	24 months Wilcoxon (*p*)	60 months Log-rank (*p*)	60 months Wilcoxon (*p*)
Demographic variables				
Gender	0.210	0.217	0.304	0.310
Age group at implant placement	0.237	0.232	0.254	0.248
Health status variables				
ASA status	0.583	0.580	0.922	0.909
Smoker	0.658	0.650	0.780	0.768
Anatomic variables				
Jaw	0.932	0.921	0.595	0.614
Tooth type	0.550	0.562	0.331	0.343
Anterior/posterior	0.753	0.762	0.691	0.700
Implant brand	0.700	0.684	0.964	0.988
Type of implant tooth	0.100	0.102	0.241	0.240
Type of implant site	0.328	0.334	*0.037*	*0.042*
Pre-loading status	*0.015*	*0.015*	*0.046*	*0.044*
Diameter of implant placed	0.092	0.098	*0.011*	*0.013*
Length of implant placed	0.353	0.359	0.145	0.151

Note: Those variables which have significant association (with *p*-value at 0.05 or less) with survival time are set in italics.

4.5 Cox proportional hazards regression model

Table 4 gives us some hints on the choice of variables to be included in the Cox's model. By fitting different combinations of variables to the Cox's model, the variable 'pre-loading status 1' was selected in the final Cox's model for the dataset with an observation period of 24 months, while 'diameter of implant placed', 'pre-loading status 1', 'implant site 3' and 'implant site 7' were selected in the final Cox's model for the dataset with an observation period of 60 months according to the Akaike's information criterion (AIC)[2] and Schwarz's Bayesian criterion (SBC)[3]. Table 5 shows the results of the final Cox's models.

[2] Given a set of candidate models for the data, the preferred model is the one with the minimum AIC value.

[3] Given a set of candidate models for the data, the preferred model is the one with the minimum SBC value.

Table 5. Final Cox's Models

Variable[4] included in Cox's model	Parameter (β)	*p*	Hazard ratio[5]	AIC	SBC
24 Months					
Pre-loading status 1 only				**393.541**	**394.942**
Pre-loading status 1 (namely, two-stage technique)	-1.06834	*0.0074*	0.344		
60 Months					
Diameter of implant placed + Pre-loading status 1 + Implant site 3,7				**443.322**	**449.544**
Diameter of implant placed	0.78829	*0.0087*	2.200		
Pre-loading status 1 (namely, two-stage technique)	-1.18295	*0.0089*	0.306		
Implant site 3 (namely, immediate extract + graft)	0.92536	*0.0288*	2.523		
Implant site 7 (namely, edentulous + bone graft)	1.17986	*0.0136*	3.254		

5. Discussion

In this paper, we assume all covariates are time-invariant. Further study can be carried out by modifying Cox's model to allow for time-dependent covariates[6], the computation of the resulting partial likelihood is more time-consuming, and the practical issues surrounding the implementation can be quite complex.

6. Conclusion

In this cohort, the first 24-month cumulative survival rate of all dental implants was 96.1% and the 60-month rate reduced to 94.4%. Therefore, the dental implant cumulative failure within 2 years after placement was only 3.9% that further implant failure probability for the next 3 years was trivial at 1.8%. Hence, this could institute a practical surveillance protocol for such a long-term dental rehabilitation.

'Pre-loading status' has significant impact on equality of survival functions and has highly significant association with survival time.

By building the Cox's models, we found that the significant implant failure predictor for 24 months was 'pre-loading status 1 (two-stage technique)' (HR=0.344), while the significant implant failure predictors for 60 months were 'diameter of implant placed' (HR=2.200), 'pre-loading status 1 (two-stage technique)' (HR=0.306), 'implant site 3 (immediate extract + graft)' (HR=2.523) and 'implant site 7 (edentulous + bone graft)' (HR=3.254). All other covariates were insignificant.

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[4] In building Cox's model, we create *K* dummy binary variables for each categorical variable with *K* possible values.

[5] The 'hazard ratio (HR)' is just exp(β).

[6] Time-dependent covariates are those that may change in value over the course of observation.