CLINICAL ORAL IMPLANTS RESEARCH

David French Hannu Lariava Ronen Ofec

Retrospective cohort study of 4591 Straumann implants in private practice setting, with up to 10-year follow-up. Part 1: multivariate survival analysis

Authors' affiliations:

David French, Hannu Larjava, Faculty of Dentistry, Division of Periodontics, University of British Columbia, Vancouver, BC, Canada David French, Private Practice, Calgary, AB,

Ronen Ofec, Department of Statistics and Operations Research, Tel-Aviv University & Private Dental Practice, Tel-Aviv, Israel

Corresponding author:

David French

Faculty of Dentistry, Division of Periodontics, University of British Columbia, Room: JBM 366, 2199 Wesbrook Mall, Vancouver, British Columbia, Canada V6T 173

Tel.: 1 403 247 8656 Fax: 1 403 247 8657 e-mail: Drfrench@shaw.ca Key words: bone implant interactions, bone regeneration, clinical research, cohort study, Intraclass correlation, patient centered outcomes, sinus floor elevation, smoking, survival analysis, time to implant failure

Objective: The purpose of this retrospective, noninterventional, open cohort study is to report on the long-term survival of dental implants, in private practice representing the daily realities of implant treatment. The data are analyzed to discern statistical relationships between explanatory variables and implant failure.

Materials and methods: A total of 4591 Straumann implants were placed in 2060 patients between 1999 and 2012. Patients were evaluated after 2-3 months, 1, 3, 5, and 7 years and, in some cases, up to 10 years. The cumulative survival rate (CSR) was calculated according to the life table method and illustrated with Kaplan-Meier survival curves. Univariate analysis was performed to investigate the association between study variables and time to implant-failure. Variables with P -value < 0.15 were further selected for a multivariate analysis. Statistical methods which take into account the fact that some patients have more than one implant (therefore, dependency between implants within mouth) had been applied.

Results: At the implant level, the cumulative survival rates at 3, 5, and 7 years were 99.3%, 99.0%, and 98.4%, respectively, and at the patient level, they were 98.6%, 97.7%, and 95.9%, respectively. After adjustment to possible confounders, the multivariate analysis identified a relationship between the following risk indicators for implant failure: implant location, length and design, timing of implantation, bone grafting procedures and gender. Tissue-Level implants (n = 3863) had a very high survival rate of 99% at 3 years, which was maintained over the entire study period. Bone-Level implants (n = 600) were as predictable with a survival rate of 99% up to 3 years, while Tapered Effect implants (n = 128) demonstrated a lower survival rate of 95% at 5 years. Short 6mm implants in the mandibular posterior sites had a high survival rate of 100%, while in maxillary posterior positions a survival rate of only 87% was achieved. Patient factors such as smoking, autoimmune disease, and penicillin allergy were tending to associate with higher failure rates. Conclusion: High long-term survival rates were observed for a large cohort of Straumann implants. Tissue- and Bone-Level implants had higher survival rates than Tapered Effect implants, and although short implants faired well in the mandibular posterior sites, they faired less well in the maxillary posterior sites. The study represents private practice insight into large-scale, long-term implant results.

The use of dental implants is now a widely accepted treatment modality for fully and partially endentulous patients. The success of this approach is rooted in the inherent ability of some dental materials, titanium in particular, to osseointegrate, thereby creating direct bone-to-implant contact (Branemark 1983). Further improvements toward the successful osseointegration of dental implants have involved modifications to both surface

topography and surface chemistry (Buser 2001; Buser et al. 2004). Implant design (i.e., type and dimensions), surgical procedure, timing of implant placement, and time prior to loading have also been shown to influence implant survival rates (Renouard & Nisand 2006; Ganeles et al. 2008; Penarrocha-Diago et al. 2012; Jung et al. 2013). In spite of these many variables, the survival rate of dental implants has been reported to be quite high,

Accepted 4 July 2014

To cite this article:

French D, Larjava H, Ofec R. Retrospective cohort study of 4591 Straumann implants in private practice setting, with up to 10-year follow-up. Part 1: multivariate survival analysis. Clin. Oral Impl. Res. 00, 2014, 000-000 doi: 10.1111/clr.12463

often >90%, particularly up to the 5-year mark

Long-term survival data, however, is required to better assess the safe and predictable use of dental implants. A few studies have reported long-term results (Buser et al. 1997; Karoussis et al. 2003; Simonis et al. 2010), showing more favorable survival statistics for solid screw over hollow cylinder implants, for mandibular sites over maxillary, and lower survival statistics for patients presenting with a history of periodontitis (Levin et al. 2011). Long-term results of implants placed with guided bone regeneration (GBR) (Jung et al. 2013), and outcomes for the treatment of atrophic posterior maxilla (Corbella et al. 2013) have also been reported. Thus, it is apparent that the more data available, regarding the various implants frequently used in private clinical practice, the better we are able to assess implant reliability and predictability.

The purpose of this retrospective, noninterventional, open cohort study is to report on cumulative survival data for 4591 Straumann® dental implants, with a mean of 2.23 implants per patient, placed between 1999 and 2012 in a private practice, with a longterm follow-up of up to 10 years. Furthermore, the study aims to assess any statistical relationships between explanatory variables and implant failure. Numerous variables were evaluated for impact on survival, including implant location, implant type and dimension, insertion torque, timing of implant, and the use of bone grafting. Patient factors were evaluated for the risk of failure, including smoking, periodontal disease, and bisphosphonate use. Further analysis of this same cohort is planned with attention to soft tissue inflammation and bone loss over time as well as risk factors for biologic and technical complications.

Material and methods

Study design

This retrospective observational study consisted of 2060 patients with a total of 4591 implants. The study cohort includes 922 (44.8%) men and 1138 (55.2%) women with a mean age at surgery of 50.58 ± 12.96 years and a range of [15, 85]. All implants were placed between 1999 and 2012, in Calgary, Alberta, Canada, with all surgeries being performed by one Periodontist (DF). Restorations were performed by a variety of General Dentists and Specialists in the Calgary region. All measurements were taken by the same examiner who placed the implants (DF).

The inclusion criterion was the presentation of edentulous or partially edentulous sites, and the only exclusion criterion was the use of ASA class 3 or higher (Owens et al. 1978). Implants were placed according to manufacturer guidelines and used for approved indications. All potential implant locations were used, and the location of implants was determined based on individual patient's requirements; no set location or group of locations were planned or declined. Patient education and consent to implant surgery was obtained, and the study is part of an ongoing long-term evaluation of dental implants associated with a University of British Columbia retrospective clinical study on dental implants. The study was approved by the Clinical Research Ethics Board at the University of British Columbia (Vancouver, Canada). Data analysis was designed to preserve the anonymity of the patients.

Surgical protocols included placement in mature ridge with and without bone grafting and immediate placement in extraction sockets. Implants were placed using open flap surgery except for immediate placement in extraction sockets, which were carried out flapless. In sites of an atrophic mature ridge that required bone graft, particulate graft with membrane was performed at the time of implant placement using autogenous bone, bovine xenograft or combinations with an ePTFE or collagen membrane. Sinus procedures were divided into two groups. In one group, a lateral window sinus lift was performed prior to implant placement using a mixture of about 20% autogenous and 80% bovine xenograft in combination with a slowly degrading collagen membrane. In the other group, an osteotome indirect sinus lift was performed using straight wall osteotomes with no added bone graft.

Loading protocols varied according to individual case requirements but were separated into three categories; immediate loading (within 48 h of placement), conventional loading (2–3 months after placement) and delayed loading (6 months after placement if very low-density bone and low insertion stability). When adjacent implants were placed, they were typically splinted together, and when 6-mm implants were used, they were always splinted to adjacent implants.

The patients were evaluated at 2–3 months postimplant insertion for implant stability, via a 35 Ncm torque test and radiographic bone measurements, which provided a baseline for future evaluation. Follow-up was then scheduled on 1-, 3-, and 5-year intervals. Subsequent to 5 years, the follow-up was less

defined with patients either returning because additional implant surgery was needed or patients with a potential concern noted by the referring dentist. In this study, follow-up was up to 10 years.

Study variables

Dates of the following clinical events were recorded: implant placement, implant loading, and last follow-up visit, as well as implant removal where applicable. The major outcome variable of this study was implant failure. Failure was defined as the removal of an implant for any reason. Early failures were defined as failures occurring before implant loading, while late failures occurred after loading. Survival time was defined as the time from implant insertion to implant removal or to last follow-up for surviving implants. Additional implant outcome variables, like bleeding on probing and marginal bone loss, were also recorded during follow-up and will be described in future publications.

The study was comprehensive in terms of the investigated explanatory variables. These variables were grouped into the following categories: implant related, surgery related, prosthesis related, and patient related. A description of investigated variables can be seen in Table 1, while a description of the health status variables is see in Table 2.

Four main types of Straumann implants (Institut Straumann AG, Basel, Switzerland) were used as described in Table 1. The majority of implants used had an SLA surface, while a limited number of implants had a hydrophilic SLActive surface (0.6% or 30/4591). Implant diameters and lengths were used as described in Table 1 and Fig. 1.

Data management and Statistical analysis

In dental implants studies, it is reasonable to assume that patients are independent from each other, but implants within patient mouth are correlated for some extent, a phenomenon that can be measured by the Intraclass Correlation Coefficient (ICC). Ignoring this correlation during the statistical analysis might lead to biased statistical estimates. To overcome the issue of ICC, we distinguished between two levels of analysis. The primary units were 2060 patients, while the elementary units were 4591 implants. Failures as the main outcome variable were analyzed at both levels. At patient level, failure was defined as a patient with at least one implant that was removed. To describe our survival data-set, we calculated the cumulative survival rate [CSR] according to the life table

Table 1. Investigated variables at implant level (n = 4591)

Variables		Frequency	Percent	Remark
Anatomic				
Location	Ant. Maxilla	625	13.6	Anterior maxilla as FDI
Location	Post. Maxilla	1717	37.4	tooth 13–23, the
	Ant. Mandible	291	6.3	anterior mandible as
	Post. Mandible	1958	42.7	tooth 34–44 (Buser
	r ost. Mariansie	1330	12.7	et al. 1997)
mplant-characteristics				
Diameter [mm]	3.3	341	7.4	
	4.1	2282	49.7	
	4.8	1968	42.9	
Length [mm]	6	308	6.7	
	8	1211	26.4	
	10	1727	37.6	
	12	1256	27.4	
	14	89	1.9	
Design	Standard	3795	82.7	
	Standard plus	68	1.5	
	Tapered effect	128	2.8	
	Bone level	600	13.1	
Neck	Narrow neck	26	0.6	
	Regular neck	2362	51.4	
	Wide neck	1603	34.9	
	Bone level	600	13.1	
Surgery related and augme	ntation procedures			
Insertion torque*[Ncm]		$33.3.8 \pm 12.77$,		n = 3459
		[5–70]		
Immediate implantation		521	11.3	
Immediate loading		226	4.9	6 1 11 1 1 1 1 1
Bone defect		338	7.4	Subdivided into horizontal, vertical and fenestration
Sinus elevation	Osteotomy	942	54.8	n = 1717 implants in
Sirius cievation	Lateral window	126	7.3	the posterior maxilla
GBR	Editor di Timido II	1459	31.8	Include sinus elevation
Fissue graft		27	0.6	ciaac siiras cicration
Prosthesis related				
Abutment type	Customized titanium	634	13.8	91 implants not restore
	Customized zirconia	81	1.8	
	Stock abutment	3552	77.4	
	Nonintermediate	161	3.5	
	Bar	44	1.0	
	Locator	28	0.6	
Prosthesis type	Single crown	1651	36	91 implants not restore
	Multiple unit bridge	2777	60.5	
	Removable on bar	44	1.0	
	Removable on ball	28	0.6	
Occlusion*	Hyperocclusion	56	1.95	n = 2869
	0 shim	1397	48.7	
	1–9 shim	1311	25.7	
	10–20 shim	105	3.65	

Table 2. Prevalence of patient related and health status variables (n = 2060)

Variables	Frequency	Percent	Definition
Bruxism	39	1.9	Only significant cases of severe wear
Autoimmune disease	14	0.7	Steroid medication and/or autoimmune disease
Bisphosphonate therapy	34	1.7	Any Bisphosphonate current or historic use
Diabetic	27	1.3	Type 1 and 2 Controlled and uncontrolled
Advanced periodontal disease	65	3.2	(4 quadrants and ≥6 mm)
Heavy smoker	29	1.4	>15 cigarettes per day, patient reported
Penicillin allergy	162	7.9	Reported allergy, clindamycin used

method and illustrated the results with Kaplan-Meier survival curves. Estimates for the Hazard Ratios [HR] were calculated to

estimate the association between explanatory variables and failure time. The hazard ratio for categorical variables was defined as, the

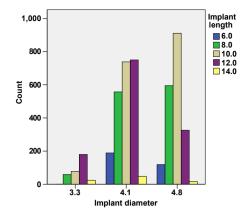


Fig. 1. Joint distribution of implant length and diameter (n = 4591).

ratio between hazards for implant failure among one group compared with another group. A ratio equal to 1 would indicate that hazards are equal across groups, while HR <1 and HR >1 would indicate protective versus risk effect, respectively. Hazard ratios were obtained by constructing the proportional hazard Cox regression model. In our model, we accounted for possible ICC (as a result of multiple implants within certain patients) by calculating sandwich-type robust standard errors. The method is described in the context of dental research by Chuang et al. (2002). Selection of variables into the final model was carried out in steps. First, we performed a univariate analysis (one by one explanatory variable), and then, all variables with a P-value < 0.15 entered to a multivariate analysis. The multivariate model enabled an estimate of the HR with adjustment to possible confounders. For example, if a multivariate model include implant type as explanatory variable and implant location as a confounder, the model actually estimate the net effect of implant type on implant failure, no matter what is the value of implant location.

Lastly, to use the Cox model, it was essential to check the underlying proportional hazard (PH) assumption, which states that HR is constant throughout the time under investigation. In the current analysis, the PH assumption was tested by using the Grambsch-Therneau test. In case of violation, we included a time-variant covariate. This method in the context of implant research is described by Levin et al. (2011). The statistical analysis was performed with SPSS (IBM Corp, Version 19.0, Armonk, NY, USA) and with R 2.15 (R Foundation for Statistical Computing, Vienna, Austria) software. With R, we used the {Survival} library. The significance level was set to 0.05.

Results

Description of the implant and patient cohort

The study cohort consisted of 922 (44.8%) men and 1138 (55.2%) women with no significant difference between men and women with regard to age and follow-up. A bimodal distribution was observed for the age distribution with a peak at 50 years and also at 19–20 years when congenitally missing teeth cases were typically treated. Follow-up was up to 11 years (133 months) with a mean of 32.2 months, and there was no significant difference between men and women with regard to age and follow-up time.

The 2060 study participants received a total of 4591 implants with a mean of 2.23 implants per patient and a SD of 1.68. The majority of patients had one implant (n = 911), 572 patients had two implants, 238 patients had three implants, and 339 patients received four implants or more. The maximum number of implants in one patient was 14 implants.

Implants, irrespective of type and/or dimension, were distributed as follows: n = 625 (13.7%) in the anterior maxilla, n = 1717 (37.4%) in the posterior maxilla, n = 291 (6.3%) in the anterior mandible and n = 1958 (42.6%) in the posterior mandible. Positions were defined according to Buser et al. (1997), whereby the anterior maxilla included FDI tooth positions 13-23, the anterior mandible included positions 34-44. The distribution of implant length and diameter is shown in Fig. 1. In general with regard to size and location, there was a trend to long, narrow implants in narrow applications such as incisors and short, wide implants in posterior locations, such as molars. Among the narrow 3.3 mm diameter implants, the most prominent length was 12 mm, but as implants became wider, shorter implants (6, 8 mm, or 10 mm) became more frequently used.

Descriptive survival analysis at implant level and patient level

During the study period, there were 32 implant failures (0.7%) documented in this study; 22 failures occurred before loading (0.5%), and 10 failures occurred after loading (0.2%). At patient level, we observed 22 patients (1.1%) who experienced at least one implant failure before loading and nine patients (0.4%) with implant failure after loading. Among these 31 patients, only one patient had two failing implants, while all the rest experienced a single implant failure.

According to the life table analysis (Table 3), at implant level, the cumulative survival rates (CSR) at 3, 5, and 7 years were 99.3%, 99.0%, and 98.4%, respectively. While at the patient level, the CSRs at 3, 5, and 7 years were 98.6%, 97.7%, and 95.9%, respectively. The Kaplan–Meier survival curves at patient and implant level are illustrated in Fig. 2.

Univariate analysis for risk indicators associated with implant failure

Table 4 summarizes the univariate association between the study variables and implant failure. Variables with a P-value < 0.15 were selected for subsequent multivariate analysis. At implant level, the selected variables for further analysis were the following: implant location, length and design as well as immediate implantation, GBR and bone grafting. Insertion torque tended to associate with implant failure (HR = 0.96, P = 0.07), suggesting that higher torque may relate to a lesser hazard to fail. However, this variable was not included in the multivariate analysis as measurements

of insertion torque had been performed only after 2006 and inclusion would limit the power of multivariate analysis. At patient level, the variables were the following: gender, autoimmune disease, smoking, and allergy to penicillin were also selected for multivariate analysis. The number of implant units within a patient was significantly associated with implant failure. When patients had more than one implant, there was a higher risk of failure compared to patients with only one implant (HR = 3.12 P = 0.002).

Multivariate analysis for risk indicators associated with implant failure

Table 5 presents the hazard ratio obtained from a multivariate PH Cox regression including all relevant variables from the univariate analysis. After adjustment to possible confounders, failure time was related to implant location, implant length and design, timing of implant, GBR procedures during implantation and gender (border line). Beyond 7 years, there were insufficient numbers of cases for statistical validity regarding risk

Table 3. Life table analysis at implant and patient level

	Implant level			Patient level		
Interval start Time[month]	Number entering interval	Number of failures	Cumulative surviving at end of interval	Number entering interval	Number of failures*	Cumulative surviving at end of interval
0	4591	23	0.99	2060	22	0.99
12	3439	1	0.99	1522	1	0.99
24	2329	1	0.99	988	1	0.99
36	1781	2	0.99	738	2	0.98
48	1137	2	0.99	449	2	0.98
60	732	2	0.99	261	2	0.97
72	461	1	0.98	152	1	0.96
84	276	0	0.98	70	0	0.96
96	141	0	0.98	36	0	0.96
108	61	0	0.98	13	0	0.96
120	18	0	0.98	2	0	0.96

*Patient with at least one implant failure.

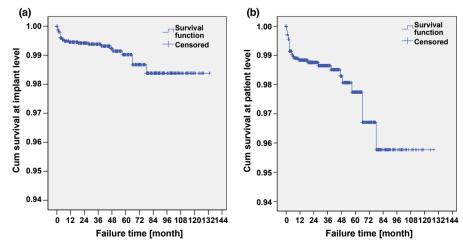


Fig. 2. Kaplan Meier survival curve (a) at implant level, n = 4591 and (b) at patient level, n = 2060.

Table 4. Univariate analysis for risk indicators associate with implant failure (n = 4591)

	Variables	Hazard ratio	95% confidence interval	Robust P _{value}
Anatomic	Location [post. maxilla](1)	0.51	0.21, 1.22	0.13
	Location [ant. mandible](1)	0.23	0.03, 1.81	0.16
	Location [post. mandible](1)	0.30	0.12, 0.77	0.01
	Jaw [maxilla]	2.18	1.03, 4.61	0.04
Implant-characteristics	Diameter	1.35	0.55, 3.31	0.52
•	Length	0.78	0.62, 0.99	0.04
	Design [Standard Plus](2)	2.55	0.35, 18.38	0.35
	Design [Tapered Effect](2)	4.88	1.72, 13.83	< 0.01
	Design [Bone Level](2)	1.06	0.32, 3.60	0.92
	Neck [Narrow](3)*	N.A.		
	Neck [Wide](3)	1.13	0.52, 2.43	0.76
	Neck[Bone Level](3)	0.96	0.27, 3.33	0.95
Surgery related and	Insertion torque†	0.96	0.93, 1.00	0.07
augmentation	Immediate implantation	2.03	0.85, 4.83	0.11
procedures	Immediate loading	1.71	0.50, 5.83	0.39
	Bone defect	0.96	0.3, 4.04	0.96
	GBR	2.28	1.13, 4.62	0.02
	Bone graft	2.28	1.13, 4.62	0.02
	Membrane use	1.74	0.68, 4.47	0.25
	Tissue graft*	N.A.		
Prosthesis related	Abutment type:	N.A.		
	Prosthesis‡	N.A.		
	Retention type:	N.A.		
	Occlusion‡	N.A.		
Patient related and	Gender [Male]	2.05	0.97, 4.31	0.06
health status	Age	1.00	0.97, 1.04	0.70
	Bruxism*	N.A.		
	Autoimmune disease	5.61	1.11, 28.49	0.04
	Bisphosphonate*	N.A.		
	Diabetic*	N.A.		
	Periodontal disease	1.12	0.27, 4.70	0.87
	Heavy smoker	3.38	0.79, 14.43	0.10
	Antibiotic*	N.A.		
	Penicillin allergy	2.16	0.84, 5.56	0.11

^{*}Estimates are not reliable due to high standard error.

Table 5. Hazard ratios obtained from a multivariate PH Cox regression*

Effect	Variables	Hazard ratio	95% confidence interval	Robust P _{value}
Main effect	Location [post. Maxilla](1) Location [Ant. Mandible](1) Location [post. Mandible](1) Length [6 mm]	0.26 0.30 0.31 7.92	0.11, 0.64 0.04, 2.19 0.10, 0.96 2.83, 22.18	<0.01 0.24 0.04 <0.01
	Design [Standard Plus](2) Design [Tapered Effect](2) Design [Bone Level](2)	2.52 3.71 0.53	0.41, 15.53 1.19, 11.52 0.13, 2.12	0.32 0.02 0.37
Interaction terms	Immediate implantation GBR Gender [male] Time*Immediate implantation	3.24 3.42 2.22 0.95	1.27, 8.29 1.27, 8.29 1.01, 4.83 0.89, 1.00	0.01 <0.01 0.05 0.05
	6 mm*Location [post. Maxilla]	19.85	2.09, 188.61	<0.01

^{*}With robust standard errors accounting for Intra Class Correlation. (1) Compared with Anterior Maxilla. (2) Compared with Standard design.

indicators so 7 years was chosen for long-term comparison.

Implant location

At 7 years, the CSR for implants at the anterior maxilla was 97%, while the CSRs were 98%, 100%, and 99% for implants at the posterior maxilla, anterior mandible, and posterior mandible, respectively (Fig. 3a). According

to our model, implants located in the posterior maxilla (HR = 0.26) and posterior mandible (HR = 0.31) were at lower risk of failure compared with implants in the anterior maxilla.

Implant length

The CSRs at 7 years for implants of 6, 8 mm, and ≥10 mm were 96%, 98%, and

99%, respectively. For 6-mm implants, a HR = 7.92 was determined (Table 3), which means that 6-mm implants have a 7.92 times greater risk of implant failure compared with all other length groups. Our model revealed a significant interaction between 6-mm implants and location. As reported, the marginal survival of 6-mm implants was 96% (Fig. 4a). Stratifying the results by implant location showed that the survival at 7 years was 99% at the posterior mandible (Fig. 4b), but dropped to 87% at the posterior maxilla (Fig. 4c).

Implant design

Tissue-Level implants (n = 3863) had a CSR of 99% at 3 years, which was maintained over the entire duration of the study (Fig. 3b). Bone-Level implants (n = 600) were as predictable with a CSR of 99% after 3 years. Hence, there was no difference with regard to failure time between the Standard, Standard Plus, and Bone-Level implants. In contrast, Tapered Effect implants (n = 128) demonstrated a lower CSR of 95% at 5 years. Compared with Standard Tissue-Level implants, the Tapered Effect implants were found to be at a greater risk of failure (HR = 3.71).

Immediate implantation

Immediate implantation (n = 521) was a risk indicator for failure with a hazard ratio of 3.24. Of the immediate implantations by implant design, there were 115 bone-Level, 95 Tapered Effect, and 312 tissue-Level implants. Immediate provisional loading was rare [2.3%] in mature ridge sites but accounted for 25.1% (n = 131) of the immediate implantation group. There were five maxillary anterior implant failures to infection when placed immediately in extraction sockets and in three of these the patients were penicillin allergic. According to our model, immediate implantation interacts significantly with time, which means that during the surgical phase there was an advantage to conventional or delayed implantation in terms of survival. However, this advantage did not last over the years with long-term CSR being equal for all placement protocols (Fig. 3c).

GBR

Guided bone regeneration during implantation was a significant risk indicator for implant failure (HR = 3.42) (Fig. 3d).

Gender

The CSR at 7 years was 97% among women compared with 94% among men. The hazard

[†]Based on 3459 observations. Measurements of insertion torque started at 2006.

[‡]Estimates are not reliable. Only 9 implant failure after loading. (1) Compared with Anterior Maxilla. (2)Compared with Standard design. (3) Compared with regular neck.

Shaded cells are for variables with P -value < 0.15 selected for further multivariate analysis.

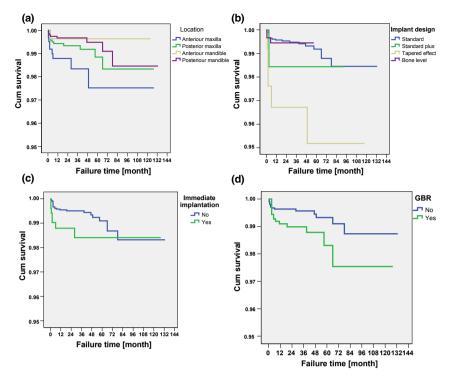


Fig. 3. Kaplan Meier survival curve by (a) implant location (b) implant design (c) immediate implantation and (d) guided bone regeneration during implantation.

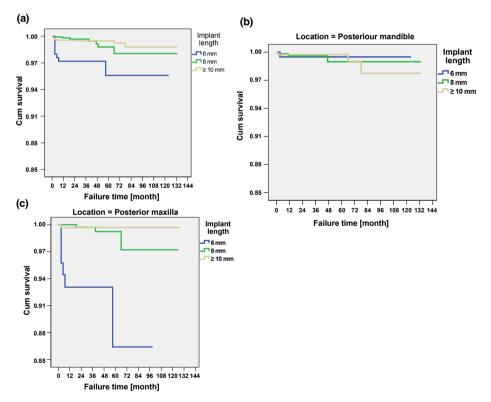


Fig. 4. Kaplan Meier survival curve by implant length. (a) marginal survival (b) at the posterior mandible and (c) at the posterior maxilla.

for a failure among men was 2.22 times greater compared with women (Table 3). However, the significance of 0.05 was borderline, and interpretation should be made cautiously.

Discussion

Survival analysis

In this open cohort, retrospective study of 4591 implants, placed in 2060 patients, the

cumulative survival rates (CSR) at the implant level were found to be relatively high with values of 99%, 99%, and 98%, at the 3-, 5-, and 7-year time-points, respectively. The cumulative survival rates at the patient level were also found to be high with CSR of 99%, 98%, and 96% at the 3-, 5-, and 7-year time-points, respectively. Although these CSR values are on par with another study reporting on long-term survival of Straumann implants, showing 99.4% and 98.3% for the 5- and 10-year marks, respectively (Nixon et al. 2009), they are higher than CSR reported in a number of other studies. For example, a systematic review showing a meta-analysis of 24 papers, reported an implant survival rate of 97.2% and 95.2% at the 5- and 10-year mark, respectively (Jung et al. 2012).

Furthermore, the results presented herein are higher than rates reported for other systems such as porous oxide-coated titanium implants whereby a recent report revealed a cumulative survival of 93% after 1-2 years (Becker et al. 2013), as well as a study on a tapered implant with double-helical steep thread pitch reporting a survival of only 87% at the 1-year mark (Ho et al. 2013). The high implant-level survival rate of 99%, reported herein, is also in stark contrast to a study utilizing flapless guided surgery showing CSR of 90% and 83% at 1- and 3-year mark, respectively (Landazuri-Del Barrio et al. 2013) and in another study making use of guided surgery showing a survival rate of only 83.5% after 3 years (Lal et al. 2013). Furthermore, with the introduction of generic type implants to the market, with no or only minimal clinical documentation, it is increasingly important to note the higher rates of implant survival achievable when using established and thoroughly tested implant materials, designs and surfaces as well as established placement procedures. results in our study may be higher than typically reported because this represents data from a single clinic with an experienced operator. Furthermore, based on reported literature, penicillin allergy testing was performed prior to immediate implantation in sockets. If penicillin class antibiotics could not be used, then the cases were usually treated as delayed implantations.

In the present study, only 32 implants failed of the 4591 implants placed. Of the implant failures observed, it was favorably noted that failures occurred before final prosthetic loading in the majority of the cases (22/32). The survival of single-unit implant analysis, at the patient level, was 100% at

the 7 year time point. This is a remarkable result, much higher than has been reported in an earlier report comparing conventional three unit bridge to single implants (Pjetursson et al. 2007), and it provides support for the use of implant treatment as an alternative to the conventional 3 unit bridge. In addition, the fact that 80% of the implants in this cohort were placed in posterior regions, together with the high survival rate, lends support to other studies showing Straumann implants as a highly successful option in single molar applications (Levine et al. 2007).

Multiple implants

Although having multiple units increased the risk of implant failure, it was somewhat surprising to find that among the 31 failing patients in this study, only one patient had more than one failing implant. This is in contrast to an earlier study reporting a clustering of removals within patients, with the odds of having a second implant removed found to be 1.3 times greater if the patient had already had one implant removed (Weyant & Burt 1993). In another study, reporting on 3609 implants with a survival rate of 97.3% over an 8-year period, it was also found that implants tend to fail in clusters with one-third of the patients accounting for over half of all failures (Schwartz-Arad et al. 2008). One possible explanation for the nonclustered failing pattern, in our study, is the fact that many of the patients received only one implant, and therefore, clusters of failure cannot be seen. Nevertheless, among the 31 failing patients, 30 of these patients received multiple implants, therefore theoretically had the chance to experience multiple failures. Cluster failures may, however, be more common with increased numbers of implants per patient and in particular on patients with full arch reconstruction. In this study, there were only 10% of patients (n = 204) with five or more implants. One other potential explanation is that the study had only five patients (0.2%) identified as having generalized aggressive periodontal disease and it has been shown that these patients are at higher risk of implant failure compared even with chronic periodontal disease patients so our low prevalence of aggressive periodontal disease cases may explain the lack of clustering (Mengel et al. 2001).

Implant variables: location, length, and design

Implant location

All potential implant locations were utilized in this study with exact location being determined by each individual patient's requirements. Interestingly, the distribution of implants was found to be relatively even with regard to maxillary and mandibular sites, showing 2342 [51%] implants located in the maxilla and 2249 [49%] implants in the mandible.

There was significantly higher trend toward failure in the anterior maxilla position and this trend remained present even after taking into account any confounding effect of the use of GBR and/or immediate placement, which were common at this location. The majority of failures occurred before final prosthetics in the upper anterior region most likely because there was more demand for interim esthetics. In relation to this, we noted that three maxillary anterior implants failed to premature mobility likely due to loading from provisional's during integration period. As mentioned, five maxillary anterior implants failed to infection when placed in immediate socket.

Implant length

Implant length was investigated as a factor in survival and, although 8-mm implants had no difference in survival rate when compared to 10-mm implants, the 6-mm implants trended to lower survival, though the differences were not found to be statistically significant due to the low overall number of failure. The cohort of 308 short implants (6 mm) was subsequently evaluated by stratifying the results to implant location, whereby the survival at the 5-year time-point was 100% in the posterior mandible position versus 87% in the posterior maxilla position. This high survival rate, particularly in the posterior mandible, for 6-mm implants, has not previously been reported for such a large number of implants and over such a long time period as is offered by this study. These results may further provide support for the use of short, splinted implants, in place of bone grafting, as the survival rate for short implants in the posterior mandible was higher than that found for the bone-grafted group in this study.

Conversely, the relatively higher failure rate in the posterior maxilla for 6-mm implants is also worthy of further discussion. This may be related to limited residual bone height as 54.8% of maxillary posterior implants were placed with the osteotome technique. In the case of the short, 6-mm implants in the posterior maxillary region, the implants were placed as multiple splinted units in bone that was 2–5 mm in height as an alternative to a lateral window procedure. In these instances, they were prone to failure

prior to loading from under a denture. The lateral window, sinus lift procedure has a number of complicating factors including rates of infection, membrane tear (19% on average) (Pjetursson et al. 2008) and graft dislodgement. In a systematic review of twentynine studies, accounting for 6940 implants placed in 2707 sinuses augmented through the lateral technique, implant survival rates varied from 75.57% to 100% (Corbella et al. 2013). In another review, survival for the lateral window technique varied between 61.7% and 100%, with an average survival rate of 91.8% (Wallace & Froum 2003). Furthermore. in a prospective study evaluating cumulative implant survival rates for sites grafted with the lateral window technique, a cumulative survival rate of 86.1% was reported (Barone et al. 2011). Thus, our finding of 87% survival with the osteotome technique, in short bone, is within the range of expected and acceptable outcomes, and has the added advantage of time and cost savings relative to lateral window augmentation.

Implant design

Straumann Standard and Standard Plus Tissue-Level implants had a very high survival rate of 99% at 3 years and remained viable up to the full length of the study period. This result indicates that the Tissue-Level implant is very reliable, which may be owing to the straight wall design and machined collar interface well above the bone crest to reduce potential biologic complications and remodeling. However, the Straumann Tissue-Level implant is less likely to be used in more complex bone grafting scenarios as well as in immediate applications where the Bone-Level and Tapered Effect implants are more often used.

The Bone-Level implant was as reliable with a survival rate of 99% after 3 years. This implant was introduced in 2008 and is a platform switching design. This study represents one of the largest, long-term clinical reports, for this implant type. Furthermore, the results of this study lend support to other studies on this implant design as seen, for example, in a multicenter study on 538 patients with 908 implants reporting a 1-year cumulative implant survival of 98.5% (Filippi et al. 2013).

The Tapered Effect implant had a good survival rate of 95% but which was slightly lower than a 2–5 year reported survival rate of 97.7% of the same implant design (Wilson et al. 2013). The significant trend to lower survival in our study may be explained by the fact that this implant was used in more

complex and challenging applications of immediate placement cases with 74% (n = 95) of the sites being immediate socket placements. However, even after accounting for potential confounders of timing and location, it is noted that this implant type remained at a greater risk of failure. It has been reported that there exists a learning curve for the use of tapered implants whereby a risk of compression may account for the higher failures (Menicucci et al. 2012; Ho et al. 2013) as such the lower survival may relate to tapered designs in general. With the introduction of the Bone-Level implant we stopped using the Tapered Effect implant primarily because the bone level implant offered improved restorative flexibility in demanding anterior locations, as such the Tapered Effect implant design was only used for a brief period between 2002 and 2005.

Surgical variables: timing, GBR

Implant timing

Implant placement into extraction sockets played only a minor role on implant survival according to the Kaplan-Meier analysis results that revealed an apparent effect only in the early phase of implant life. This is a significant finding with a follow-up period of up to 10 years and lends support to shortterm data seen in a systematic review of at least 1 year on 46 prospective studies that shows a 98.4% survival rate of implants in sockets (Lang et al. 2012). Of note in the systematic review was that only antibiotic selection factors affected survival rates, and we report on this later in this paper in patient variables regarding penicillin allergic patients.

GBR procedure

The survival of implants with GBR is lower than nonbone-grafted sites in this study, the implant survival in GBR sites still remains higher than the reported 95.7% in a systematic review of GBR procedures to correct peri-implant dehiscences (Chiapasco & Zaniboni 2009). Of the failed implants, in this study, that were placed with the GBR procedure, none of the sites experienced membrane exposure. Therefore, membrane exposure was not found to be a cause of implant failure herein.

Patient variables

Patient factors including male gender, smoking, autoimmune disease and penicillin allergy trended to higher failure rates, based on the univariate analysis.

There was a fairly even distribution of male patients at 45% to female patients at 55%, which allowed for a comparison of the effect of gender on survival. Gender was found to be a significant indicator for implant failure with a greater risk among men in the univariate analysis; however, this may be related to confounding variables, as it became marginally significant in the multivariate analysis. The increased risk may be due to the increased bite force expected in male patients; however, the failure risk was also greater even before prosthetic loading. It could still be that implants failed at a higher rate in men before prosthetic loading due to load under the provisional denture.

Heavy smoking had a potential impact on implant survival with univariate analysis indicating a greater risk of failure (HR = 4.83, P = 0.07). However, this did not remain significant in multivariate analysis. Of note is that all the implants used in our study were SLA surfaced and our result is similar to other retrospective studies that have found that smoking has minimal effect on survival for rough surfaced implants (Alsaadi et al. 2008; Balshe et al. 2008). One limitation is the low prevalence of heavy smokers at <2%, which may limit the power of the study. We recorded heavy smoking at >15 cigarettes per day, so light to moderate smokers were not recorded; furthermore, it is probable that not all patients were reporting their smoking status accurately. Also, the cohort drawn is located in an area with a high socio-economic status and in this group <2% for heavy smoking is not far from an expected rate in Canada (Reid et al. 2010).

Surprisingly, the history of periodontal disease did not have a significant impact on implant survival. Our result differs from other reports showing an increased risk in periodontal patients. In one study on Straumann hollow cylinder implants, patients with implants replacing teeth lost to periodontitis demonstrated a lower survival rate of 90.5%, compared with normal (96.5%) survival rate over a 10-year maintenance period (Karoussis et al. 2003). That periodontal disease did not significantly affect survival in this study may be related to the different implant design as it is documented that the hollow cylinder had a lower survival rate and used a rougher TPS surface compared with SLA (Levine et al. 2007). In this study, we also treated active periodontal disease prior to implant therapy and any patients with moderate to advanced periodontal disease were maintained on regular periodontal recall. It has been shown that compliance to

periodontal treatment affects implant survival (Roccuzzo et al. 2013). As noted earlier, we had a low incidence (0.2%) of generalized aggressive periodontitis patients. Furthermore, considering our average time of follow-up was 32.3 months, and the overall number of failed implants was low, our study may not reflect the long-term risk from periodontal disease as the effect on peri-implantitis may be chronic bone loss. Periodontal disease as a risk factor for progressive peri-implant bone loss, in this same cohort, is a topic of future study.

Patients taking steroids for chronic conditions or with active autoimmune disease were pooled and at the patient level were found to have marginally increased risk for (HR = 9.05,P = 0.07). implant failure Patients taking steroids are known to have immune suppression and steroids are also osteopenic and may therefore impair initial bone healing events required for reliable integration (Parrillo & Fauci 1979; Waters et al. 2000). Furthermore, patients with autoimmune disease may have impaired healing and reduced resistance to infection as can be seen by higher rates of tooth loss and periodontal disease in patients with rheumatoid arthritis (Pischon et al. 2008). The impact of steroids as a cofactor complicating bone-healing in patients with osteonecrosis related to bisphosphonate use is also noted and further implicates steroids as a risk factor for dental implants (Sonis et al. 2009).

Bisphosphonate therapy in our study did not impact survival, and this is in keeping with findings from a review of one prospective and three retrospective case series involving 217 patients demonstrating that the placement of implants is a safe procedure for such patients. However, in our study, we did not detail the duration or dose of bisphosphonate medication, and in the review noted above, the majority of the data reported in the above review are for patients with 4 years or less of bisphosphonate medication [Madrid & Sanz 2009].

The ability of a penicillin allergy to affect survival rates is a function of the routine use of premedication with antibiotics for dental implant placement, as well as the use of postoperative antibiotics in bone graft, sinus lift or immediate socket cases. In a recent systematic review of controlled trials comparing amoxicillin versus placebo in 927 patients, it was noted that 2 g of amoxicillin given orally 1 h preoperatively reduced the probability of implant failure (Esposito et al. 2010). In the cases where amoxicillin was not used, clindamycin was given as an alter-

nate. From our results, it would suggest there is a possible increased failure when clindamycin is used for antibiotic coverage. Our reported HR of 2.16 indicates a potential doubling of failure rate in patients allergic to penicillin; however, due to low numbers of failures, this did not achieve significance (P = 0.11). Penicillin allergic patient risk has also been shown in a retrospective study of 1925 implants placed in sockets, where it was found that patients unable to utilize postsurgical amoxicillin had an implant failure rate 3 times that of patients who received amoxicillin (Wagenberg & Froum 2006).

Although allergy to penicillin, autoimmune disease, and heavy smoking tend to be significant risk indicators for implant failure, it is important to note the power of the statistical analysis for these factors. Even with minimal exclusion criteria, that is, including all implant candidates, and the small number of implant failures observed in this study, taken together with the low prevalence of certain categories (e.g., heavy smokers, periodontal disease), the power of the statistical analysis in this study is low and, thus, limits the probability to identify significant differences between groups. Further analysis of the same cohort is planned to look at periimplant bone loss, inflammation, and infection, and this may provide the higher prevalence rates needed to better evaluate these variables.

As noted earlier, one major limitation to the study is the low number of implant failure overall, which reduces the power of the study to analyze risk indicators for implant failure particularly in that we do not find similar results for periodontal disease, smoking and cluster failures, as published previously. Another limitation is that all work has been done in one center by one clinician so results may not translate to different centers. Another limitation of this study, with regard to long-term results is that although implant follow-up appointments were scheduled at 3 months, 1 year, 3 years, and 5 years, the actual time between appointments varied from patient to patient and the variation was largest for the longest time-points. There was a trend showing a higher ratio of patient follow-up being seen at the specified intervals up to 3-5 years and then a reduction in the ratio of patients seen after 5 years. Furthermore, the subset of patients seen after 5 years was larger multiarch cases or patients returning due to potential implant complication, or additional tooth loss as such with a higher relative ratio of problem cases seen.

Conclusions

This study presents implant survival analysis from a retrospective cohort study of 2060 patients with 4591 implants placed in private practice over a period of up to 10 years. The cumulative survival rate at the implant level was found to be 99%, 99%, and 98%, at 3-, 5-, and 7-year mark, respectively. At the patient level, cumulative survival rates of 99%, 98%, and 96%, were observed at 3, 5, and 7 years, respectively. Straumann Tissue-Level implants had a very high survival rate of 99% at 3 years, which was maintained over the 9 years of the study. Bone-Level implants were as predictable with a survival rate of 99% up to 3 years, while Tapered

Effect implants demonstrated a lower survival rate of 95% at 5 years. Single site implants were highly predictable with 100% survival up to 7 years. Conversely, patients with multiple implant locations had higher failure rates, although this study did not show a trend toward cluster failure. Short implants in the mandibular posterior sites had a high survival rates of 100%, while the same was not true for the maxillary posterior position whereby 6-mm implant had a survival rate of only 87%. Patient factors, including male gender, smoking, autoimmune disease and allergy to penicillin, were found to trend to higher failure rates. In conclusion, very high survival rates are achievable, over long periods, for Straumann implants placed in private practice. This study is of value as a representation of private practice experience providing insight into the realities of large-scale, long-term implant results. Further analysis of this same cohort is planned with attention to soft tissue inflammation and bone loss over time as well as risk factors for biologic and technical complications.

Acknowledgements: This study was carried out independent of financial support with the exception of financial assistance from Institut Straumann AG, Basel, Switzerland for statistical analysis performed at the department of Statistics and Operations Research, Tel-Aviv University, Israel. The authors would also like to thank Dr. Michelle Brown for her assistance in manuscript preparation.

References

Alsaadi, G., Quirynen, M., Komarek, A. & van Steenberghe, D. (2008) Impact of local and systemic factors on the incidence of late oral implant loss. Clinical Oral Implants Research 19: 670–676.

Balshe, A.A., Eckert, S.E., Koka, S., Assad, D.A. & Weaver, A.L. (2008) The effects of smoking on the survival of smooth- and rough-surface dental implants. *International Journal of Oral and Maxillofacial Implants* **23**: 1117–1122.

Barone, A., Orlando, B., Tonelli, P. & Covani, U. (2011) Survival rate for implants placed in the posterior maxilla with and without sinus augmentation: a comparative cohort study. *Journal of Periodontology* 82: 219–226.

Becker, W., Becker, B.E., Hujoel, P., Abu Ras, Z., Goldstein, M. & Smidt, A. (2013) Prospective clinical trial evaluating a new implant system for implant survival, implant stability and radiographic bone changes. Clinical Implant Dentistry and Related Research 15: 15–21. Branemark, P.I. (1983) Osseointegration and its experimental background. *Journal of Prosthetic Dentistry* 50: 399–410.

Buser, D. (2001) Titanium for dental applications (ii): implants with roughened surfaces. In: Brunette, D., Tengvall, P., Textor, M. & Thomson, P., eds. Titanium in Medicine, 232–239. Berlin: Springer.

Buser, D., Broggini, N., Wieland, M., Schenk, R.K., Denzer, A.J., Cochran, D.L., Hoffmann, B., Lussi, A. & Steinemann, S.G. (2004) Enhanced bone apposition to a chemically modified sla titanium surface. *Journal of Dental Research* 83: 529–533.

Buser, D., MericskeStern, R., Bernard, J.P., Behneke, A., Behneke, N., Hirt, H.P., Belser, U.C. & Lang, N.P. (1997) Long-term evaluation of non-submerged iti implants.1. 8-year life table analysis of a prospective multi-center study with 2359 implants. Clinical Oral Implants Research 8: 161–172. Chiapasco, M. & Zaniboni, M. (2009) Clinical outcomes of gbr procedures to correct peri-implant dehiscences and fenestrations: a systematic review. Clinical Oral Implants Research 20: 113–123

Chuang, S.K., Wei, L.J., Douglass, C.W. & Dodson, T.B. (2002) Risk factors for dental implant failure: a strategy for the analysis of clustered failuretime observations. *Journal of Dental Research* 81: 572–577.

Corbella, S., Taschieri, S. & Del Fabbro, M. (2013) Long-term outcomes for the treatment of atrophic posterior maxilla: a systematic review of literature. Clinical Implant Dentistry and Related Research doi: 10.1111/cid.12077 [Epub ahead of print].

Esposito, M., Grusovin, M.G., Loli, V., Coulthard, P. & Worthington, H.V. (2010) Does antibiotic prophylaxis at implant placement decrease early implant failures? A cochrane systematic review.

- European Journal of Oral Implantology **3**: 101–110.
- Filippi, A., Higginbottom, F.L., Lambrecht, T., Levin, B.P., Meier, J.L., Rosen, P.S., Wallkamm, B., Will, C. & Roccuzzo, M. (2013) A prospective noninterventional study to document implant success and survival of the straumann bone level slactive dental implant in daily dental practice. *Quintessence International* 44: 499–512.
- Ganeles, J., Zollner, A., Jackowski, J., ten Bruggenkate, C., Beagle, J. & Guerra, F. (2008) Immediate and early loading of straumann implants with a chemically modified surface (slactive) in the posterior mandible and maxilla: 1-year results from a prospective multicenter study. *Clinical Oral Implants Research* 19: 1119–1128.
- Ho, D.S.W., Yeung, S.C.H., Zee, K.Y., Curtis, B., Hell, P. & Tumuluri, V. (2013) Clinical and radiographic evaluation of nobelactivetm dental implants. Clinical Oral Implants Research 24: 297–304.
- Jung, R.E., Fenner, N., Hammerle, C.H.F. & Zitzmann, N.U. (2013) Long-term outcome of implants placed with guided bone regeneration (gbr) using resorbable and non-resorbable membranes after 12-14 years. Clinical Oral Implants Research 24: 1065–1073.
- Jung, R.E., Zembic, A., Pjetursson, B.E., Zwahlen, M. & Thoma, D.S. (2012) Systematic review of the survival rate and the incidence of biological, technical, and aesthetic complications of single crowns on implants reported in longitudinal studies with a mean follow-up of 5 years. Clinical Oral Implants Research 23: 2–21.
- Karoussis, I.K., Salvi, G.E., Heitz-Mayfield, L.J.A., Bragger, U., Hammerle, C.H.F. & Lang, N.P. (2003) Long-term implant prognosis in patients with and without a history of chronic periodontitis: a 10-year prospective cohort study of the iti (r) dental implant system. Clinical Oral Implants Research 14: 329–339.
- Lal, K., Eisig, S.B., Fine, J.B. & Papaspyridakos, P. (2013) Prosthetic outcomes and survival rates of implants placed with guided flapless surgery using stereolithographic templates: a retrospective study. *International Journal of Periodontics & Restorative Dentistry* 33: 661–667.
- Landazuri-Del Barrio, R.A., Cosyn, J., De Paula, W.N., De Bruyn, H. & Marcantonio, E. (2013) A prospective study on implants installed with flapless-guided surgery using the all-on-four concept in the mandible. Clinical Oral Implants Research 24: 428–433.
- Lang, N.P., Pun, L., Lau, K.Y., Li, K.Y. & Wong, M.C. (2012) A systematic review on survival and success rates of implants placed immediately into fresh extraction sockets after at least 1 year. Clinical Oral Implants Research 23(Suppl 5): 39–66.

- Levin, L., Ofec, R., Grossmann, Y. & Anner, R. (2011) Periodontal disease as a risk for dental implant failure over time: a long-term historical cohort study. *Journal of Clinical Periodontology* 38: 732–737.
- Levine, R.A., Ganeles, J., Jaffin, R.A., Clem, D.S., Beagle, J.R. & Keller, G.W. (2007) Multicenter retrospective analysis of wide-neck dental implants for single molar replacement. *International Journal of Oral & Maxillofacial Implants* 22: 736–742.
- Madrid, C. & Sanz, M. (2009) What impact do systemically administrated bisphosphonates have on oral implant therapy? A systematic review. Clinical Oral Implants Research 20(Suppl 4): 87–95.
- Mengel, R., Schroder, T. & Flores-de-Jacoby, L. (2001) Osseointegrated implants in patients treated for generalized chronic periodontitis and generalized aggressive periodontitis: 3-and 5-year results of a prospective long-term study. *Journal of Periodontology* 72: 977–989.
- Menicucci, G., Pachie, E., Lorenzetti, M., Migliaretti, G. & Carossa, S. (2012) Comparison of primary stability of straight-walled and tapered implants using an insertion torque device. *Inter*national Journal of Prosthodontics 25: 465–471.
- Nixon, K.C., Chen, S.T. & Ivanovski, S. (2009) A retrospective analysis of 1000 consecutively placed implants in private practice. Australian Dental Journal 54: 123–129.
- Owens, W.D., Felts, J.A. & Spitznagel, E.L.J. (1978) As aphysical status classifications: a study of consistency of ratings. *Anesthesiology* 49: 239–243.
- Parrillo, J.E. & Fauci, A.S. (1979) Mechanisms of glucocorticoid action on immune processes. Annual Review of Pharmacology and Toxicology 19: 179–201.
- Penarrocha-Diago, M., Demarchi, C.L., Maestre-Ferrin, L., Carrillo, C., Penarrocha-Oltra, D. & Penarrocha-Diago, M.A. (2012) A retrospective comparison of 1022 implants: immediate versus nonimmediate. *International Journal of Oral & Maxillofacial Implants* 27: 421–427.
- Pischon, N., Pischon, T., Kroeger, J., Guelmez, E., Kleber, B.M., Bernimoulin, J.P., Landau, H., Brinkmann, P.G., Schlattmann, P., Zernicke, J., Buttgereit, F. & Detert, J. (2008) Association among rheumatoid arthritis, oral hygiene, and periodontitis. *Journal of Periodontology* 79: 979– 986.
- Pjetursson, B.E., Bragger, U., Lang, N.P. & Zwahlen, M. (2007) Comparison of survival and complication rates of tooth-supported fixed dental prostheses (fdps) and implant-supported fdps and single crowns (scs). Clinical Oral Implants Research 18: 97–113.
- Pjetursson, B.E., Tan, W.C., Zwahlen, M. & Lang, N.P. (2008) A systematic review of the success of

- sinus floor elevation and survival of implants inserted in combination with sinus floor elevation part i: lateral approach. *Journal of Clinical Periodontology* **35**: 216–240.
- Reid, J.L., Hammond, D. & Driezen, P. (2010) Socio-economic status and smoking in canada, 1999–2006: has there been any progress on disparities in tobacco use? Canadian Journal of Public Health 101: 73–78.
- Renouard, F. & Nisand, D. (2006) Impact of implant length and diameter on survival rates. *Clinical Oral Implants Research* 17: 35–51.
- Roccuzzo, M., Bonino, L., Dalmasso, P. & Aglietta, M. (2013) Long-term results of a three arms prospective cohort study on implants in periodontally compromised patients: 10-year data around sandblasted and acid-etched (sla) surface. Clinical Oral Implants Research doi: 10.1111/clr.12227 [Epub ahead of print].
- Schwartz-Arad, D., Laviv, A. & Levin, L. (2008) Failure causes, timing, and cluster behavior: an 8year study of dental implants. *Implant Dentistry* 17: 200–203.
- Simonis, P., Dufour, T. & Tenenbaum, H. (2010) Long-term implant survival and success: a 10-16year follow-up of non-submerged dental implants. Clinical Oral Implants Research 21: 772–777.
- Sonis, S.T., Watkins, B.A., Lyng, G.D., Lerman, M.A. & Anderson, K.C. (2009) Bony changes in the jaws of rats treated with zoledronic acid and dexamethasone before dental extractions mimic bisphosphonate-related osteonecrosis in cancer patients. Oral Oncology 45: 164–172.
- Wagenberg, B. & Froum, S.J. (2006) A retrospective study of 1925 consecutively placed immediate implants from 1988 to 2004. *International Jour*nal of Oral and Maxillofacial Implants 21: 71– 80.
- Wallace, S.S. & Froum, S.J. (2003) Effect of maxillary sinus augmentation on the survival of endosseous dental implants. A systematic review. Annals of periodontology 8: 328–343.
- Waters, R.V., Gamradt, S.C., Asnis, P., Vickery, B.H., Avnur, Z., Hill, E. & Bostrom, M. (2000) Systemic corticosteroids inhibit bone healing in a rabbit ulnar osteotomy model. Acta Orthopaedica Scandinavica 71: 316–321.
- Weyant, R.J. & Burt, B.A. (1993) An assessment of survival rates and within-patient clustering of failures for endosseous oral implants. *Journal of Dental Research* 72: 2–8.
- Wilson, T.G., Jr, Roccuzzo, M., Ucer, C. & Beagle, J.R. (2013) Immediate placement of tapered effect (te) implants: 5-year results of a prospective, multicenter study. *International Journal of Oral and Maxillofacial Implants* 28: 261–269.