Early Implant Failures in Patients Treated with Brånemark System Titanium Dental Implants: A Retrospective Study

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Implant failure has been associated with factors such as poor bone quality, insufficient bone volume, implant instability, unfavorable implant loading, and smoking habits. Infections and host responses may also be important factors in dental implant failure. The objectives of the present study were to identify various explanatory factors associated with titanium implant failure. Forty subjects with stage 1 non-osseointegrated titanium dental implants (NOTI) ad modum Brånemark and 40 age- and gender-matched control subjects with successfully osseointegrated titanium implants (SOTI) were studied. Clinical data and gamma G immunoglobulin (IgG) antibody titers were studied. An independent t test revealed that significantly longer implants were placed in subjects with SOTI ($P < .05$). Statistically significant differences in bone shape and resorption (BSR) scores were found between SOTI and NOTI ($P < .05$). Logistic regression analysis identified 3 significant explanatory outcome variables: serum antibody avidity scores for Bacteroides forsythus *($P < .0001$), serum antibody titers to* Staphylococcus aureus *($P < .001$), and the BSR scores ($P < .05$). Antibody avidity to* B forsythus *and antibody titer to* S aureus *were therefore the 2 most important factors associated with early implant failures and with a significant predictive ability. This indicates that immunologic factors are involved in osseointegration.*
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Key words: *early implant failure, endosseous dental implantation, osseointegration, titanium*

Implant failures have been associated with factors such as poor bone quality, insufficient jawbone volume, initial implant instability, and overload.[1–5] Implants may be lost prior to stage 2 surgery (early failures) or after prosthetic rehabilitation (late failures).[1,2] Most implant failures have been observed in the maxilla, with almost 3 times more implant losses than in the mandible in totally edentulous situations.[2] Early failures have been reported to vary between 1.5% and 21%.[1–3,6]

The majority of reports found in the literature claim that the main reasons for early implant failures are related to factors such as anatomic conditions, surgical trauma, lack of operator surgical implant experience, and infections.[1,2,5,7–12] In several reports, smoking habits were associated with the outcome of implant treatment.[13–15] In an analysis of the outcome of 2,066 implants representing 310 patients, cigarette smoking was found to be the primary factor for implant failure reported at second-stage surgery.[15] It has also been confirmed that a significantly greater percentage of early implant failures occurred in smokers than in nonsmokers.[14] Cigarette smoking has also been identified as a significant factor in periodontal disease, and local cofactors, such as poor oral hygiene, seem to be responsible for the higher incidence of peri-implantitis in smokers.[16]

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There are still other factors that may be associated with early implant failures. A previous study showed that humoral immunity factors relative to *Bacteroides forsythus* and *Staphylococcus aureus* may be associated with the osseointegration of titanium dental implants.[17]

In animal studies, *S aureus* has been identified as a rapid colonizer of implanted titanium metal plates and discs.[18,19] The same biomaterials are currently used in artificial joints and as orthopedic devices.[18,19] In this context, the biomaterial-bacterial attachment was reported to be of special interest. Glycoproteins have been reported to promote *S aureus* attachment to the surfaces of implanted biomaterials.[18–21] Implant surface properties are also suggested to be a factor of importance.[22] The objectives of the present study were to identify various explanatory factors associated with early failures of titanium dental implants.

MATERIALS AND METHODS

At the time of stage 2 surgery, a group of 43 adults with failing and non-osseointegrated titanium dental implants (NOTI) was identified and constituted the study group. The study group consisted of all patients with early implant failures treated at the Department of Prosthetic Dentistry, Central Hospital, Skövde, Sweden, during the years 1992 to 1997. Three patients declined to participate in the study, resulting in a sample size of 40 subjects. All patients were treated with Brånemark System implants (Nobel Biocare, Göteborg, Sweden). A gender- and age-matched control group of 40 subjects with long-term successfully osseointegrated titanium dental implants (SOTI) ad modum Brånemark was identified and included in the study. However, it was not possible to match each patient in the NOTI group with a control in the SOTI group with respect to jaw, oral surgeon, and edentulism etiology. For both groups, information concerning social and demographic factors, systemic conditions, and oral condition was also collected.

The patients signed an IRB (Internal Review Board) approval consent form and agreed to participate in the present study. Four experienced oral surgeons at the Department of Oral and Maxillofacial Surgery, Central Hospital, Skövde, Sweden, had placed all the implants, which had been placed using standard surgical protocol.[23] All patients were given systemic antibiotic prophylaxis with oral phenoxymethylpenicillin (pc-V). Two g of antibiotic were administered 1 hour preoperatively, and 1 g was administered every 8 hours for 10 days postoperatively. No preoperative mouthrinse with chlorhexidine solution was prescribed.

Information concerned with bone quality and jawbone resorption was obtained by the surgeons and registered according to the classification of Lekholm and Zarb.[24] For each of the implants, information about length, position, and initial stability was recorded by the surgeons. For each patient, reason for tooth loss was registered using information from earlier dental records and radiographs.

All failing implants in the NOTI group were removed immediately after being diagnosed as non-osseointegrated. A 5-mL venous blood sample was collected from each subject after the removal of non-osseointegrated implants and wound healing in subjects with NOTI, and after prosthetic rehabilitation in subjects with SOTI. The time interval between implant loss and sample harvesting varied among the subjects in the NOTI group. Also among the subjects in the SOTI group, variations were seen between the time of implant placement and sera harvesting. All the blood samples were obtained at the Central Hospital in Skövde, Sweden. The sera were separated, labeled, and frozen at –80°C and shipped on dry ice to the University of Washington for analyses using enzyme-linked immunosorbent assay techniques. The analytic method is fully described elsewhere.[17]

Statistical Methods

Descriptive statistics were used to characterize the distribution of values for study parameters. Binary logistic regression analysis using the method of forward Wald statistics was used to explore explanatory variables for loss of implants. Non-parametric statistical methods were used to study group differences for non-parametric data, as well as for antibody titer and avidity data, because the serology data were not normally distributed. All analyses were done using the SPSS statistical package (version 10.0, Chicago, IL). Statistical significance was set at $P < .05$.

RESULTS

The mean ages of the study (NOTI) and control (SOTI) group subjects were 64.5 years (SD ± 9.7) and 65.7 years (SD ± 9.8), respectively. Gender was evenly distributed (half males, half females) in both groups. In the study group, 27 subjects had lost their teeth because of periodontitis, and 13 subjects had lost their teeth as a result of dental caries. The corresponding figures for the control group were 20 and 16, respectively, while 4 subjects had received implant treatment because of congenitally missing teeth. In both groups, 23 subjects had remaining teeth. The number, length, and distribution of implants in the groups are presented in Table 1.

Table 1 Number and Length of Implants Placed in Investigated Subjects

Implant length (mm)	NOTI (n = 40)*	SOTI (n = 40)
7	1 (1)	1
10	36 (21)	28
13	86 (31)	87
15	75 (24)	68
18	11 (2)	11
Total	209 (79)	195

*No. of failing implants is indicated in parentheses.

Table 2 Bone Quality Scores for the Subjects Studied According to the Lekholm-Zarb Classification System[24]

Bone quality scores	NOTI (n = 40)		SOTI (n = 40)	
	n	%	n	%
1	0	0	1	2.5
2	11	27.5	17	42.5
3	22	55.0	18	45.0
4	7	17.5	4	10.0

Table 3 Percent Distribution of Bone Shape and Resorption (BSR) Scores According to Lekholm-Zarb[24] and Outcomes for the Subjects Studied

BSR score	Surgeon #1		Surgeon #2		Surgeon #3		Surgeon #4	
	NOTI	SOTI	NOTI	SOTI	NOTI	SOTI	NOTI	SOTI
A	0.0	0.0	0.0	0.0	0.0	0.0	0.0	12.5
B	7.1	16.7	11.8	22.2	0.0	33.3	16.1	43.8
C	14.2	25.0	29.4	33.3	33.3	33.3	29.9	37.5
D	57.1	33.3	35.3	22.2	0.0	33.3	54.9	6.3
E	21.4	25.0	23.5	22.2	66.7	0.0	0.0	0.0

In the study group, 37 subjects had implants placed in the maxilla, while the corresponding number for the control group was 29. There were 9 smokers in the study group and 3 smokers in the control group, all of whom smoked between 10 and 20 cigarettes per day. For the smokers in the NOTI group, no changes in smoking habits were reported between the time of implant placement and the time of implant failure. Among the 40 patients in the NOTI group, 28 had implants placed by the same oral surgeon as the age- and gender-matched control subjects in the SOTI group. The mean time period between removal of non-osseointegrated implants and serum sampling was 2.6 years (range 0.5 to 6.3 years). No patient in the NOTI group reported any severe infections or changes in general health status during the healing period or up to the time of collection of sera. No correlation was found between the time interval between implant removal and sampling of sera versus serum gamma G immunoglobulin (IgG) titer to any of the pathogens studied.

The scores for bone quality, bone shape, bone resorption (BSR), and implant stability can be seen in Tables 2 to 4. The relationships between BSR scores, surgeon, and failing or successful outcome are presented in Table 3. Statistically significant differences in BSR scores were found between SOTI and NOTI ($P < .05$, non-parametric Mann-Whitney U test), indicating less favorable outcomes for implants placed in resorbed jawbone. No difference in the assessment of primary implant stability was found between surgeons.

Table 4 Implant Primary Stability Scores for the Subjects Studied

Score	NOTI		SOTI	
	n	%	n	%
1 (good stability)	37	92.5	40	100
2 (poor stability)	3	7.5	0	0.0

No difference in the distribution of successful vs failing implants was found among the 4 different surgeons who performed implant placement. The distribution of implant lengths among the surgeons versus outcomes is presented in Fig 1. Analysis by independent *t* test revealed that significantly longer implants had been placed in subjects with successful outcomes ($P < .05$).

Logistic regression analysis demonstrated that the most significant explanatory variables for implant failure or success prior to stage 2 surgery were antibody avidity score for *B forsythus* ($P < .0001$), antibody titer to *S aureus* ($P < .001$), and BSR scores ($P < .05$) (Table 5). The significance of antibody titers to *S aureus* as a predictor of successful implant outcome is illustrated by a receiver operator characteristic (ROC) diagram (Fig 2a). The poor ability of the BSR index to predict outcome is also presented (Fig 2b).

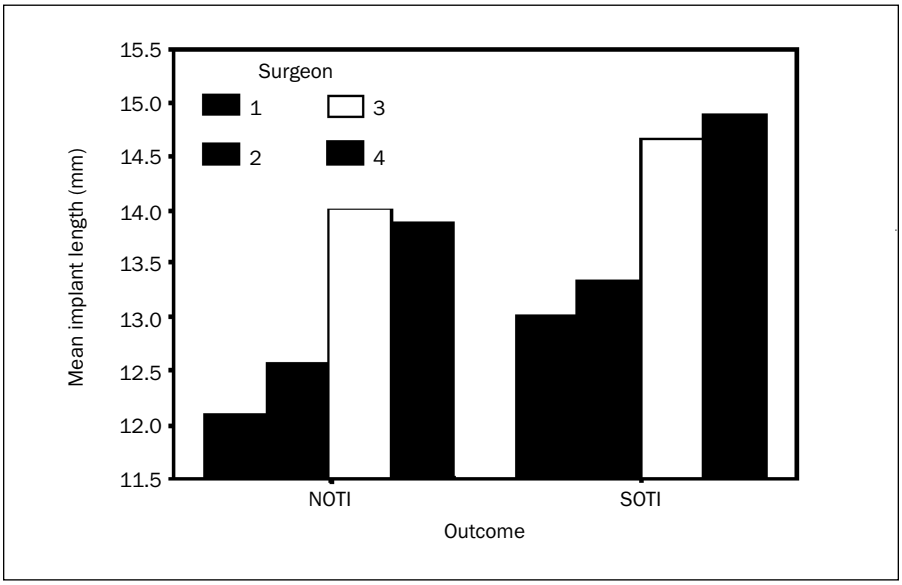

Fig 1 Distribution of mean implant lengths among the surgeons and outcome.

Table 5 Binary Logistic Regression Analysis (Wald Statistics) for Variables of Significance in Equation

Variable	β coeff	SE	Wald coefficient	*P* value	*R*	Chi-squared	*P* value
B forsythus avidity	5.68	1.41	16.2	.0001	0.37	26.2	.000
S aureus titer	4.75	1.48	10.31	.001	0.29	15.2	.000
BSR score	–1.69	1.52	0.34	.01	0.21	9.0	.003

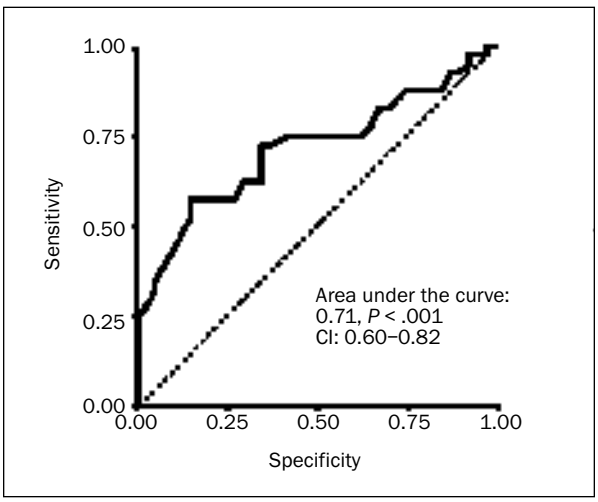

Fig 2a Receiver operator characteristic diagram illustrating the prediction for serum IgG titer to *S aureus* to predict a successful outcome. (The further away the represented variable curve characteristic is from the dotted diagonal line, the better the predicted value for the parameter.)

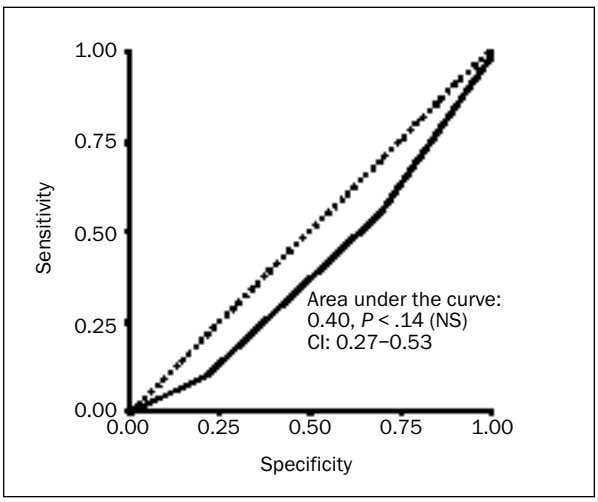

Fig 2b Receiver operator characteristic diagram illustrating the prediction for bone shape and resorption score to predict a successful outcome. (The closer the represented variable curve characteristic is to the dotted diagonal line, the less predictive value for the parameter. A curve below the dotted line also suggests a negative trend of the parameter's ability to predict outcome.)

DISCUSSION

The study and control groups were gender- and age-matched. However, it was not possible to match the study group with the control group in all respects, ie, factors such as reason for tooth loss, number of implants, and position and length of the implants. The time interval between implant loss and when the sera were harvested varied among the subjects in the study group, but the time of harvest also varied similarly in the control group. Data analysis failed to identify the time interval between implant removal and sampling of sera as an explanatory factor for the serological differences between groups.

The present study demonstrated that antibody avidity to *B forsythus* and antibody titer to *S aureus* were highly significantly associated with early implant failures (Table 5). The data suggested that subjects with failing implants were unable to mount protective serum IgG titer levels to pathogens studied. This indicates that humoral immunity factors may play an important role in the process of osseointegration of titanium dental implants. However, at what level antibody titers/avidity are protective or indicative of immune susceptibility remains to be studied. Other host immunity factors may also be of importance and should be studied further.

The prevalence of postsurgical wound infection associated with oral titanium implants is not known. However, in general, postsurgical infections and complications are caused by *S aureus* in varying degrees up to 20%.[25] *Staphylococcus aureus* has been identified with the microflora associated with titanium dental implants.[26] Recently, observations of colonization by *S aureus* at failing implant sites have also been reported.[27] Rapid bone destruction may be caused by bacterial cell surface proteins that stimulate the release of bone-resorbing cytokines such as TNF-α and interleukins.[28,29]

Nasal carriage of *S aureus* is approximately 20%. Subjects with nasal carriage of *S aureus* infection are at greater risk for *S aureus* infections following invasive procedures.[30,31] If nasal carriage of *S aureus* is associated with *S aureus* infection of maxillary dental implants, presurgically administered anti-*S aureus* nasal ointments may be effective in reducing this risk.[30,31] To reduce the production of cytokines, systemic treatment with anti-inflammatory drugs such as indomethacin may effectively reduce bone loss around titanium implants.[28] *Staphylococcus aureus* has a specific predilection for causing infections of prosthetic restorations that may be difficult to treat. Removal of the implant may be the most predictable way to cure the infection.[20,21,32]

The presence of fibronectin, a family of glycoproteins found on the surfaces of titanium implants, augments the colonization of staphylococci.[19–22,33] Surface characteristics of the implant may influence such colonization. Results from in vitro studies indicate that a rough titanium surface may reduce the affinity of fibronectin and thereby reduce the risks for staphylococcal infections.[22]

The present study did not allow investigation of the microflora at the time of implant failure, and therefore this was not studied at successful implant sites either. Studies of experimentally induced periimplantitis have shown that a mixed flora can be identified that includes *B forsythus*.[34] *Bacteroides forsythus* is a predominant pathogen in older subjects with either periodontitis or gingivitis.[35] Thus, it appears important to study both the presence of *B forsythus* at implant sites and serum IgG antibody titers to this pathogen.

In the present study, it was not possible to collect blood samples at the time of stage 2 surgery or when the implant was identified as non-osseointegrated. At the time of blood sampling in the NOTI group, all subjects had had the failing implants removed and did not show any clinical signs of oral infection. Elevated serum IgG antibody titers can be expected at the time of acute infection and should provide long-term memory functions and protection against new infections.[36] However, the titer differences as represented by the 2 groups suggest that subjects in the NOTI group either did not carry antibody memory functions relative to the pathogens studied or that they were potentially unable to surmount protective antibody titers. Future prospective studies must be conducted to further elucidate the role of humoral immunity and infections in subjects receiving titanium dental implants.

The finding that reduced bone volume (BSR score) was significantly associated with implant failure ($P < .05$) is in accordance with the results of other studies.[1–8] In the literature, bone quality and bone quantity have been considered factors of decisive importance for implant survival.[1–8] Poor bone quality and advanced jawbone resorption have also been recognized as factors influencing primary implant stability.[1,2,4–8] However, in the present study, the ROC analysis of BSR index failed to demonstrate that BSR index had predictive value for implant success or failure (Fig 2b).

Optimal primary implant stability is generally suggested as a prerequisite for successful treatment outcome. Bicortical anchorage in the maxilla is suggested as one way to improve primary implant stability.[23] However, there have been reports of 10% higher failure rates for maxillary implants that perforated the

floor of the nasal cavity and maxillary sinus.[37] Bacterial contamination of the implant surface may lead to lack of osseointegration.[30,31] The risk of bacterial contamination may increase when implants penetrate nasal or maxillary cavities that are infected with *S aureus.*[30,31] A successful treatment outcome with an implanted biomaterial requires tissue integration of the implant surface. It has been suggested that a "contest" between tissue cell integration and bacterial adhesion to the implant surface takes place, which has been dubbed a "race for surface."[20,21] If the tissue cells are successful and win this race, the implant surface is covered and defended and thus less available for bacterial colonization.[21]

There are a limited number of reports focusing on early implant failures, and no studies of humoral immunity and early dental implant failures have been found. Surgical trauma, bone quality, and jawbone resorption are believed to be the most important etiologic factors for early implant failures. Smoking habits have also been suggested to be a significant factor in that context.[13–15] Results from the present study failed to demonstrate significant differences between smokers and non-smokers with respect to a successful or failing treatment outcome. The analysis of the data set revealed that antibody avidity to *B forsythus*, antibody titer to *S aureus*, and BSR scores were the only significant factors associated with early implant failures.

CONCLUSION

The results of the present study showed that antibody avidity to *B forsythus* and antibody titer to *S aureus* were found to be the 2 most important factors associated with early implant failures. This would seem to indicate that immunologic factors are involved in osseointegration. Poor bone quality, initial implant stability, surgical trauma, and smoking habits were, in this study, not the most important factors associated with early implant failures.

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