Dental Implant Failure Rates and Associated Risk Factors

Peter K. Moy, DMD[1]/Diana Medina, DDS[2]/Vivek Shetty, DDS, Dr Med Dent[3]/Tara L. Aghaloo, DDS, MD[4]

Purpose: *To guide treatment planning by analyzing the rates of dental implant failure to determine associated risk factors.* ***Materials and Methods:*** *All consecutively treated patients from January 1982 until January 2003 were included in a retrospective cohort study, as defined in the hierarchy of evidence for dental implant literature. Data regarding gender, age, implant location, bone quality, bone volume, and medical history were recorded. Correlations between these data and implant survival were calculated to establish relative risk (RR) ratios.* ***Results:*** *Increasing age was strongly associated with the risk of implant failure. Compared to patients younger than 40 years, patients in the 60-to-79 age group had a significantly higher risk of implant failure (RR = 2.24;* P < *.05). Gender, hypertension, coronary artery disease, pulmonary disease, steroid therapy, chemotherapy, and not being on hormone replacement therapy for postmenopausal women were not associated with a significant increase in implant failure. Smoking (RR = 1.56), diabetes (RR = 2.75), head and neck radiation (RR = 2.73), and postmenopausal estrogen therapy (RR = 2.55) were correlated with a significantly increased failure rate. Overall, implant failure was 8.16% in the maxilla and 4.93% in the mandible (*P < *.001).* ***Discussion:*** *Patients who were over age 60, smoked, had a history of diabetes or head and neck radiation, or were postmenopausal and on hormone replacement therapy experienced significantly increased implant failure compared with healthy patients.* ***Conclusion:*** *Overall, dental implant failure is low and there are no absolute contraindications to implant placement. Conditions that were found to be correlated with an increased risk of failure should be considered during treatment planning and factored into the informed consent process.* (More than 50 references.) Int J Oral Maxillofac Implants 2005;20:569–577

Key words: *dental implants, implant failure, medical risk factors, osseointegration*

Despite the predictability of dental implants for orofacial rehabilitation, a small but significant subset of patients continue to experience implant failure. The identification of patients most at risk for dental implant failure is essential to the informed consent process and for treatment planning. Empirical information has associated a variety of risk factors ranging from implant design to coexisting systemic disease with adverse outcomes. With the continuing refinement of the technical aspects of implant surgery, increasing interest is focused on patient- and disease-related variables that may influence implant integration and success.

In some articles, diabetes, osteoporosis, steroid therapy, chemotherapy, and head and neck irradiation have been regarded as contraindications for dental implant placement.[1–4] However, other studies have shown that individual medical problems do not correlate with increased implant failure and that implant success is influenced rather by bone quantity and quality and by surgical technique.[3,5–11] Because of conflicting data from studies with small sample sizes or case series, or studies involving multiple surgeons, clinicians are unable to provide con-

[1]Adjunct Associate Professor, Oral and Maxillofacial Surgery, University of California at Los Angeles, School of Dentistry, Los Angeles, California.
[2]Resident, Temple University, Oral and Maxillofacial Surgery, Philadelphia, Pennsylvania.
[3]Professor, Oral and Maxillofacial Surgery, University of California at Los Angeles, School of Dentistry, Los Angeles, California.
[4]Assistant Professor, Oral and Maxillofacial Surgery, University of California at Los Angeles, School of Dentistry, Los Angeles, California.

Correspondence to: Dr Tara L. Aghaloo, Oral and Maxillofacial Surgery, UCLA School of Dentistry, 10833 Le Conte Avenue, Room A0-156, Los Angeles, CA 90095-1668. Fax: +310 794 2198. E-mail: taghaloo@ucla.edu

This paper was presented at the 18th Annual Meeting of the Academy of Osseointegration, February 17–21, 2003, Boston, Massachusetts.

crete answers to questions posed by patients seeking dental implant treatment. It would be helpful to identify a minimal set of patient- and disease-related factors that increase the risk of implant failure. With this information, the clinician would be able to take additional precautionary measures where indicated (eg, placing an extra implant, using longer healing periods, using pre-implantation hyperbaric oxygen in radiated patients).

To test the hypothesis that coexisting conditions (such as smoking, diabetes, and radiation therapy) lead to increased rates of implant failure, a retrospective cohort analysis of dental implants placed in a consistent manner by a single surgeon was carried out.

MATERIALS AND METHODS

The study cohort consisted of a consecutive series of patients who had dental implants placed by the same surgeon over a 21-year period. Prior to surgery, a detailed health history was collected, and informed consent was obtained. Putative risk factors abstracted from the patient records included gender, age, location of implant, smoking history, and coexisting medical conditions such as insulin and non-insulin dependent diabetes, hypertension and coronary artery disease, asthma, steroid therapy, history of chemotherapy or head and neck radiation therapy, and treatment (or lack of treatment) with postmenopausal hormone replacement therapy (PMHRT). All implants were placed by the same surgeon using a consistent surgical protocol. The implant systems used over this long-term study evolved with the changes in implant technology. However, most of the implants, especially those with the longest follow-up, were machine-surfaced implants. Most of the cohort patients were followed longitudinally for up to 20 years. They were screened for complication by both the surgeon and the hygienist during implant maintenance care. Implant failure was defined as any condition that led to removal of the implant, both short- and long-term. Failure was recorded from the day of placement of the implant. Conditions that resulted in implant failure included implant mobility, pain, infection, fracture, intolerable paresthesia, anesthesia or dysesthesia, and radiographic bone loss greater than 50%.

Data Analyses

Patients consented to inclusion in the study and were assigned numbers to keep their identities anonymous during data analysis. Baseline characteristics of patients were summarized in terms of frequencies and percentages for the categorical variables (SPSS v. 10; SPSS, Chicago, IL). Univariate and multivariate logistic regression analyses were performed to evaluate the relationships between baseline characteristics and the occurrence of implant failure. Relative risks and odds ratios were calculated to compare the risk of developing implant failure with respect to patients who had an uneventful course. A full multivariate regression model was derived that included all the potential predictors. This model was simplified according to statistical criteria. Variables that showed no significant association with implant failure were excluded. To assess individual influence, a cumulative model was constructed starting with patient-related factors (age, gender, smoking behavior, and number of coexisting medical conditions). Subsequently, factors associated with compromised wound healing (diabetes, head and neck radiotherapy) were added. Finally, the total number of implants placed was included in the model.

RESULTS

A total of 4,680 implants were placed in 1,140 patients between December 1,1982 and July 21, 2003. The patients ranged in age from 12 to 94 years (median age = 58 years); there were more female patients than male patients (59.4% versus 40.6%). A total of 778 patients (68%) had 1 or more coexisting condition, and 69 patients (6%) had 3 or more conditions. Most patients (74%) were treated with 1 to 5 implants; 26% received 6 or more implants, and 1 patient received a total of 24 implants. Implants were successful in most patients (85.1%); however, 170 patients (14.9%) experienced at least 1 implant failure.

Table 1 shows the univariate relative risk of developing implant failure for all variables in relation to a successful outcome.

Implants placed within the maxilla experienced almost twice the failure rate of those placed in the mandible ($P < .001$). Of the implants placed in the maxilla, 198 (8.16%) failed; of those placed in the mandible, 111 (4.93%) failed. Table 2 further elaborates the specifics of implant failure by location. Implants placed in the anterior mandible had the lowest failure rate (2.89%) of any location. The failure rates in other locations ranged from 5.08% to 9.66%.

Multiple linear regression was performed to explore predictors of the number of failed implants per patient, using age, gender, coexisting conditions, and total implants placed as independent variables. Only total implants placed ($P = .001$), diabetes (($P = .044$), and PMHRT ($P = .001$) were significant predictors ($P < .05$) of implant failure. Subsequently, with respect to failed implants, stepwise logistic regres-

Table 1 Univariate Analysis—Relative Risk of Implant Failure

Variable	No. of patients (N = 1140)	Patient: Failure n (%)	Patient: Success n (%)	RR	95% CI
Age					
< 40	181	16 (8.84)	165 (91.16)	1.00	1.00
40–59	418	58 (13.30)	360 (86.70)	1.66	0.93, 2.98
60–79	499	89 (17.90)	410 (82.10)	2.24	1.28, 3.93*
> 79	42	7 (16.67)	35 (83.33)	2.06	0.78, 5.39
Gender					
Male	463	77 (16.63)	386 (83.37	1.00	1.00
Female	677	93 (13.74)	594 (86.26)	0.80	0.57, 1.11
Coexisting conditions					
Smoker	173	35 (20.23)	138 (79.77)	1.56	1.03, 2.36*
Hypertension	202	29 (14.36)	173 (85.64)	0.95	0.62, 1.46
Cardiac disease	106	16 (15.09)	90 (84.91)	1.02	0.58, 1.78
Pulmonary disease	75	10 (13.33)	65 (86.67)	0.87	0.44, 1.73
Diabetes	48	15 (31.25)	33 (68.75)	2.75	1.46, 5.18*
Steroids	78	9 (11.54)	69 (88.46)	0.73	0.36, 1.49
Chemotherapy	10	1 (10.00)	9 (90.00)	0.63	0.08, 5.02
Radiation therapy	22	7 (31.82)	15 (68.18)	2.73	1.10, 6.81*
PMHRT	161	44 (27.33)	117 (72.67)	2.55	1.72, 3.77*
No PMHRT	304	49 (16.12)	255 (83.88)	1.14	0.79, 1.63

RR = Relative risk of failure.
*Significant at $P < .05$.

sion was performed using the variables location, sex, age, smoking, hypertension, coronary artery disease, asthma, diabetes, steroids, chemotherapy, head and neck radiation therapy, PMHRT, and no PMHRT. Diabetes (RR = 1.94; ($P = .003$), smoking (RR = 1.39; ($P = .03$), and head and neck radiation (RR = 1.87; ($P = .05$) were significant predictors of implant failure. Furthermore, location of the implant had a significant effect on the failure rate. Keeping the other covariates constant, implants in the maxilla had a greater probability of failing compared with implants in the mandible (RR = 1.79, $P = .001$).

Implants in all patients were compared with implants in healthy and medically compromised patients to determine a difference in time when implants failed in a life table analysis (Fig 1). Failure trends were similar between healthy and medically compromised patients. However, after 10 years, more implants had failed in healthy patients than in medically compromised patients.

More implants failed in diabetics and in patients with previous head and neck radiation than in smokers. In smokers, most failures occurred within the first year, with very few failing at later time points. Diabetes patients had failures from the first few months, and the failures continued over the following 10 years. Radiation patients, however, experienced most failures within the first 2 years and had fewer failures after 5 or 10 years (Fig 2).

Table 2 Implant Failure as a Function of Location

Location	Implants: Placed	Implants: Failed	Failure rate (%)
Posterior right maxilla	687	61	8.88
Anterior maxilla	1,067	72	6.75
Posterior left maxilla	673	65	9.66
Posterior left mandible	793	52	6.56

DISCUSSION

The ability to anticipate outcomes is an essential part of risk management in an implant practice. Recognizing conditions that place the patient at a higher risk of failure will allow the surgeon to make informed decisions and refine the treatment plan to optimize the outcomes. Also, focusing on a select group of risk factors for implant failure and collecting data in a standardized manner allows for uniform surgical audit and reporting. This retrospective cohort study reviewed the outcomes of a large set of implants placed in a consistent fashion by a single oral and maxillofacial surgeon. In a hierarchy of evidence for evaluating dental implant literature, this individual cohort study observes subjects with different exposure levels over a long period of time to compare the incidence of failure. It is recognized, as stated by Eckert and associates, that transfer bias is possible, as are

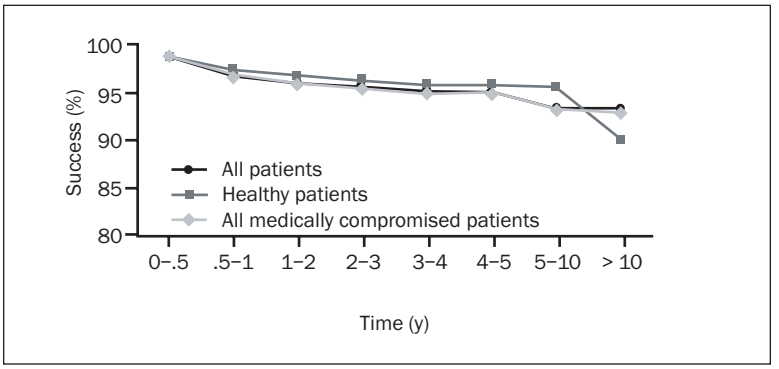

Fig 1 Life table analysis of implant failures over time. Data is shown for all implants, implants placed in healthy patients, and implants placed in medically compromised patients.

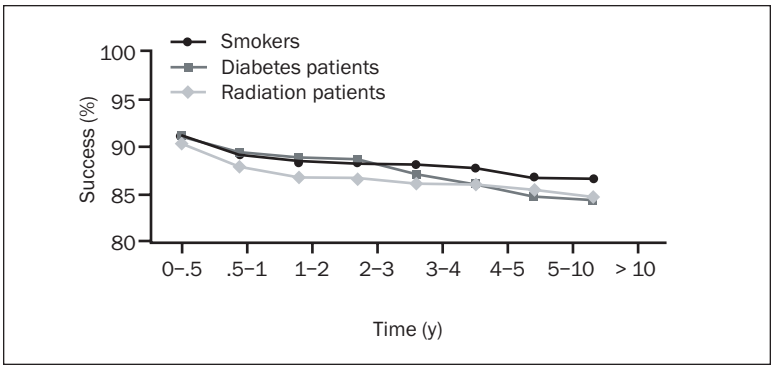

Fig 2 Life table analysis of implant success in smokers, patients with diabetes, and patients with previous head and neck radiation.

confounding variables related to incomplete control of prognostic baseline characteristics.[12] In general, the low failure rates documented reflect the predictability of dental implants. Not surprisingly, most of the variables associated with increased rates of implant failure corresponded closely with previously described risk factors for adverse surgical outcomes. Young, healthy patients had an implant success rate of 91.16%, which is consistent with previous studies.[13–18] Advanced age increased the risk of implant failure; patients older than 60 years were twice as likely to have adverse outcomes. Surprisingly, the risk of failure decreased slightly for patients older than 79 years. This observation may simply be a function of sample size, as there were more than 10 times the number of patients in the 60–79 age group than in the > 79 age group. One explanation for this phenomenon may be the loss of bone mineral associated with increasing age.[19] In an animal study regarding aging and implants, young rats had favorable, new trabecular bone growth around implants, with rapid contact at the implant bone interface. In contrast, the older rat group had a much smaller quantity of trabecular bone and less bone-to-implant contact.[20] Even though patient age is not classically thought of as a factor influencing implant success[21,22] or perioperative morbidity,[5] this study did show a statistically significant increase in failure in patients 60 to 79 years old. By itself, gender did not appear to influence the surgical outcomes relative to implant failure. The percentage of implant failures was comparable for both male and female groups, which corresponds closely to the results of Smith and coworkers.[5]

Not unexpectedly, patients who disclosed a history of smoking had a failure rate of 20%, with a 1.56 RR of failure compared to nonsmokers ($P < .05$). From the life table analysis, the majority of the failures in smokers occurred within the first year, with only few implants failing later in the follow-up period. These failure rates are somewhat higher than the previously reported rates of 6.50% and 11.28% in smokers.[23,24] Smoking causes both systemic and local injury to tissues. Smoking is a common contributor to decreased tissue oxygenation.[25] Carbon monoxide, oxidating radicals, nitrosamines, and nicotine are released during smoking. Nicotine causes a systemic increase in epinephrine, norepinephrine, and carboxyhemoglobin, and also decreases blood flow, collagen deposition, prostacyclin formation; it increases platelet aggregation, causes Polymorphonuclear neutrophil dysfunction, and increases fibrinogen, hemoglobin, and blood viscosity,[26–31] all of which negatively affect wound healing.[31–33] It has been concluded that long-term smoking results in poor bone quality and a poorer prognosis for implants.[34–36] Although a smoking cessation protocol was used in all patients, its relative success was not evaluated by this study.

Many of the patients seeking dental implant placement in this study were age 50 or older and had either coronary artery disease or hypertension. Of the 1,365 implants placed in these patients, the RR of implant failure was close to that of patients without these conditions. The data from this study suggest that there is no apparent contraindication to placing implants in patients with cardiovascular disease. These results are similar to those reported previously, where medical conditions such as cardiomyopathy, pericarditis, coronary artery disease, hypertension, cardiac arrhythmias, rheumatic heart disease, and congestive heart failure did not appear to contribute to perioperative implant complications.[5] A similar trend was observed in patients with asthma or chronic obstructive pulmonary disease. Asthma has not shown previously to have adverse effects on implant success. The effect of steriod therapy on dental implant failure is not known.

Although a patient with well-controlled diabetes may not be at a greater risk for impaired wound healing than a nondiabetic patient, the current study suggested otherwise. Even patients with controlled diabetes were almost 3 times as likely to develop implant failure compared to other patients. Diabetes has been mentioned as a relative contraindication to implant placement[1] and has been associated with life-threatening complications.[37] Microvascular disease of the gingiva in diabetic patients may adversely affect blood supply and contribute to delayed oral wound healing and susceptibility to infection.[38] Although there has been some conflicting evidence, diabetic patients may be more prone to infection.[5] Strict control of blood glucose is important in diabetic patients, and even starting non–insulin-dependent patients on an insulin regimen has been suggested.[38,39] Tissue hyperglycemia impacts every aspect of wound healing by adversely affecting the immune system, including neutrophil and lymphocyte function, chemotaxis, and phagocytosis.[40] Uncontrolled blood glucose hinders red blood cell permeability and impairs blood flow through the critical small vessels at the wound surface. The hemoglobin release of oxygen is impaired, resulting in an oxygen and nutrient deficit in the healing wound. Wound ischemia and impaired recruitment of cells resulting from small vessel occlusive disease renders the wound vulnerable to infections.[31] This study showed a 68.75% success rate in diabetic patients and an RR of failure of 2.75, which was statistically significant. These patients had failures beginning a few months postplacement and continuing for more than 10 years. Even though most of these patients were under adequate blood glucose control, this study was not specifically stratified for control of diabetes. Further studies are required to correlate implant failure with control of diabetes and other wound healing problems.

Patients take glucocorticoids for a variety of reasons, including, but not limited to, ulcerative colitis, Crohn's disease, asthma, systemic lupus erythematosus, pemphigus vulgaris, allergic reactions, organ transplantation, and Addison's disease.[41] Patients may take steroids for years or have only a short course. Steroids are known to cause a number of complications, including osteoporosis, delayed wound healing, and increased susceptibility to infection.[42] The success rate in patients in this study on steroid therapy was 88.46%. However, patients were not stratified for steroid dose or duration.

Many patients who have undergone chemotherapy with pre-existing implants have suffered serious complications and lost multiple implants.[43] However, in other cases, implants have been successful with chemotherapy treatments before and after implant placement.[7–9] Some studies have shown that chemotherapy is not detrimental to the survival or success of dental implants in the mandible,[44] and that it may not have a deleterious effect on implant osseointegration, particularly in early stages.[9] In the present study, data analysis revealed a success rate of 90% (RR = 0.63) in patients undergoing chemotherapy treatment. Although the sample size for these patients was small, no significant increase in implant failure was seen when compared with the healthy population.

Radiation has many deleterious effects, the most relevant to bony and soft tissue healing being hypocellularity, hypovascularity, and hypoxemia.[45–47] These changes in irradiated tissues contribute to an increased failure rate during the osteophyllic or osteoconductive phases of osseointegration.[48] Controversy exists with regard to head and neck irradiation patients and dental implants. Patients are living longer and functioning for long periods of time after curative head and neck cancer resection with adjuvant radiation. Prostheses improve patient quality of life, and dental implants often improve the success of these prostheses.

In this study, the 68.18% success rate is lower than those (83% to 88%) previously reported in studies of success in irradiated jaws,[48,49] and is significantly lower than that observed in healthy patients. For these patients, the risk of implant failure was 2.73 times higher, which was the highest of all medically compromised patients. Most of the implants failed in these patients within the first 2 years, and fewer failures were seen after 5 or 10 years. However, the benefits of dental implants may be greater than the risk of failure to improve patients' oral rehabilitation and quality of life. One controversy becomes apparent

when discussing hyperbaric oxygen (HBO) therapy and osteoradionecrosis.[50–52] A review of head and neck radiation found that overall incidence of osteoradionecrosis was between 3% and 22%.[53] Marx and colleagues reported a 24% reduction of osteoradionecrosis in HBO treated patients compared to non-HBO treated patients where both groups received antibiotics pre- and post-operatively.[54] Implant-associated osteoradionecrosis has been reported as 0.5% in patients who received HBO therapy.[48] However, when implant-associated osteoradionecrosis without HBO therapy was evaluated, only 3 cases were found in the literature.[55,56] No cases of osteoradionecrosis occurred in this study after implant placement. The risk of osteoradionecrosis exists with any surgical procedure after head and neck irradiation, regardless of HBO use.

A protocol has been previously described to maximize implant success and long-term survival in patients who have undergone head and neck irradiation. This protocol involves a delay in implant placement surgery until 6 months after radiation, thorough informed consent, smoking cessation, preoperative HBO therapy, increasing integration time by 3 months before uncovering and loading, overengineered/implant-supported prostheses, and a strict oral hygiene regimen.[52] Some very important surgical points include minimal and careful reflection of the periosteum, since it is the dominant blood supply in irradiated mandibles. Also, the largest and widest-diameter implants should be used to increase the surface area for osseointegration.[48] However, it is imperative for the surgeon to realize that the wider and deeper the drill goes, the more prevalent heat trauma to the fragile bone site becomes. It has been recommended that the time allowed for osseointegration before stage-2 surgery and loading be increased to 5 to 6 months in irradiated bone.[48,50]

Though increased age may be associated with increased implant failure, this study also evaluated systemic osteoporosis and its effect on implant failure. Well-known risk factors for osteoporosis include advanced age, smoking, steroid use, inadequate calcium intake, leanness, genetic predisposition, alcohol or coffee consumption, a sedentary lifestyle, and menopause.[57] Decreased bone mass in postmenopausal women involves the alveolar ridges, similar to other bones in the body.[19] Estrogen replacement therapy is associated with decreased risk of ischemic heart disease, decreased risk of cerebrovascular accident, and an improved cholesterol panel. In postmenopausal patients in this study, women on estrogen replacement had a significantly lower success rate. The likelihood of failure was 2.55 times higher for these patients than for the healthy population. Postmenopausal women not on hormone replacement therapy did not have this increased failure rate. The patients on estrogen therapy in this study may be a surrogate marker for osteoporosis. One study has indicated that hormone replacement therapy is not linked with improved outcome of endosseous dental implant placement in the mandible in postmenopausal women.[58] However, 1 study did show a reduced maxillary implant failure rate in postmenopausal women on estrogen therapy, although the difference was not statistically significant.[59] In patients with significant osteoporosis, it may be difficult to achieve immediate implant stability because of decreased trabecular bone mass. These patients may benefit from screw-type implants with large surface areas to maximize stability and facilitate integration.[2] In this study, patients were not stratified for the presence or absence of osteoporosis or number of postmenopausal years. A paucity of literature exists regarding this variable, and more research is necessary to draw definitive conclusions.

It has been hypothesized among implant practitioners that dental implant failure rate is higher in the maxilla than in the mandible,[17,60–64] with the area of lowest failure rate being the anterior mandible[62] and the highest being the posterior maxilla.[65] This study showed that implants placed in the maxilla had almost twice the failure rate of those placed in the mandible. The anterior mandible had a failure rate of 2.89% (20 of 692), followed by the posterior mandible (5.89%); 92 of 1,561) ($P < .001$), the anterior maxilla (6.75%; 72 of 1067), and the posterior maxilla (9.26%); 126 of 1360) ($P < .022$). Failure rates differed significantly between the anterior and posterior regions. The overall failure rate, including all areas of the mouth, was 6.60%, which is consistent with previous studies.[65] This study did not further stratify for area of implant placement with each individual medical risk factor. That is an important data set for future analysis.

When evaluating dental implants and their success and failure, it may be pertinent to compare them to other surgical prostheses such as total hip replacements. Dental implants are technically sensitive and rely on patient-related, clinician-related, and mechanical factors for predictable results. A recent study evaluated total hip replacement failure in patients to determine whether specific sociodemographic factors influenced failure.[66] Smoking was included, but it was not associated with an increase in relative risk of failure. However, the study included far fewer smokers than nonsmokers. Interestingly, the most common reasons for failure of total hip replacements are mechanical and biochemical, with loosening associated with postoperative patient activity, problems with cementation, wear particles of the

implants, tissue responses, and inflammatory mediators.[67] Local reaction causing granulomatous tissue in the area of the bone-to-implant interface has also been implicated.[68] One study also showed less failure with surgeons who performed high volumes of replacement surgeries.[69] Few studies have evaluated specific medical risk factors contributing to implant failure, such as age, smoking, diabetes, or osteoporosis.[66,70] However, one study did identify host factors such as osteoporosis as a risk factor for femoral fractures, leading to revision of total hip prosthesis.[71] Further studies have evaluated bisphosphonates as prophylactic therapy to reduce bone loss after total hip replacement, though pre-existing osteoporosis was not cited as a major reason for this bone loss and implant failure.[72,73]

Some limitations of this study include the presence of multiple confounding factors that could not be accounted for, based on the hierarchy of evidence.[12] These include the type of prosthetic restoration, expertise of the restorative dentist, and the evolution of dental implant systems throughout the long study period. Also, the single surgeon placing the implants in the study is very experienced, which may make the results of this study difficult to generalize to most practitioners. More long-term studies of dental implant success and failure are necessary to maximize the information available to patients so they can make educated decisions regarding risks and benefits of dental implant treatment.

CONCLUSION

Certain medical risk factors, including asthma, hypertension, and chronic steroid usage were not correlated with a significant increase in failure of dental implants. Significantly increased failure rates were seen in smokers, diabetics, patients with a history of head and neck radiation, and postmenopausal women on hormone replacement therapy. Even though these patients had a significantly increased failure rate in this study, the overall rate of failure is low. This study did not identify any medical risk factors that are absolute contraindications to dental implant placement.

ACKNOWLEDGMENTS

The authors would like to thank Gabriella Djerrahian and Sylvia Koo for assistance with data collection and Jun Xing for statistical support.

REFERENCES

1. Oikarinen K Raustia AM, Hartikainen M. General and local contraindications for endosseal implants- an epidemiological panoramic radiographic study in 65 year old subjects. Community Dentistry Oral Epidemiology 1995;23:114–118.
2. Blanchaert R. Implants in the medically challenged patient. Dent Clin North Am 1998;42 (1):35–45.
3. Matukas V. Medical risks associated with dental implants. J Dent Educ 1988;52:745–747.
4. Fugazotto P. Success and failure rates of osseointegrated implants in function in regenerated bone for 6 to 51 months: A preliminary report. Int J Oral Maxillofac Implants 1997;12:17–24.
5. Smith RA, Berger R, Dodson T. Risk factors associated with dental implants in healthy and medically compromised patients. Int J Oral Maxillofac Implants 1992;7:367–372.
6. Steiner M, Ramp W. Endosseous dental implants and the glucocorticoid-dependent patient. J Oral Implantol 1990;16(3):211–216.
7. Sager R, Theis R. Dental implants placed in a patient with multiple myeloma: Report of a case. J American Dent Assoc 1990;121:699–701.
8. Steiner M, Windchy A, Gould A, Kushner G, Weber R. Effects of chemotherapy in patients with dental implants. J Oral Implantol 1995;21(2):142–146.
9. McDonald A, Pogrel MA, Sharma A.Effects of chemotherapy on osseointegration of implants: a case report. J Oral Implantol 1998;24:11–13.
10. Cuenin M, Billman MA, Kudryk VL, Hanson BS. Estrogenic hormones and dental implant therapy: The effects of estrogen and progesterone levels on osseointegration of dental implants. Mil Med 1997;162:582–584.
11. Fritz M. Implant Therapy II. Ann Periodontol 1996;1:796–815.
12. Eckert S, Choi YG, Koka S. Methods for comparing the results of different studies. Int J Oral Maxillofac Implants 2003;18:697–705.
13. Kent J, Block MS, Finger IM, et al. Biointegrated hydroxylapatite-coated dental implants: 5-year clinical observations. J Am Dent Assoc 1990;121:138–144.
14. Adell R, Lekholm U, Rockler B, Brånemark P-I. A 15 year study of osseointegrated implants in the treatment of the edentulous jaw. Int J Oral Surg 1981;10:387–416.
15. Albrektsson T. A multicenter report on osseointegrated oral implants. J Prosthet Dent 1988;60:75–84.
16. Albrektsson T, Dahl E, Enbom L, et al. Osseointegrated oral implants: A Swedish multicenter study of 8139 consecutively inserted Nobelpharma implants. J Periodontol 1988;59:287–296.
17. Adell R, Eriksson B, Lekholm U, Brånemark PI, Jemt T. A long-term follow-up study of osseointegrated implants in the treatment of totally edentulous jaws. Int J Oral Maxillofac Implants 1990;5:347–359.
18. Brånemark PI, Hansson BO, Adell R, et al. Osseointegrated implants in the treatment of edentulous jaws. Scand J Plast Reconstr Surg Suppl 1977;16:1–32.
19. Humphries S. A radiographic investigation into bone resorption of mandibular alveolar bone in elderly edentulous adults. J Dent 1989;17:94–96.
20. Shirota T, Ohno K, Suzuki K, et al. The effect of aging on the healing of hydroxylapatite implants. J Oral Maxillofac Surg 1993;51:51–56.
21. Garg A, Winkler S, Bakaeen LG, et al. Dental implants and the geriatric patient. Implant Dent 1997;6:168–173.

22. Dao TT, Anderson JD, Zarb GA, et al. Is osteoporosis a risk factor for osseointegration of dental implants? Int J Oral Maxillofac Implants 1993;8:137–144.
23. Bain C, Moy P. The association between the failure of dental implants and cigarette smoking. Int J Oral Maxillofac Implants 1993;8:609–615.
24. Gorman LM, Lambert PM, Morris HF, Ochi S, Winkler S. The effect of smoking on implant survival at second stage surgery: DICRG Interim Report No. 5. Implant Dent 1994;3:165–168.
25. Krueger JK, Rohrich RJ. Clearing the smoke: The scientific rationale for tobacco abstention with plastic surgery. Plast Reconstr Surg 2001;108:1063–1073.
26. Cryer P, Haymond MW, Santiago JV, Shah SD. Norepinephrine and epinephrine release and adrenergic mediation of smoking-associated hemodynamic and metabolic events. New Eng J Med 1976;295:573–577.
27. Sarin C, Austin JC, Nickel WO. Effects of smoking on digital blood-flow velocity. J Am Med Assoc 1974;229:1327–1328.
28. MacFarlane G, Herzberg MC, Wolff LF, Hardie NA. Refractory periodontitis associated with abnormal polymorphonuclear leukocyte phagocytosis and cigarette smoking. J Periodontol 1992;63:908–913.
29. Noble R, Penny, B. Comparison of leukocyte count and function in smoking and nonsmoking young men. Infect Immun 1975;12:550–555.
30. Kenney EB, Kraal JH, Saxe SR, Jones J. The effect of cigarette smoke on human oral polymorphonuclear leukocytes. J Periodont Res 1977;12:227–234.
31. Shetty V, Bertolami C. Wound healing. In: Moloro M (ed). Peterson's Principles of Oral and Maxillofacial Surgery, ed 2. St Louis: BC Decker, 2004:3–15.
32. Mosely L, Finseth F, Goody M. Nicotine and its effect on wound healing. Plast Reconstruct Surg 1978;61:570–575.
33. Jones J, Triplett R. The relationship of cigarette smoking to impaired intraoral wound healing. J Oral Maxillofac Surg 1992;50:237–239.
34. Haas R, Haimbock W, Mailath G, et al. The relationship of smoking on peri-implant tissue: A retrospective study. J Prosthet Dent 1996;76:592–596.
35. Lindquist LW, Carlsson GE, Jemt T. Association between marginal bone loss around osseointegrated mandibular implants and smoking habits: A 10 year follow-up study. J Dent Res 1997;76:1667–1674.
36. Crews KM, Cobb GW, Seago D, Williams N. Tobacco and dental implants. Gen Dent 1999:484–488.
37. Li K, Varvares MA, Meara JG. Descending necrotizing mediastinitis: A complication of dental implant surgery. Head Neck 1996;18:192–196.
38. Shernoff AF, Colwell JA, Bingham SF. Implants for type II diabetic patients: Interim report. Implant Dent 1994;3:183–185.
39. Farzad P, Andersson L, Nyberg J. Dental implant treatment in diabetic patients. Implant Dent 2002;1:262–267.
40. Goodson WH, Hunt TK. Wound healing in well-controlled diabetic men. Surg Forum 1984;35:614–616.
41. Holland E, Taylor A. Glucocorticoids in clinical practice. J Family Pract 1991;32:512–519.
42. Haick A, Johnson D, Raju S. Vitamin A does not alter immunosuppressive properties of simultaneously administered steroids. Am Surgeon 1981;47:533–537.
43. Karr R, Kramer DC, Toth BB. Dental implants and chemotherapy complications. J Prosthet Dent 1992;67:683–687.
44. Kovacs A. Influence of chemotherapy on endosteal implant survival and success in oral cancer patients. Int J Oral Maxillofac Surg 2001;30:144–147.
45. Marx R, Johnson R. Studies in the radiobiology of osteoradionecrosis and their clinical significance. Oral Surg Oral Med Oral Pathol 1987;64:379–390.
46. Marx R. Osteoradionecrosis: A new concept in its pathophysiology. J Oral Maxillofac Surg 1983;41:283–288.
47. Marx R. A new concept in the treatment of osteoradionecrosis. J Oral Maxillofac Surg 1983;41:351–357.
48. Marx RE, Morales MJ. The use of implants in the reconstruction of oral cancer patients. Dent Clin North Am 1998;42:177–202.
49. Arcuri M, Fridrich KL, Funk GF, Tabor MW, LaVelle WE. Titanium osseointegrated implants combined with hyperbaric oxygen therapy in previously irradiated mandibles. J Prosthet Dent 1997;77:177–183.
50. Brogniez V, D'Hoore W, Gregoire V, Munting E, Reychler H.. Dental prosthetic reconstruction of osseointegrated implants placed in irradiated bone. Int J Oral Maxillofac Implants 1998;13:506–512.
51. Keller EE. Placement of dental implants in the irradiated mandible: A protocol without adjunctive hyperbaric oxygen therapy. J Oral Maxillofac Surg 1997;55:972–980.
52. Larsen PE. Placement of dental implants in the irradiated mandible: A protocol involving adjunctive hyperbaric oxygen. J Oral Maxillofac Surg 1997;55:967–971.
53. Aitasalo K. Bone tissue response to irradiation and treatment model of mandibular irradiation injury. Acta Otolaryngol 1986; 428:0(suppl):1–54.
54. Marx R, Johnson RP, Kline SN. Prevention of osteoradionecrosis: A randomized prospective clinical trial of hyperbaric oxygen versus penicillin. J Am Dent Assoc 1985;111:49–54.
55. Watzinger F, Ewers R, Ewers R, et al. Endosteal implants in the irradiated lower jaw. J Craniomaxillofac Surg 1996;24:237–244.
56. Esser E, Wagner W. Dental implants following radical oral cancer surgery and adjuvant radiotherapy. Int J Oral Maxillofac Implants 1997;12:552–557.
57. Jeffcoat M, Chesnut C. Systemic osteoporosis and oral bone loss: Evidence shows increased risk factors. J Am Dental Assoc 1993;124:49–56.
58. Minsk L, Polson AM. Dental implant outcomes in postmenopausal women undergoing hormone replacement. Compendium 1998;19:859–864.
59. August M, Chung K, Chang Y, Glowaki J. Influence of estrogen status on endosseous implant osseointegration. J Oral Maxillofac Surg 2001;59:1285-1289.
60. Buser D, Mericske-Stern R, et al. Long-term evaluation of non-submerged ITI implants. Part 1: 8-year life table analysis of a prospective multi-center study with 2359 implants. Clin Oral Implants Res 1997;8:161–172.
61. Lekholm U, Gunne J, Henry P, et al. Survival of the Brånemark implant in partially edentulous jaws: A 10-year prospective multicenter study. Int J Oral Maxillofac Implants 1999;14:639–645.
62. Davarpanah M, Martinez H, Etienne D, et al. A prospective multicenter evaluation of 1,583 3i implants: 1- to 5- year data. Int J Oral Maxillofac Implants 2002;17:820–828.
63. Eckert SE, Wollan PC. Retrospective review of 1170 endosseous implants placed in partially edentulous jaws. J Prosthet Dent 1998;79:415–421.
64. Parein AM, Eckert SE, Wollan PC, Keller EE. Implant reconstruction in the posterior mandible: A long-term retrospective study. J Prosthet Dent 1997;78:34–42.
65. Weng D, Jacobson Z, Tarnow D, et al. A prospective multicenter clinical trial of 3i machined-surface implants: Results after 6 years of follow-up. Int J Oral Maxillofac Implants 2003;18:417–423.

66. Inoue K, Ushiyama T, Tani Y, Hukuda S. Sociodemographic factors and failure of hip arthroplasty. Int Orthopaedics 1999;23:330–333.
67. El-Warrak AO, Olmstead M, Schneider R, et al. An experimental animal model of aseptic loosening of hip prostheses in sheep to study early biochemical changes at the interface membrane. BMC Central Musculoskelet Disord 2004;5:7.
68. McCombe P, Williams SA. A comparison of polyethylene wear rates between cemented and cementless cups. A prospective, randomized trial. J Bone Joint Surg Br 2004;86:344–349.
69. Losina E, Barrett J, Mahomed NN, Baron JA, Katz JN. Early failures of total hip replacement: Effect of surgeon volume. Arthritis Rheum 2004;50:1338–1343.
70. Wu CC, Au MK, Wu SS, Lin LC. Risk factors for postoperative femoral fracture in cementless hip arthroplasty. J Formos Med Assoc 1999;98:190–194.
71. Nelson CL. Periprosthetic fractures of the femur following hip arthroplasty. Am J Orthop 2002;31:221–223.
72. Yamaguchi K, Masuhara K, Yamasaki S, Nakai T, Fuji T. Cyclic therapy with etidronate has a therapeutic effect against local osteoporosis after cementless total hip arthroplasty. Bone 2003;33:144–149.
73. Wilkinson JM, Stockley I, Peel NF, et al. Effect of pamidronate in preventing local bone loss after total hip arthroplasty: a randomized, double-blind, controlled trial. J Bone Miner Res 2001;16:556–564.