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Risk Factors for Endosseous Dental Implant Failure

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A recent report published by the American Dental Association Council on Scientific Affairs recognized the consistently high rate of endosseous dental implant success or survival in human clinical trials [1]. For example, in 14 trials spanning follow-up periods of 2 to 16 years and involving over 10,000 dental implants placed in edentulous, partially edentulous, or single-tooth replacement cases, the overall mean survival rate was 94.4% with a range between 76% and 98.7% [2–15]. Implant survival rates also remain high for grafted bone (86.8%) [16–24] and for immediate loading protocols (94.0%) [25–27]. Still, these figures indicate a small but relevant implant failure rate of less than 10% overall, in which the implant is lost, fractured, or mobile; is a source of irreversible pain or infection; or coincides with peri-implant radiolucency or critical crestal bone loss [28]. Implant failures are usually classified either as early, when osseointegration fails to occur, or as late, when the achieved osseointegration is lost after a period of function. Implant failures may also be categorized as biological (eg, due to infection) or mechanical (eg, fracture). This article examines the available evidence on risk factors for implant failure. This should provide the basis for clinicians to better understand the role of device, procedural, anatomic, systemic, occlusal, microbial, immuno-inflammatory, and genetic factors that may indicate or cause an implant loss. With this understanding, clinicians can select appropriate cases or interventions that may enhance dental implant success.

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Device and procedural factors

Esposito and coworkers [29] conducted a recent systematic review and meta-analysis to determine whether different dental implant materials, shapes, and surface properties affect success rates. Twelve randomized clinical trials spanning at least 1 year were identified and included in the review. Overall, these trials represented 512 patients and constituted 12 implant types, all commercially pure titanium but with different shapes and surface preparations. On a per-patient basis, rather than a per-implant basis, no significant differences were observed between various implant types for implant failures. There were statistically significant differences for peri-implant bone-level changes on intraoral radiographs in three comparisons in two trials. However, these differences disappeared in the meta-analysis. More implants with rough surfaces were affected by peri-implantitis (relative risk = 0.80; 95% CI 0.67–0.96). This meta-analysis of the available evidence indicates that titanium implants with different shapes and surface preparations have similar success rates, but that smooth implants, compared to rough implants, appear to be less prone to peri-implantitis.

Several recent trials suggest that different implant dimensions are associated with different failure rates (Fig. 1). In a secondary analysis of 2,917 implants, Winkler and coworkers [30] reported a significantly lower mean 3-year survival for implants <4 mm in diameter (90.7%) versus survival for implants ≥ 4 mm in diameter (94.6%). Survival also significantly differed for 7-mm long (66.7%) implants versus 16-mm implants (96.4%). These outcomes did not change when clustering was considered, although the *P* values increased slightly. Chuang and coworkers [31] similarly conducted a multivariate analysis of clinical data on 677 patients and 2,349 implants. These investigators also found a significant association between short implants and implant failure. Shin and coworkers [32] compared survival rates for 64 wide-bodied implants placed consecutively in the posterior jaws of 43 patients and those for 64 regular-diameter implants (3.75 mm or 4 mm in

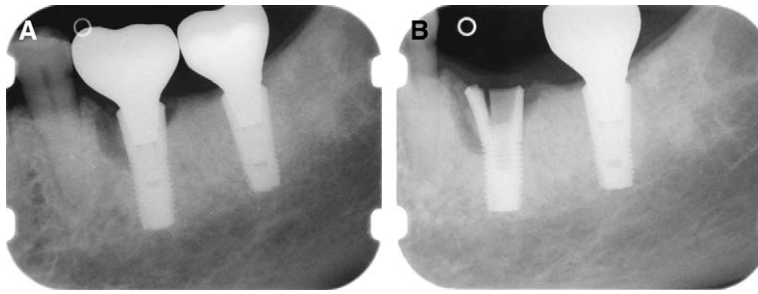

Fig. 1. Periapical radiograph of endosseous implant indicating peri-implant bone loss (*A*) and following removal of the prosthesis and abutment (*B*). The case was diagnosed with a fractured implant (technical failure) most likely due to short implant length and occlusal load.

diameter) placed in the posterior jaws of 25 of the same patients plus 14 others. The investigators observed 10 failures among the wide-bodied implants versus 2 for regular-diameter implants Multivariate analysis demonstrated a significant predictive relationship between overall cumulative survival rates and the ratio of implant volume to remaining-bone volume. The investigators postulated that the increased failure susceptibility for wide-bodied fixtures may relate to either implant design or the relative relationship of implant to host-bone dimensions. Hence, implant length and diameter, while selected on the basis of bone volume, present differences in risk for implant failure.

Degini and coworkers [33] recently assessed the relationship between implant dimension and survival in the context of immediate functional loading of the edentulous maxilla. For 388 implants in 43 patients, the crude 5-year survival rate was 98% with all failures occurring within 6 months from loading. Significant factors determining survival included implant diameter (99.37% for diameter $\leq$5.25 mm versus 93.8% for diameter $>$5.25 mm), the number of implants placed (99.3% for $\leq$10 implants versus 96.3% for $>$10) and gender (97.1% for males versus 99.5% for females). Cox regression analysis showed that diameter of implants adjusted for patient age and gender was associated to an average risk of failure (hazard rate) of 3.13 (95% CI 1.04–9.43) per mm (from 3 to 6.5). These findings indicate that wider diameter implants are associated with a higher risk of failure in maxillary edentulous cases with immediate functional loading.

In contrast, different surgical techniques in placing dental implants do not appear to be associated with different survival rates. Coulthard and coworkers [34] tested this hypothesis in a systematic review and analysis that included four randomized controlled trials (six publications). Two different aspects of implant surgical technique were reported in these trials. These were (1) two versus four implants to support a mandibular overdenture, and (2) crestal versus vestibular incision for implant placement. At the patient level, the investigators found no statistically significant differences for any of these alternative techniques with respect to implant failures, marginal bone levels, morbidity, or patient satisfaction.

Anatomic and osseous factors

Clinical studies consistently demonstrate patient anatomy and bone quality as important determinants of dental implant survival. For example, Herrmann and coworkers [35] recently analyzed an extant database involving 487 implants followed for 5 years. Significant determinants for implant failure were poor bone quality (type 4), a resorbed jaw, short implant length (7 mm), overdenture treatment protocol, and combination jawbone-related characteristics. Accordingly, 65% of the patients with a combination of poor bone quality and resorbed jaw (3% of the total study population) experienced implant failure (Fig. 2). These data indicate that patient

anatomic and bone characteristics independently or simultaneously can affect implant success.

Naert and coworkers [36] collected outcomes on 1,956 dental implants in 660 partially edentulous patients to identify anatomic and other factors predictive of implant success. The estimated cumulative survival rates were 91.4% for all implants and 95.8% for all restorations over a period of 16 years. Neither jaw site (maxilla versus mandible) nor implant position (anterior versus posterior) had any significant effect on implant survival. The investigators also reported that short implant length, high number of implants per patient, low number of implants per prosthesis, implants loaded by acrylic-veneered restorations, and implants combined with bone grafting present a higher risk for implant failure.

Clinicians should recognize peri-implant bone resorption occurring in the interval between first- and second-stage surgeries (for two-stage implant systems) as predictive of implant failure. In a retrospective cohort study, Strietzel and coworkers [37] assessed treatment outcomes for 504 patients constituting 1,554 implants followed for approximately 6 years on average. Overall, the implant survival rate of 92.6% in the maxilla remained constant after 68 months of observation. In the mandible, the implant survival rate of 96.7% showed no changes after 76 months. Statistically significant correlations were found between the incidence of implant failure and vertical bone loss adjacent to the implant at the time of second-stage surgery. In addition,

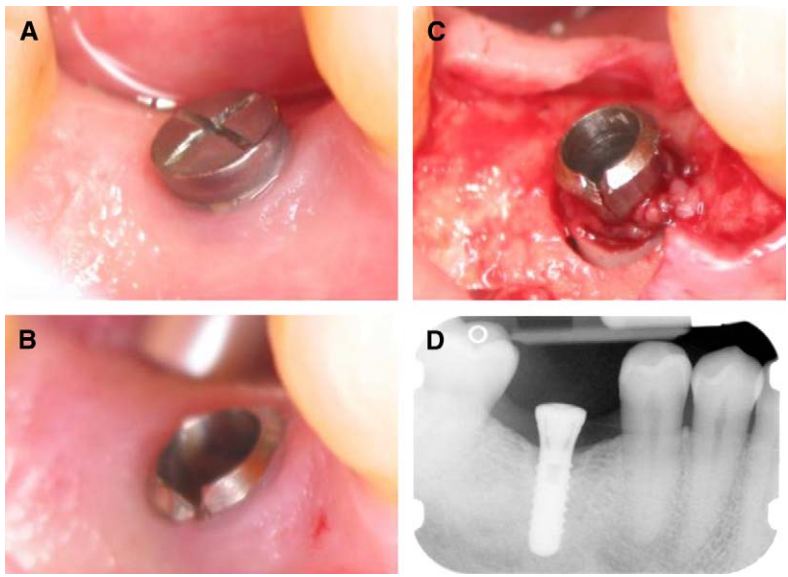

Fig. 2. (*A*) Implant with soft tissue inflammation and suppuration. (*B*) Implant fracture revealed after healing abutment removed. (*C*) Flap elevation and trephining to remove the fractured fixture. (*D*) Preoperative periapical radiograph indicates peri-implant bone loss.

a multivariate Cox regression showed that subject gender (male), jaw (maxilla) and the occurrence of postoperative complications were factors that increased the risk of implant loss. Hence, peri-implant bone resorption before loading along with other factors may compromise implant success.

In a recent, small clinical trial, Widmark and coworkers [38] randomized 43 subjects with resorbed maxillae to one of three treatment groups: (1) bone grafting and implant placement, (2) modified implant placement but no bone grafting (nongrafted control), or (3) optimized complete dentures (negative control). At the 1-year follow-up, 10% (22 of 221) of the implants had been lost, and at the 2-year follow-up, 18% of the implants had been lost (40 of 221 with 25% in the grafted versus 13% in the nongrafted control group). Following years 2 to 5, no further losses occurred. Life-table analysis showed cumulative success rates of 82% in the grafted group and 96% in the nongrafted control group after 1 year, and 74% in the grafted group and 87% in the nongrafted control group at the final examination after 3 to 5 years. Woo and coworkers [39] conducted a larger cohort study involving 677 patients, each with one implant, randomly selected for analysis. The overall implant survival rates were 95.2% after 1 year and 90.2% after 5 years. In the multivariate model, patients with osseous grafting (ie, dento-alveolar reconstructive procedures including sinus augmentation, onlay bone grafting and guided bone regeneration with autogenous bone or substitutes) did not have a statistically significant increased risk for implant failure (odds ratio = 1.4, 95% CI 0.7–2.9). Bivariate analyses revealed that only four factors were statistically or nearly statistically associated with implant failure. These included current tobacco use, implant length, implant staging, and type of prosthesis. The results of this comprehensive study indicate that the use of bone-grafting procedures to reconstruct deficient implant recipient sites is not an independent risk factor for implant failure.

Factors related to occlusion or loading

While restoration of occlusal function is a principal objective of implant therapy, parafunctional and excessive loading may present different risks for failure, including implant fracture [40]. Bragger and coworkers [41] compared the frequency of technical or occlusal complications occurring for implant-supported fixed partial dentures (FPDs), tooth-supported FPDs and mixed (implant- and tooth-supported) FPDs. Eighty-eight partially edentulous subjects were treated and followed for 4 to 5 years with FPDs in function. Complete failures resulted in the loss of one FPD per group. Significantly more technical complications were found for implant-supported FPDs and for cases with bruxism. Of the 10 bruxers, 6 (60%) exhibited a technical complication whereas 13 of the 75 (17%) nonbruxers exhibited a complication. Extensions (cantilevers) were associated with more technical complications (37% with extensions versus 11%

without). These data indicate that bruxism and extensions were associated with more technical failures for implants loaded under a conventional protocol.

Glauser and coworkers [42] reported on treatment outcomes for 41 patients receiving 127 immediately loaded implants (76 maxillary and 51 mandibular). Of these patients, 71% received their prosthetic restoration the same day and the others within 11 days [43]. All prosthetic constructions were in full contact in centric occlusion. At 1 year, 21 implants (17.3%) were lost in 13 patients (including 7 maxillary implants lost in 1 patient). Implants in patients with a parafunctional habit (bruxers) were lost more frequently than those placed in patients with no parafunction (41% versus 12%, respectively). Of the immediately loaded implants placed in regions other than the posterior maxilla, 91% were successful, compared with 66% of immediately loaded implants placed in the posterior maxilla. Immediately loaded implants subjected to guided bone regeneration were more successful compared with those not subjected to regeneration procedures (90% versus 67%). Therefore, patient bruxism, clenching, and the posterior maxilla may reduce the likelihood of implant success under an immediate-loading protocol.

The opposing occlusion or dentition may also be a relevant determinant of implant success. Becktor and coworkers [43] retrospectively analyzed data obtained from 90 consecutive patients with edentulous maxillae autogenous bone grafting and endosseous implants (mean patient follow-up of 64.2 months). Accordingly, the investigators recorded the presence and distribution of the opposing mandibular teeth as a dependent variable. Of 643 maxillary implants placed, 118 (18.4%) were lost between implant placement and definitive prosthesis delivery. The type of mandibular dentition was significantly associated with implant failure during this time interval. In particular, patients with implants opposing unilateral occlusal support showed the highest rate of implant failure (43.8%). Implants that opposed a mandibular implant-supported fixed prosthesis demonstrated an implant failure rate of 14.3%, and in patients with a removable mandibular denture, the implant failure rate was 6.2%. Thus, unfavorable concentration of forces on the maxilla may contribute to increased risk of implant failure.

Esposito and coworkers [44] recently presented results from another systematic review and meta-analysis demonstrating no differences in implant survival with different times of loading. Five randomized control trials constituting 124 patients met study inclusion criteria. Within these studies, implants were immediately loaded after insertion (2 to 3 days), early loaded (6 weeks), or conventionally loaded (3 to 8 months) in edentulous mandibles of adequate bone quality and shape. On a per-patient basis, rather than per-implant basis, the investigators failed to detect any statistically significant differences for prosthesis failures, implant failures, and marginal bone loss on intra-oral radiographs among the three loading strategies.

While it is possible to successfully load oral implants immediately after their placement in carefully selected patients with mandibles of adequate bone density and height, it is yet unknown how predictable this approach is in other cases.

Systemic risk factors

Smoking, a prevalent behavior in our population, constitutes a systemic exposure or risk factor for several adverse health outcomes, including tooth and implant loss [45,46]. The rationale for poorer oral health among smokers is related to vasoconstriction and tissue hypoxia, reduced polymorphonuclear cell function, enhanced inflammatory mediator secretion, and persistence of the pathogenic biofilm [47]. Cohort and clinical trials of endosseous implants consistently rate smoking as a primary patient-centered risk factor for implant loss. In one retrospective cohort study, McDermott and coworkers [48] identified predictor variables (eg, demographic, medical history, implant-specific, anatomic, prosthetic, and reconstructive variables) for 677 patients receiving implant therapy and followed for 13 months on average. These investigators observed an overall frequency of implant complications of 13.9% (10.2% inflammatory, 2.7% prosthetic, and 1.0% operative). A multivariate Cox model revealed that smoking was statistically associated with an increased risk for overall complications or failure. Similarly, Vehemente and coworkers [49] conducted a retrospective study of predictor variables for implant success versus failure involving 677 patients. After adjusting for other covariates in a multivariate model, tobacco use was statistically associated with an increased risk for failure (hazard ratio = 4.36, 95% CI 1.94–9.77). These cumulative findings indicate that subjects who smoke are over four times more likely than nonsmokers to experience implant loss.

Endocrine disease, particularly diabetes, may also pose a systemic risk for implant failure among patients. Morris and coworkers [50] compared treatment outcomes for 255 implants placed in type-2 diabetic patients and 2,632 implants in nondiabetic controls. The primary model assuming independence showed that type-2 diabetic patients exhibited significantly more failures. Although surgeon experience did not affect implant survival overall, the use of adjunctive antimicrobials (eg, preoperative antibiotics or postoperative chlorhexidine mouth rinses) improved implant survival in type-2 diabetics relative to nondiabetics. This association between implant loss and diabetes is likely related to the formation of advanced glycation endproducts, exaggerated production of inflammatory mediators, and impairment in leukocyte function [51]. A recent report by Attard and Zarb [52] documents no differences in implant success rates for hypothyroid patients with replacement therapy versus matched controls.

Postmenopausal women may constitute another at-risk patient group because of decreased estrogen and progesterone levels and altered bone

metabolism. Indeed, this patient group does exhibit reduced alveolar bone density and mass [53]. August and coworkers [54] conducted a retrospective study to test the hypothesis that postmenopausal women have lower rates of osseointegration of endosseous dental implants than premenopausal women and male controls. Five hundred and twenty-six participants were grouped in five categories: (1) postmenopausal women without estrogen replacement therapy (ERT), (2) postmenopausal women with ERT, (3) premenopausal women, (4) men younger than 50, and (5) men older than 50. Successful osseointegration was defined as stability at uncovering using a manual torque wrench plus radiographic confirmation. Postmenopausal women without ERT exhibited the highest maxillary failure rate (13.6%), which was significantly greater than the rate for premenopausal women (6.3%) and for men over 50 (7.6%). Other comparisons in success rates for maxillary and mandibular fixture failed to reach statistical significance. These results suggest that estrogen deficiency and the resultant bony changes associated with menopause may be systemic risk factors for dental implant failure in the maxilla.

Microbial and host immuno-inflammatory factors

Peri-implantitis, defined as infection and inflammation affecting implant-supporting tissues, is a leading cause of late implant failures (Fig. 3). This prompts the question as to whether certain microbial exposures or inflammatory biomarkers may indicate increased risk for subsequent implant failure or loss. Rutar and coworkers [55] conducted a retrospective study to explore the relationship between the clinical and microbiological peri-implant conditions in 45 partially edentulous patients (64 implants). During 5 to 10 years between implant installation and final examination, 9 implants experienced one episode and an additional 6 implants two episodes of peri-implantitis (23% overall). Of the peri-implantitis sites, 4 implants showed cultural evidence for presence of *Porphyromonas gingivalis*, and 2 implants were positive for *Actinobacillus actinomycetemcomitans*. Statistical analysis also revealed a significant relationship between peri-implant probing depth

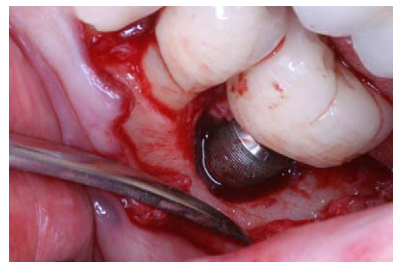

Fig. 3. Peri-implantitis and bony defect formation upon flap elevation and debridement (biological complication).

and the total anaerobic cultivable microbiota, as well as the frequency of detection of *P gingivalis*. These data implicate two putative pathogens of periodontitis with peri-implantitis and implant failure.

Salcetti and coworkers [56] conducted a case-control study comparing levels of bacterial pathogens, inflammatory mediators, and growth factors for failing (eg, evidence of peri-implant radiolucency or vertical bone loss >2 mm after 1 year of function) versus healthy implants. Twenty-one patients with failing implant sites (experimental group) and 8 patients with only healthy implants (control group) were included. Fifteen of the 21 failing-implant patients also presented with at least one stable nondiseased implant. Plaque samples were examined, using checkerboard DNA–DNA hybridization techniques. Peri-implant sulcus fluid samples were collected and analyzed for prostaglandin E_2 (PGE_2), interleukin-1β (IL-1β), IL-6, transforming growth factor-β (TGF-β), and platelet-derived growth factor (PDGF). Although positive trends were noted, there were no significant differences in any of the microbial factors, inflammatory mediators, or growth factors comparing failing to stable implants within the experimental group. In contrast, the investigators detected higher frequencies of *Prevotella nigrescens, Peptostreptococcus micros, Fusobacterium nucleatum ss vincentii,* and *F nucleatum ss nucleatum*, as well as significant elevations in sulcus fluid levels of PGE_2, IL-1β, and PDGF in mouths with failing-implant sites as compared with mouths with healthy control implants. The investigators concluded that risk appears to be primarily at a patient level and secondarily at a site or implant level from a clinical, microbial (*P micros and P nigrescens*), and biochemical (PGE_2 and IL-1β,) perspective. Furthermore, the counts of *P nigrescens* and *P micros* correlated with concentrations of PGE_2 at a site level. These data indicate that specific microbial exposures (orange complex) and the ensuing host inflammatory response are predictive of early implant disease [57].

Specific microbial exposures as assessed with serum antibody levels may also indicate elevated risk for implant failure. Kronstrom and coworkers [58] measured serum IgG antibody titers and avidity in 40 subjects with implant failure (nonosseointegration) and 40 age- and gender-matched control subjects with successful implants. The investigators noted significant elevations in serum IgG antibody titers to *Staphylococcus aureus* subjects with implant failures as compared with control subjects. They also observed significantly higher serum IgG antibody avidity to *P gingivalis* and *Tannerella forsythensis* in subjects with implant failures versus controls. Further analysis failed to demonstrate antibody titer or avidity differences for any of the other pathogens studied. The investigators concluded that serum IgG antibodies or exposure to *T forsythensis, P gingivalis*, and *S aureus* may be associated with the poor implant outcomes.

At least three clinical studies indicate that local elevations in matrix metalloproteinases (MMPs) accompany implant inflammatory and destructive tissue changes occurring around dental implants. Kivela-Rajamaki and

coworkers [59] analyzed peri-implant sulci fluid sampled from healthy versus untreated diseased implant sites for MMP concentrations using immunologic techniques. Accordingly, levels of active MMP-8 and MMP-7 were significantly elevated in diseased peri-implant sulcus fluid as compared with healthy controls. Furthermore, MMP-8 and MMP-7 levels correlated significantly to each other and to gingival index scores. Other cross-sectional studies have documented elevated peri-implant sulcular fluid levels for laminin-5 and gelatinase B at diseased sites relative to healthy sites [60,61]. Cumulatively, these findings demonstrate that host inflammatory biomarkers are up-regulated secondary to infection and that these biomarkers may be predictive of peri-implant tissue changes and ultimately implant failure.

Evidence on genetic risk markers for implant failure

To date, there is inconsistent evidence on any genetic risk factors for implant therapy. Studies in general have focused on genetic variations or polymorphisms for cytokines, such as IL-1, that are involved in bone turnover and resorption. Independent research has demonstrated that these cytokine polymorphisms indicate increased risk for advanced periodontitis or tooth loss in human populations [62,63]. Gruica and coworkers [64] demonstrated a positive association for the combination of IL-1 genotype plus heavy smoking with implant complications. These investigators conducted a retrospective analysis of 180 consecutive Swiss subjects followed for at least 8 years following implant and prosthetic treatments. Biological complications (Fig. 3) were defined as suppuration, fistula, and peri-implantitis with radiographic bone loss. Subjects were further classified on the basis of smoking status. Overall, 36% of subjects tested positive for the IL-1 genotype, and 17% of fixtures presented with a biological complication. Failures in general clustered in heavy smokers with the IL-1 genotype (50%). Jansson and coworkers [65] conducted a similar clinical study involving 22 partially edentulous Swedish patients who were treated with implants and who consented to genetic testing. For this cohort, the implant failure rate was 30.1%. Of these, 45% were smokers and 27% were IL-1 genotype positive. Patients positive for IL-1 genotype were more prone to implant loss, however, a synergistic effect between IL-1 genotype and smoking was noted. At least two other clinical studies report no detected association between the IL-1 genotype and implant failures in nonsmoking populations [66,67]. In addition, Campos and coworkers [68] report no association for TNF-α polymorphism and implant failure among a cohort of 66 Brazilian nonsmoking subjects. The limited data suggest that genetic polymorphisms related to cytokines may confer increased risk for dental implant failure at least among patients who smoke.

Summary

Clinical trials document a consistently high success rate for endosseous dental implants in partially and completely edentulous patients. Failures occur at a low rate but tend to cluster in those with common profiles or risk factors. These risk factors may be categorized as related to implant devices, procedures, anatomy, systemic health or exposures, occlusion, microbial biofilm, host immuno-inflammtory responses, and genetics. In general, factors related to the patient appear to be more critical than those related to the implant in determining the likelihood of implant failure [69]. Several of these risk factors can be modified. For example, the patient can modify smoking habits and the clinician can modify implant selection, site preparation, and loading strategy. Both the patient and clinician are important for long-term oral biofilm management and maintenance. In identifying these factors and making appropriate interventions, clinicians can enhance dental implant success rates for better oral function, esthetics, and patient well-being.

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