

Risk of Dental Implant Failure Associated With Medication Use

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Keywords

Clinical outcome; patient-based; risk assessment.

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The authors declare no conflict of interest related to this study.

Accepted November 27, 2017

doi: 10.1111/jopr.12773

Abstract

Purpose: The probability of achieving important clinical outcomes is an increasingly important factor for patients considering various treatment options for tooth loss. For oral reconstruction involving dental implants, the patient-specific risks of implant failure may be influenced by the patient's medication profile. The purpose of this study was to identify associations between dental implant failure and medication use in a consecutive series of patients seen from October 1983 through December 2014 at the Department of Dental Specialties, Mayo Clinic (Rochester, Minnesota).

Materials and Methods: In this patient-level analysis, demographic, implant-specific, and medical profile data were abstracted from a prospective clinical database and individual medical records and used to determine the time to first implant failure. Implant failure-free survival at the patient level was estimated using the Kaplan-Meier method. Associations of demographic characteristics and medication use with implant failure were evaluated by using Cox proportional hazards regression models and summarized with hazard ratios and 95% confidence intervals.

Results: In the 31-year study period, 6358 patients received their first dental implant (median age, 53 years). The median follow-up duration of the 5645 patients whose implants did not fail was 5.8 years, and 713 patients had implant failure (median, 0.6 years). All associations were adjusted for age, sex, and era of implantation because these features strongly influence medication use and implant failure. After adjustment, no medication increased the risk of implant failure in the cohort; specifically, medication use at the time of implant placement or starting a medication after implant placement did not increase the risk of implant failure. Among the medications used at the time of implant placement, corticosteroids were associated with a reduced risk of implant failure (hazard ratio, 0.82; 95% CI, 0.67-0.99; $p = 0.04$). This association was not seen when corticosteroids were started after implant placement.

Conclusion: In the population studied, medication use was not associated with an increased risk of dental implant failure.

Patients have multiple care options when seeking interventions for tooth loss. Clinicians can greatly facilitate the decision-making process by sharing information about the comparable risks and benefits of the available options within the context of short- and long-term outcomes.^{1,2} Prosthodontic options have expanded with the inclusion of dental implant-supported prostheses, and the field of prosthodontics believes achieving a core set of outcomes helps facilitate patient-provider discussions and quality improvement.³ The risk of implant failure is an outcome worth monitoring and discussing.⁴

The probability of achieving future outcomes is an increasingly important consideration.⁵ When applied to clinical prediction models, risk can be used to better inform individual patients when the risk model's variables match the patient's personal characteristics.⁶

Health care outcomes can be influenced by the individual patient's systemic condition and possibly the medications used to manage that condition. The medication profile is a particular concern, especially in patients with multiple chronic conditions.⁷ In 2012, about half of all American adults had more than one chronic health condition, and one in four adults had more than two chronic health conditions.⁸ Given this prevalence rate, and to better predict individual patient risk, understanding the potential impact of systemic conditions and medication use on dental implant failure is important.

The challenge is to identify the systemic risks that influence important processes related to implant wound healing and establishing and maintaining osseointegration when those systemic risks lead to implant failure.^{9,10} This patient-risk perspective seeks to answer the question, "Am I at greater risk for

implant failure because of my medication(s)?" The purpose of this study was to identify associations between implant failure and medication use in a cohort of consecutive patients.

Materials and methods

Patient selection

After receiving Mayo Clinic Institutional Review Board approval, we identified 6384 patients who received a dental implant at the Department of Dental Specialties, Mayo Clinic (Rochester, Minnesota) from October 1983 to December 2014. The patient cohort included more than 20,600 implants, but for analytic purposes, the date of first implant placement was used to establish the "at-risk" patient cohort.

Demographic features and systemic conditions

The collected demographic features included age at first implant placement, sex, race/ethnicity, and the era of the first implantation (1983-2000 or 2001-2014). The era of implantation reflects changes in Nobel Biocare implants (a turned screw that produces a surface with no design-specific roughness) relative to the TiUnite implant surface characteristics. The analyzed medications were divided into aspirin and six prescription drug classes: anticonvulsants, bisphosphonates (oral and intravenous [IV]), antihypertensives, antidepressants, and corticosteroids (Table 1). Aspirin, an over-the-counter medication, was included because of its prevalent use. Two temporal relationships of medication use and implant failure were analyzed: (1) when the medication was in use at the time of implant placement, and (2) when the medication was started after implant placement. In addition, the number of medications in use at the time of implant placement was analyzed to assess cumulative effects on implant failure.

Statistical analysis

The statistical analysis was applied at the patient level to determine the patient risk of implant failure. Continuous features are summarized as the medians, interquartile ranges (IQRs), and ranges; categorical features are summarized as frequency counts and percentages. The outcome of concern—implant failure—was defined as the first implant that failed in the patient. Implant failure-free survival at the patient level was estimated using the Kaplan-Meier method. For each patient, the follow-up duration was calculated as the date of first implant placement to the date of first implant failure or the date of the last follow-up. Using "first implant failure" as an outcome established the patient's experience with implant failure and statistically does not require the repeated-measures or cluster effect analyses that are needed when implant-level data are collected for device rate analyses.

The associations between the demographic features and medication use—medications in use at the patient's first implant placement and medications started after implant placement—and implant failure were evaluated using Cox proportional hazards regression models and are summarized with hazard ratios (HRs) and 95% confidence intervals (CIs). For patients identified who started medication use after implant placement, the analysis included medications as time-dependent covariates in the Cox proportional hazards regression models.

Table 1 List of prescription medications^a

| Generic name | Brand name ^b |
|---|---|
| Anticonvulsants | |
| Rufinamide | Banzel |
| Carbamazepine | Tegretol, Carbatrol |
| Methsuximide | Celontin |
| Divalproex sodium | Depakote, Depakote ER |
| Ethosuximide | Zarontin |
| Felbamate | Felbatol |
| Gabapentin | Neurontin |
| Tiagabine HCl | Gabitril |
| Lamotrigine | Lamictal, Lamictal ODT, Lamictal XR |
| Levetiracetam | Keppra, Keppra XR |
| Pregabalin | Lyrica |
| Oxcarbazepine | Trileptal |
| Ethotoin | Peganone |
| Phenytoin sodium | Dilantin |
| Primidone | Mysoline |
| Vigabatrin | Sabril |
| Topiramate | Topamax |
| Valproic acid | Depakene, Stavzor |
| Vimpat | Lacosamide |
| Zonisamide | Zonegran |
| Oral bisphosphonates | |
| Risedronate | Actonel, Actonel with calcium, Atelvia |
| Alendronate | Fosamax |
| Ibandronate | Boniva |
| Etidronate | Didronel |
| Tiludronate | Skelid |
| Alendronate with vitamin D | Fosamax Plus |
| Intravenous bisphosphonates | |
| Ibandronate | Boniva |
| Pamidronate | Aredia |
| Zoledronic | Reclast, Zometa |
| Antihypertensives (calcium channel blockers) | |
| Nifedipine | Afedintab CR, Adalat, Adalat CC, Nifedical XL, Procardia XL, Procardia |
| Nimodipine | Nimotop, Nymalize |
| Diltiazem | Dilt-XR, Diltia XT, Tiazac, Cardizem, Cartia XT, Dilacor XR, Diltzac, Matzim LA |
| Verapamil | Isoptin SR, Verelan PM, Calan SR, Covera-HS, Calan, Covera |
| Isradipine | DynaCirc |
| Antidepressants | |
| Vortioxetine | Brintellix |
| Levomilnacipran | Fetzima |
| Vilazodone | Viibryd |
| Citalopram | Celexa |
| Escitalopram | Lexapro, Cipralex |
| Fluoxetine | Prozac, Sarafem, Pexeva |
| Fluvoxamine | Luvox |
| Paroxetine | Paxil, Paxil CR |
| Sertraline | Zoloft |
| Amitriptyline | Elavil, Endep, Levate |
| Amoxapine | Asendin |
| Clomipramine | Anafranil |

(Continued)

Table 1 Continued

| Generic name | Brand name ^b |
|----------------------------|---|
| Desipramine | Norpramin, Pertofrane |
| Dosulepin | Prothiaden, Thaden |
| Doxepin | Adapin, Sinequan |
| Imipramine | Tofranil |
| Lofepramine | Gamanil, Lomont |
| Maprotiline | Deprilept, Ludiomil, Psymion |
| Mianserin | Bolvidon, Norval, Tolvan |
| Nortriptyline | Pamelor |
| Protriptyline | Vivactil |
| Trimipramine | Surmontil |
| Desvenlafaxine | Pristiq |
| Duloxetine | Cymbalta |
| Levomilnacipran | Fetzima |
| Milnacipran | Savella |
| Venlafaxine | Effexor, Effexor XR |
| Mirtazapine | Remeron, Remeron SolTab |
| Bupropion | Wellbutrin, Wellbutrin SR, Wellbutrin XL, Zyban, Aplenzin |
| Atomoxetine | Strattera |
| Agomelatine | Valdoxan |
| Buspirone | BuSpar |
| Nefazodone | Nefadar, Serzone |
| Tandospirone | Desyrel, Apo-Trazodone, Oleptro |
| Reboxetine | Edronax, Vestra |
| Viloxazine | Vivalan |
| Vortioxetine | Viiibryd |
| Vortioxetine | Brintellix |
| Fluoxetine-olanzapine | Symbyax |
| Amitriptyline- | Etrafon, Triavil |
| perphenazine | |
| Isocarboxazid | Marplan |
| Moclobemide | Manerix |
| Phenelzine | Nardil |
| Tranylcypromine | Parnate |
| Selegiline | Emsam |
| Lithium | Eskalith, Lithane, Lithobid |
| Quetiapine | Seroquel, Xeroquel, Ketipinor |
| Brexiprazole | Rexulti |
| Corticosteroids | |
| Methylprednisolone | Medrol |
| Prednisolone | Prelone |
| Beclomethasone | QVAR |
| Budesonide | Pulmicort Flexhaler |
| Flunisolide | Aerospam |
| Fluticasone | Flovent |
| Mometasone | Asmanex, Twisthaler |
| Budesonide and formoterol | Symbicort |
| Fluticasone and salmeterol | Advair |

^aAspirin was included in the analysis.

^bMayo Clinic does not endorse the specific products included in this article.

To prospectively apply practice-specific evidence to patient care, a multivariable model was developed to predict implant failure by using the stepwise selection of the features present at implant placement, with the P value set to 0.05 for a feature to enter or leave the model. Statistical analyses were performed

Table 2 Demographic features and medications in use at the date of first implant placement (N = 6358)

| Feature | No. (%) |
|--|-----------|
| Female sex | 3707 (58) |
| Race (n = 5882) | |
| White | 5480 (93) |
| Pacific Islander or Asian | 199 (3) |
| Black | 68 (1) |
| American Indian or Alaskan Native | 7 (<1) |
| Other | 128 (2) |
| Ethnicity (n = 5032) | |
| Not Hispanic or Latino | 4954 (98) |
| Hispanic or Latino | 45 (1) |
| South American | 18 (<1) |
| Central American | 5 (<1) |
| Mexican | 4 (<1) |
| Cuban | 3 (<1) |
| Puerto Rican | 3 (<1) |
| Era of first implantation | |
| 1983-2000 | 1872 (29) |
| 2001-2014 | 4486 (71) |
| Medications in use | |
| Anticonvulsants | 1656 (26) |
| Oral bisphosphonates | 314 (5) |
| Intravenous bisphosphonates | 30 (<1) |
| Antihypertensives | 548 (9) |
| Antidepressants | 1801 (28) |
| Aspirin | 2556 (40) |
| Corticosteroids | 1944 (31) |
| Number of medications | |
| 0 | 2491 (39) |
| 1 | 1349 (21) |
| 2 | 1026 (16) |
| 3 | 784 (12) |
| 4 | 484 (8) |
| 5 | 188 (3) |
| 6 | 32 (1) |
| 7 | 4 (<1) |
| Number of medications, not including aspirin | |
| 0 | 3023 (48) |
| 1 | 1498 (24) |
| 2 | 997 (16) |
| 3 | 600 (9) |
| 4 | 203 (3) |
| 5 | 33 (1) |
| 6 | 4 (<1) |

using SAS software (v9.4; SAS Institute Inc., Cary, NC). All tests were two-sided, and $p < 0.05$ was considered statistically significant.

Results

Twenty-six patients received no follow-up after first implant placement (0.4%) and were excluded, leaving 6358 patients in the analysis. The median age at first implant placement of the 6358 included patients was 53 years (IQR, 40-64 years; range, 8-95 years). Table 2 summarizes the remaining demographic

Table 3 Associations of demographic features and medication use at the date of first implant placement with time to implant failure (N = 6358)

| Characteristic | Univariable | | Age-, sex-, era-adjusted risk | |
|--|-------------------------------|----------------|----------------------------------|----------------|
| | HR (95% CI) | <i>p</i> Value | HR (95% CI) | <i>p</i> Value |
| Age | 1.04 (1.00-1.09) ^a | 0.07 | 1.05 (1.00-1.09) ^{a, b} | 0.04 |
| Sex | | | | |
| Female | 1.0 (reference) | | 1.0 (reference) | |
| Male | 1.23 (1.06-1.42) | 0.007 | 1.24 (1.07-1.44) ^c | 0.005 |
| Race (n = 5882) | | | | |
| White | 1.0 (reference) | | 1.0 (reference) | |
| All others | 1.15 (0.85-1.56) | 0.35 | 1.21 (0.89-1.63) | 0.22 |
| Ethnicity (n = 5032) | | | | |
| Not Hispanic or Latino | 1.0 (reference) | | 1.0 (reference) | |
| All others | 0.97 (0.48-1.95) | 0.94 | 0.90 (0.45-1.81) | 0.77 |
| Era of first implantation | | | | |
| 1983-2000 | 1.0 (reference) | | 1.0 (reference) | |
| 2001-2014 | 0.66 (0.56-0.76) | <0.001 | 0.65 (0.56-0.76) ^d | <0.001 |
| Medications in use | | | | |
| Anticonvulsants | 0.96 (0.80-1.16) | 0.67 | 1.15 (0.93-1.41) | 0.19 |
| Oral bisphosphonates | 0.82 (0.55-1.21) | 0.31 | 0.94 (0.63-1.41) | 0.76 |
| IV bisphosphonates | 1.14 (0.37-3.55) | 0.82 | 1.26 (0.40-3.92) | 0.69 |
| Calcium channel blockers | 0.76 (0.56-1.03) | 0.08 | 0.77 (0.56-1.06) | 0.11 |
| Antidepressants | 0.88 (0.74-1.04) | 0.14 | 1.04 (0.87-1.25) | 0.67 |
| Aspirin | 0.92 (0.79-1.08) | 0.29 | 1.05 (0.87-1.26) | 0.65 |
| Corticosteroids | 0.72 (0.60-0.86) | <0.001 | 0.82 (0.67-0.99) | 0.04 |
| Number of medications | 0.93 (0.88-0.98) ^e | 0.010 | 0.99 (0.92-1.06) ^e | 0.69 |
| Number of medications, not including aspirin | 0.90 (0.84-0.97) ^e | 0.006 | 0.97 (0.89-1.06) ^e | 0.49 |

Abbreviations: CI, confidence interval; HR, hazard ratio.

^aHR and CI represent a 10-year increase.

^bAdjusted for sex and era of implantation only.

^cAdjusted for age and era of implantation only.

^dAdjusted for age and sex only.

^eHR and CI represent a 1-medication increase.

features and medications in use at the date of first implant placement. The total number of medications in use was calculated; given the extensive use of aspirin, the impact of multiple medications was analyzed with and without including aspirin.

A total of 713 patients had implant failure at a median of 0.6 years after first implant placement (IQR, 0.3-3.0 years; range, 2 days to 27.4 years). The median follow-up duration of the 5645 patients who did not have implant failure was 5.8 years (IQR, 2.6-11.4 years; range, 1 day to 31.2 years), including 638 patients (11%) who received less than 1 year of follow-up.

Table 3 summarizes the univariable associations of demographic features and medications in use at the date of first implant placement with time to implant failure. Medication use was significantly associated with age (older patients were more likely to have a condition requiring medication), and some medications were significantly associated with sex (e.g., women were more likely to take antidepressants, men were more likely to take aspirin). In addition, the era of implantation was the strongest predictor of implant failure on the univariable analysis. After adjusting for age, sex, and era of implantation, only corticosteroids showed a significant and protective association with implant failure. Consideration was given to the cumulative influence of multiple medications on implant failure because of

Table 4 Multivariable associations of demographic features and medication use at date of first implant placement with time to implant failure

| Feature | HR (95% CI) | <i>p</i> Value |
|---------------------------|-------------------------------|----------------|
| Age | 1.06 (1.01-1.10) ^a | 0.02 |
| Sex | | |
| Female | 1.0 (reference) | |
| Male | 1.22 (1.06-1.42) | 0.01 |
| Era of first implantation | | |
| 1983-2000 | 1.0 (reference) | |
| 2001-2014 | 0.69 (0.59-0.81) | <0.001 |
| Corticosteroid use | 0.82 (0.67-0.99) | 0.04 |

Abbreviations: CI, confidence interval; HR, hazard ratio.

^aHR and CI represent a 10-year increase.

the potential comorbid influence of multiple medications. The use of multiple medications, including and excluding aspirin, showed no significant influence on implant failure, even after incrementally increasing the number of medications.

Table 4 summarizes the multivariable model. In the multivariable analysis, each 10-year increase in age was associated with a 6% increased risk of implant failure. Men were 22%

Table 5 Associations of medications started after the date of first implant placement with time to implant failure

| Medication | No. (%) ^a | Univariable | | Age-, sex-, era-adjusted risk | |
|--------------------------|----------------------|------------------|----------------|-------------------------------|----------------|
| | | HR (95% CI) | <i>p</i> Value | HR (95% CI) | <i>p</i> Value |
| Anticonvulsants | 1729/4702 (37) | 0.92 (0.68-1.24) | 0.58 | 1.10 (0.80-1.51) | 0.57 |
| Oral bisphosphonates | 279/6044 (5) | 1.18 (0.69-2.00) | 0.55 | 1.20 (0.70-2.05) | 0.50 |
| IV bisphosphonates | 88/6328 (1) | 0.49 (0.07-3.51) | 0.48 | 0.59 (0.08-3.92) | 0.55 |
| Calcium channel blockers | 497/5810 (9) | 1.00 (0.62-1.60) | 0.99 | 0.96 (0.60-1.54) | 0.86 |
| Antidepressants | 914/4557 (20) | 0.96 (0.68-1.37) | 0.83 | 1.02 (0.72-1.45) | 0.92 |
| Aspirin | 1402/3802 (37) | 0.87 (0.63-1.20) | 0.39 | 0.87 (0.63-1.22) | 0.42 |
| Corticosteroids | 1419/4414 (32) | 0.93 (0.68-1.28) | 0.66 | 1.02 (0.74-1.40) | 0.91 |

Abbreviations: CI, confidence interval; HR, hazard ratio.

^aNumber of patients who started medication after the date of first implant divided by number of patients at risk to start the medication during follow-up (%).

more likely to have implant failure compared with women. Patients whose first implant was placed between 2001 and 2014 were significantly less likely to have implant failure compared with those whose first implant was placed between 1983 and 2000. Corticosteroid use at the date of first implant placement was associated with a reduced risk of implant failure. No other medications were significantly associated with implant failure after adjusting for age, sex, era of implantation, and corticosteroid use.

Table 5 shows the associations between medications started after first implant placement and implant failure. No medication started after implant placement was associated with an increased risk of implant failure.

Discussion

Information about implant failure risk facilitates shared decision making with patients seeking surgical prosthodontic solutions for oral disability related to missing teeth. Patients of interest at our practice comprise the patient cohort, and the observed results could be generalized to direct future patient care.⁶ The results show no increased risk of implant failure associated with any of the evaluated medication categories after adjusting for important confounding variables that were significantly associated with implant failure. As a single study on implant failure risk among many, it is useful to consider what constitutes a favorable study characteristic that can identify valid risk estimates and how these findings compare to other reports on implant failure risk.

Comparing findings with previous reports

Many patients who present to reconstructive practices have multiple chronic diseases.⁸ Understanding how combinations of conditions impact disease burden, costs, and quality of care is critical.⁷ Although prescription drug use and polypharmacy (use of ≥ 5 prescription drugs) have increased since 2000,¹¹ we are unaware of failure risk studies that assess the use of multiple medications or medications started after implant placement.

Bisphosphonates

Biphosphonate use showed no differences in the risk of implant failure between patients receiving oral bisphosphonates (6 dif-

ferent medications; $n = 314$ patients with implants), patients receiving IV bisphosphonates (3 different medications; $n = 30$ patients with implants), and patients not receiving bisphosphonates. The literature is mixed about supporting or refuting the failure risk associated with bisphosphonate use and about the appropriate analytic approach (implant-level or patient-level analyses).

In a school-based study, Al-Sabbagh et al¹² sought to determine associations between selected risk factors and implant failure by using patient-reported outcomes. Patient- and implant-level data were analyzed, including the use of bisphosphonates. Patient-level multiple logistic regression analysis showed no impact of bisphosphonate use on implant survival; however, the adjusted implant-level analysis suggested an association between implant failure and bisphosphonate use.

Most publications have not shown sufficient evidence supporting an increased risk of implant failure because of bisphosphonate use. A systematic review pooled data from eight studies involving 386 case and 902 control patients and found no significant increased risk in implant failure in bisphosphonate-using patients compared with control patients.¹³

The clinical challenge posed by implant failure risk, as influenced by the class of medication, is shown by the findings of a systematic review of 50 publications that contained little information to summarize statistically.¹⁴ Another review, which included 15 studies and 1339 patients,¹⁵ reported that the data were inconclusive, as no pooled estimate was provided because of the lack of long-term follow-up data. The systematic review by Guazzo et al¹⁶ similarly stated that, because of study heterogeneity and the high risk of bias, insufficient data quality did not allow estimates of risk to be determined. Matsuo et al¹⁷ and Tallarico et al¹⁸ reported no increased risk in failure associated with IV or oral bisphosphonate use, respectively. The association between oral bisphosphonate use and dental implant failure was investigated in a case-control study involving 337 female patients (age ≥ 40 years).¹⁹ In that study, the odds of oral bisphosphonate use was 2.69 (95% CI, 1.49-4.86) times higher in women with implant failure (compared with durable implants); however, no significant interaction was observed ($p = 0.41$). A report on the influence of selective serotonin reuptake inhibitors (SSRIs) on implant failure addresses how such a seemingly inconsistent analytic conclusion between the implant failure rate and patient-based risk can be true,²⁰ and this inconsistency may

partially explain why variable reports on implant failure risk are seen in the literature.

Antihypertensive medications

Five calcium channel blockers, the only antihypertensive medications abstracted, were used among the 548 patients with implants in the antihypertensive medication category, and no increased risk of implant failure was identified. This finding was in contrast to a published study on medication users ($n = 142$) and nonusers ($n = 586$) that reported a reduced risk of implant failure in patients receiving hypertension medications.²¹ In that study, which analyzed implant-level failure, Wu *et al* found a higher implant survival rate among the users of antihypertensive medications than nonusers (HR, 0.12; 95% CI, 0.03-0.49).

Antidepressants

In the current study, 48 medications were used among the 1801 patients with implants in the antidepressant medication category, and no increased risk of implant failure was detected. The following SSRI reports vary in support of this finding. Wu *et al*²³ studied SSRI users ($n = 50$) and non-SSRI users ($n = 440$) during a 67-month period. They reported implant failure rates of 4.6% in non-SSRI users and 10.6% in SSRI users. After adjusting for sex, age, implant diameter, implant length, bone augmentation, and smoking status, they identified an association between implant failure and SSRI use (HR, 6.28; 95% CI, 1.25-31.61). Chrcanovic *et al*²⁰ also compared implant failure rates between SSRI users and non-SSRI users. They reported that SSRI intake may not be associated with an increased risk of dental implant failure because their analysis did not show a statistically significant association between SSRI use and implant failure.

Notably, both studies reported different implant failure rates for case and control patients, and the difference between SSRI users and non-SSRI users was greater in the Chrcanovic *et al*²⁰ study (9.2% vs 6.9%, respectively). Chrcanovic *et al* specifically addressed the differences between their results and those reported by Wu *et al*²³ and suggested that the differences were due to confounding factors.

Medications with no comparable risk reports

Patients with implants who were receiving anticonvulsant medications ($n = 1656$; 20 different anticonvulsant medications) did not have a difference in implant failure compared with nonusers. No similar reports that investigated implant failure and the use of anticonvulsants could be identified in the literature for comparison with this finding.

No clinical reports on implant failure risk related to corticosteroid use were identified for comparison with the nine different corticosteroids used among the patients with implants ($n = 1944$) in this study, which found that corticosteroids had a protective association with implant failure. We did not identify any studies assessing the influence of aspirin use on implant failure for comparison with our aspirin-using cohort ($n = 2556$).

In this study, we did not assess the association between proton pump inhibitor use and implant failure. Wu *et al*²² reported

proton pump inhibitor use to be associated with an increased risk of implant failure and reported failure rates of 6.8% and 3.2% in proton pump inhibitor users ($n = 58$) and nonusers ($n = 741$), respectively.

Generalizability of risk prediction

It is appropriate to ask whether the risk estimates determined in a single group of patients from a single institution can be generalized to different groups of patients. The fact that clinical risks vary across patient groups, and that variability is in part explained by differences in medical management across geographic regions, has been discussed in descriptions of cardiac surgery risk models.²⁴

Using patient-specific surgical risk to guide decisions is a long-standing practice in cardiac surgery.²⁵ Risk models have been applied to assess the relative impact of specific risk factors on surgical outcomes, as well as counseling patients, selecting treatment options, comparing postoperative results, and evaluating quality-improvement programs. This work has led to the recognition that risk models perform best when they are applied to the patient groups in which they were developed. This suggests that variability in medical management may explain the differences in risk estimates between reported studies, and that the risk estimates of this cohort are best applied to future patients in the same medical environment.

Strengths and limitations

The favorable features of this study include the large patient cohorts in the medication groups (>300 patients/group, with the exception of IV bisphosphonate group), the long follow-up period (the maximum failure range and maximum survival range were 27.4 and 31.2 years, respectively), the large non-medication-using population, and the use of the medical profiles of the patient population derived from complete access to patient medical records.

There are also important study limitations. The exact medication exposure was assumed based on prescription medical records, not compliance records. Therefore, given concerns about medication adherence, systemic exposure of the implants to the medications cannot be assured.²⁶ Medication categories, not individual types of medication within a category, were the basis of the analysis, and although the list of medications includes 148 brands in 92 generic drug categories, it is not inclusive of all medications.

Conclusions

The decision-making process of patients in need of major oral reconstruction can be complex. Providers can help patients better manage this process by sharing pertinent information regarding the risks and benefits of various care options. The ideal outcome information to share should reflect the provider's own practice-based evidence.

This report provides practice-based estimates of implant failure risk determined by analyzing the demographic and medication profiles of our cohort of patients. This information is considered pertinent to shared decision-making discussions with patients considering reconstruction options because the

data were obtained from a specialty-specific database linked to a medical database that can provide personalized risk predictions. The major findings related to age, sex, and era of implantation were important to consider during risk adjustment, and after adjustment, no associations were identified that increase the risk of dental implant failure.

Acknowledgments

We acknowledge the valuable contribution made to this manuscript by our Implant Database team. We also acknowledge the entire team involved in data entry and accuracy verification at the Department of Dental Specialties and the Division of Oral & Maxillofacial Surgery, Department of Surgery, at Mayo Clinic, Rochester, Minnesota.

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