

Risk of Dental Implant Failure Associated With Medication Use

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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
Ethoin	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
Brexpiprazole	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

Bisphosphonate 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.

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References

- Jokstad A, Gussgard AM, Fava J, et al: Benchmarking outcomes in implant prosthodontics: partial fixed dental prostheses and crowns supported by implants with a turned surface over 10 to 28 years at the University of Toronto. *Int J Oral Maxillofac Implants* 2017;32:880-892
- Carr AB: Successful long-term treatment outcomes in the field of osseointegrated implants: prosthodontic determinants. *Int J Prosthodont* 1998;11:502-512
- Bassi F, Carr AB, Chang TL, et al: Oral rehabilitation outcomes network:ORONet. *Int J Prosthodont* 2013;26:319-322
- Parel SM, Phillips WR: A risk assessment treatment planning protocol for the four implant immediately loaded maxilla: preliminary findings. *J Prosthet Dent* 2011;106:359-366
- Han PK, Hootsmans N, Neilson M, et al: The value of personalised risk information: a qualitative study of the perceptions of patients with prostate cancer. *BMJ Open* 2013;3:e003226
- Salisbury AC, Spertus JA: Realizing the potential of clinical risk prediction models: where are we now and what needs to change to better personalize delivery of care? *Circ Cardiovasc Qual Outcomes* 2015;8:332-334
- Vogeli C, Shields AE, Lee TA, et al: Multiple chronic conditions: prevalence, health consequences, and implications for quality, care management, and costs. *J Gen Intern Med* 2007;22 Suppl 3:391-395
- Ward BW, Schiller JS, Goodman RA: Multiple chronic conditions among US adults: a 2012 update. *Prev Chronic Dis* 2014;11:E62
- Insua A, Monje A, Wang HL, et al: Basis of bone metabolism around dental implants during osseointegration and peri-implant bone loss. *J Biomed Mater Res A* 2017;105:2075-2089
- Trindade R, Albrektsson T, Wennerberg A: Current concepts for the biological basis of dental implants: foreign body equilibrium and osseointegration dynamics. *Oral Maxillofac Surg Clin North Am* 2015;27:175-183
- Kantor ED, Rehm CD, Haas JS, et al: Trends in prescription drug use among adults in the United States from 1999–2012. *JAMA* 2015;314:1818-1831
- Al-Sabbagh M, Thomas MV, Bhavsar I, et al: Effect of bisphosphonate and age on implant failure as determined by patient-reported outcomes. *J Oral Implantol* 2015;41:e287-291
- Ata-Ali J, Ata-Ali F, Penarrocha-Oltra D, et al: What is the impact of bisphosphonate therapy upon dental implant survival? A systematic review and meta-analysis. *Clin Oral Implants Res* 2016;27:e38-46
- Walter C, Al-Nawas B, Wolff T, et al: Dental implants in patients treated with antiresorptive medication: a systematic literature review. *Int J Implant Dent* 2016;2:9
- de-Freitas NR, Lima LB, de-Moura MB, et al: Bisphosphonate treatment and dental implants: a systematic review. *Med Oral Patol Oral Cir Bucal* 2016;21:e644-651
- Guazzo R, Sbricoli L, Ricci S, et al: Medication-related osteonecrosis of the jaw and dental implants failures: a systematic review. *J Oral Implantol* 2017;43:51-57
- Matsuo A, Hamada H, Takahashi H, et al: Evaluation of dental implants as a risk factor for the development of bisphosphonate-related osteonecrosis of the jaw in breast cancer patients. *Odontology* 2016;104:363-371
- Tallarico M, Canullo L, Khanari E, et al: Dental implants treatment outcomes in patient under active therapy with alendronate: 3-year follow-up results of a multicenter prospective observational study. *Clin Oral Implants Res* 2016;27:943-949
- Yip JK, Borrell LN, Cho SC, et al: Association between oral bisphosphonate use and dental implant failure among middle-aged women. *J Clin Periodontol* 2012;39:408-414
- Chrcanovic BR, Kisch J, Albrektsson T, et al: Is the intake of selective serotonin reuptake inhibitors associated with an increased risk of dental implant failure? *Int J Oral Maxillofac Surg* 2017;46:782-788
- Wu X, Al-Abedalla K, Eimar H, et al: Antihypertensive medications and the survival rate of osseointegrated dental implants: a cohort study. *Clin Implant Dent Relat Res* 2016;18:1171-1182
- Wu X, Al-Abedalla K, Rastikerdar E, et al: Selective serotonin reuptake inhibitors and the risk of osseointegrated implant failure: a cohort study. *J Dent Res* 2014;93:1054-1061
- Wu X, Al-Abedalla K, Abi-Nader S, et al: Proton pump inhibitors and the risk of osseointegrated dental implant failure: a cohort study. *Clin Implant Dent Relat Res* 2017;19:222-232
- Shahian DM, Blackstone EH, Edwards FH, et al: STS workforce on evidence-based surgery. Cardiac surgery risk models: a position article. *Ann Thorac Surg* 2004;78:1868-1877
- Prins C, de Villiers Jonker I, et al: Cardiac surgery risk-stratification models. *Cardiovasc J Afr* 2012;23:160-164
- Brown MT, Bussell JK: Medication adherence: WHO cares? *Mayo Clin Proc* 2011;86:304-314