



Association between immunologic parameters, glycemic control, and postextraction complications in patients with type 2 diabetes

Karin Sá Fernandes, DDS, PhD; Michael Glick, DMD; Mario Sérgio de Souza, DDS; Cristina Maria Kokron, MD, PhD; Marina Gallottini, DMD, PhD

he number of people living with diabetes has grown exponentially in many parts of the world. Epidemiologic data published in 2013 suggest that at least 13.4 million people in Brazil and 26 million people in the United States are currently living with a diagnosis of diabetes.¹

People with diabetes have been reported to have increased susceptibility to develop oral complications, especially periodontal diseases, and oral infections may compromise glycemic control.^{2,3} In addition, there is evidence of people with diabetes and hyperglycemia who are undergoing surgical procedures such as thoracic or abdominal surgery having an increased risk of experiencing postoperative infections.⁴⁵

There is scant clinical evidence of a relationship between diabetes, hyperglycemia, and an increased risk of experiencing infection after dental extraction. To our knowledge, investigators of few prospective longitudinal studies have attempted to examine this relationship.^{6,7} These investigators^{6,7} suggested that having an infection after dental extraction is no more common in people with diabetes than it is in people who do not have diabetes. However, these studies^{6,7} had limitations, such as small sample sizes, lack of standardization of surgical methods, and short follow-up periods.

ABSTRACT

Background. The purpose of this study was to assess the association between metabolic control and immune dysfunction, and postoperative complications and wound healing after dental extractions in people with type 2 diabetes and control participants. **Methods.** The authors performed a prospective, case-control study enrolling 53 participants with type 2 diabetes and 29 participants who did not have type 2 diabetes. Exclusion criteria included being a smoker and having teeth with periodontal pockets deeper than 4 millimeters, among others. All participants underwent an extraction of 1 erupted tooth. The investigators assessed patients' signs and symptoms at 3, 7, 21, and 60 days after surgery. The investigators measured glycemic control and immunologic profile at the time of the extraction. They compared the pattern of healing and the incidence of post-

extraction complications between the 2 groups.

Results. Even in the presence of impaired neutrophil function and poor glycemic control, we found no increase in the number of post-operative complications. There was no association between delayed wound epithelialization on postoperative day 21 and level of glycemic control, and reduced neutrophil function. On postoperative day 60, all alveolar sockets were epithelialized completely and showed no signs of infection.

Conclusions. The study results suggest that type 2 diabetes per se or glycemic control is not a risk factor for experiencing postoperative complications in people undergoing dental extractions. Although people with type 2 diabetes may have impaired neutrophil function, the study results revealed that having this condition was not associated with an increased risk of experiencing postoperative complications. Additional research studies with larger sample sizes of patients who have diabetes are needed to confirm this study's findings.

Practical Implications. The results allow clinicians to infer that people with type 2 diabetes undergoing dental extractions of erupted teeth that do not have an acute odontogenic infection should not receive antibiotic prophylaxis simply because of their diabetic status or level of glycemic control.

Key Words. Tooth extraction; diabetes mellitus; infection; wound healing; hyperglycemia.

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Although most dentists believe in the benefit of providing antibiotic prophylaxis to patients with different systemic conditions, including diabetes, before they undergo invasive dental procedures,⁸ there is limited evidence to support such a practice.⁹ Barasch and colleagues¹⁰ reviewed the literature on empirical antibiotic prophylaxis for people with diabetes undergoing dental extraction. The authors selected articles using the following search terms: "healing after tooth extraction," "infection," and "diabetes." They concluded that there was no scientific evidence that people with diabetes undergoing oral surgery were at an increased risk of postoperative infection and, consequently, that there was no evidence to support the use of prophylactic antibiotic therapy during such procedures.

Despite the paucity of studies involving patients experiencing oral complications after dental extractions and the lack of evidence to support the use of antibiotic prophylaxis in patients with diabetes, such a practice has been recommended for patients with diabetes who are undergoing invasive dental procedures.^{11,12} The medical plausibility invoked for such a practice is that people with diabetes are, to some extent, immunocompromised.

The investigators of only a few studies have evaluated the impact of diabetes on T lymphocytes, complement proteins, and immunoglobulin (Ig) levels, and the results of these studies have shown conflicting results.¹³ Regarding neutrophil function, the investigators of a large number of studies have suggested that people with diabetes can have a decrease in neutrophil chemotaxis, phagocytosis, and dihydrorhodamine oxidation.^{12,14,15} However, investigators have yet to establish the relationship between neutrophil dysfunction and diabetes metabolic control.^{16,17} Because neutrophils play a major role in the defense against bacterial infections, neutrophil dysfunction may expose patients to an increased risk of experiencing complications after invasive dental procedures, such as teeth extractions.

Having hypothesized that neither type 2 diabetes nor hyperglycemia constitute risk factors for experiencing postoperative complications in patients undergoing dental extractions, we conducted a study to compare postoperative complications and surgical wound healing in patients with type 2 diabetes and control patients who did not have type 2 diabetes, all of whom were undergoing tooth extractions. We performed an analysis to assess the association between postextraction complications, wound healing, complete blood counts, glycated hemoglobin (HbA_{1c}) levels, and immunologic profiles. A secondary goal of this study was to assess whether certain baseline characteristics (for example, HbA_{1c}, glycemic values, complete blood counts, and immunological profiles) had an impact on the socket healing process.

METHODS

The Research Ethics Committee of the School of Dentistry, University of São Paulo (USP), located in São Paulo, Brazil, approved this prospective case-control study. All participants gave written informed consent.

We screened 435 patients with type 2 diabetes and 144 patients who did not have type 2 diabetes. The inclusion criteria included being 18 years or older and requiring extraction of erupted teeth because of extensive dental decay or preprosthetic preparation. To eliminate confounding variables that could affect wound healing, we used the following exclusion criteria: having teeth with periodontal pockets deeper than 4 millimeters, use of antibiotic or anti-inflammatory drugs in the previous month; use of hormone replacement therapy; use of bisphosphonate therapy; a history of having diseases or conditions associated with immunosuppression; undergoing cancer chemotherapy or radiation therapy; having a history of smoking; use of illicit drugs; chronic use of alcohol; having a dental emergency; having a cognitive impairment; and having acute dental or periodontal infections, such as abscesses. We enrolled 65 patients with type 2 diabetes and 32 patients who did not have diabetes in the study, and we followed 53 patients with diabetes and 29 patients who did not have diabetes for 60 days after their dental extractions (Figure, Table 1).

The same experienced dentist (M.S.S.) performed all the study participants' dental extractions in accordance with the standards established by Peterson and colleagues¹⁸ at an outpatient clinic at the USP School of Dentistry. The patients received local anesthetic.

To assess whether certain participants' baseline characteristics influenced the healing process, we collected blood samples on the same day as the dental extractions. We assessed blood test results in the same laboratory and included the following: complete blood cell count; HbA_{1c} level; nonfasting blood glucose, serum IgA, IgG, and IgM levels; lymphocyte immunophenotyping $(CD_3^+ T \text{ cells}, CD_4^+ T \text{ cells}, \text{ and } CD_8^+ T \text{ cells});$ serum levels of complement components 3 and 4 (C3 and C4, respectively); and neutrophil function tests, including dihydrorhodamine oxidation test, phagocytic index determination, and neutrophil chemotaxis assay. The dihydrorhodamine oxidation test, all phagocytic index determinations, and all neutrophil chemotaxis assays were performed by the same trained and calibrated investigator (K.S.F.) using PHAGOTEST and MIGRATEST Chemotaxis (Glycotope Biotechnology) kits in the Laboratory of Clinical Immunology and Allergy of the USP School of Medicine.

We measured finger-prick glucose test and blood pressure before and after surgery to detect possible

ABBREVIATION KEY. HbA_{1c}: Glycated hemoglobin. Ig: Immunoglobulin. USP: University of São Paulo.



Figure. Flowchart of the study.

hypoglycemia and extreme elevated blood pressure unsuitable for the planned dental procedure. We did not prescribe any prophylactic antibiotics or anti-inflammatory drugs. We recorded the duration of surgery (from anesthetic to suture placement); need for forceps, elevators, or both; need for a flap approach; type and amount of local anesthetic used; need for tooth sectioning; need for osteotomy; and need for intraligamentary anesthetic. The characteristics of the tooth extracted as well as the duration and technique of the surgeries were similar between the 2 groups (Table 2).

All study participants returned on postoperative days 3, 7, 21, and 60 for follow-up evaluations. The same calibrated researcher (K.S.F.) clinically assessed wound healing. We considered epithelialization to be complete when the epithelium of the gingival mucosa totally covered the alveolus.

We used the following variables to assess postoperative complications: edema, erythema, alveolar bone exposure, halitosis, trismus, fever, cellulitis, Ludwig angina, loss of appetite, malaise, itching, moderate to severe pain (as assessed by a visual analog scale), and unpleasant taste. We did not consider mild pain, redness, or swelling on postoperative day 3 to be postoperative complications, as clinicians expect these signs and symptoms to occur as part of the normal healing process.

A second outcome was socket epithelialization. According to the literature, the dental alveolus is filled with blood clot and fibrin at 3 days after dental extraction; on postoperative day 7, the alveolus is filled with granulation tissue; on postoperative day 21, wound epithelialization is complete; and on postoperative day 60, alveolar bone formation can be observed on a dental radiographic image.¹⁸ We defined delayed wound epithelialization as an incomplete epithelial recovery at day 21.¹⁸

On postoperative day 60, we performed a follow-up evaluation. We categorized the postoperative period as "presence of complication" or "no complication" on the basis of the presence or absence of the aforementioned clinical signs and symptoms. In addition, we classified socket epithelialization as "normal" or "delayed" on the basis of the timing of the aforementioned events.

We compared the occurrence of postextraction complications and the pattern of healing between the 2 groups of study participants (those who had type 2 diabetes and those who did not have type 2 diabetes). In addition, we investigated whether the occurrence of postextraction complications and the pattern of healing were associated with HbA_{1c} levels, hyperglycemia, and immunologic profiles. We used the Fisher exact test, analysis of variance, and the Mann-Whitney test to determine statistical analysis. We used R statistical software, version 2.15.3 (R Foundation), and we set the level of significance at 5%.

RESULTS

Table 1 summarizes the demographic and baseline data of the 53 patients with type 2 diabetes and of the 29

TABLE 1

patients in the control group, matched for sex and race. Among the patients with type 2 diabetes, the median number of years after diagnosis was 8 (range, 1-36 years). At the time of the initial evaluation, 32 (60%) were using oral hypoglycemic medications, 9 (17%) were using insulin, and 12 (23%) were using a combination of oral hypoglycemic medications and insulin.

Among the 53 patients with type 2 diabetes, 1 (1.9%) had a postoperative complication: unpleasant taste. Among the 29 control patients, 7 (24%) had postoperative complications, including 3 (10.3%) with unpleasant taste; 2 (6.9%) with malaise; 1 (3.4%) with trismus; and 1 (3.4%) with loss of appetite. The 2 groups of patients differed significantly in terms of the occurrence of complications (P = .005). On postoperative day 21, 9 of the 53 patients (17%) with type 2 diabetes and none of the 29 controls showed incomplete epithelialization of the alveolar socket, the difference being statistically significant (P =.023). On postoperative day 60, all

Demographic and baseline data of the 53 study participants with type 2 diabetes and the 29 control participants.

CATEGORY	PATIENTS W DIABETES	ITH TYPE 2 (N = 53)	CONTROL	5 (N = 29)	<i>P</i> VALUE		
	Value	95% CI*	Value	95% CI			
Female Sex, No. (%)	27 (50.9)	37.0-64.7	12 (41.4)	24.1-60.9	.401†		
Age, y, Mean (Interquartile Range)	58 (39-82)	55.0-61.0	48 (28-82)	45.1-53.2	.001 ^{‡§}		
White Race, No. (%)	34 (64.2)	49.7-76.5	21 (72.4)	52.5-86.6	.463†		
Preoperative Glycemia, mg/dL, [¶] Mean (Interquartile Range)	186 (75-412)	180.0-213.5	103 (79-161)	82.6-127.9	< .001‡§		
Glycated Hemoglobin, %, Mean (Interquartile Range)	7.6 (5.4-12.4)	7.6-8.4	5.5 (4.8-5.8)	4.8-5.9	< .001 ^{‡§}		
Participants With Reduced Oxidative Burst Function, No. (%)	13 (24.5)	14.2-38.6	0 (0)	0-14.6	.01 ^{†§}		
Participants With Reduced Neutrophil Phagocytosis Function, No. (%)	9 (17.0)	8.5-30.3	0 (0)	0-14.6	.047 ^{†§}		
Participants With Reduced Neutrophil Chemotaxis, No. (%)	39 (73.6)	59.4-84.3	0 (0)	0-14.6	< .001†§		
Participants With Reduced Monocyte Phagocytosis Function, No. (%)	1 (1.9)	0.1-11.4	0 (0)	0-14.6	.684 [†]		
 * CI: Confidence interval (for mean or proportions). † <i>P</i> values obtained using the Fisher exact test. ‡ <i>P</i> values obtained using the Mann-Whitney test. § Statistically significant finding. 							

§ Statistically significant finding.

¶ mg/dL: Milligrams per deciliter.

alveolar sockets, in both groups, were completely epithelialized and asymptomatic, showing no signs of infection. During the postoperative period, we did not prescribe any antibiotics or nonsteroidal antiinflammatory drugs. Table 2 summarizes the postoperative characteristics.

The 9 patients with type 2 diabetes (17%) who exhibited incomplete alveolar epithelialization on postoperative day 21 had HbA_{1c} levels ranging from 5.4% to 12.4% and nonfasting glucose levels ranging from 78 milligrams per deciliter to 182 mg/dL. Assessing delay in epithelialization with HbA_{1c} levels or nonfasting glucose levels did not reach statistical significance (P =.467). Also, age, surgical technique, neutrophil function, time since diagnosis of diabetes, serum IgA levels, serum IgG levels, serum IgM levels, serum C3 levels, serum C4 levels, number of $CD4^+$ T cells, or number of CD8⁺ T cells did not correlate with the delay of epithelialization on postoperative day 21. In addition, we did not detect any statistical significance between delayed wound healing and reduced neutrophil function (Table 3).

At the time of the extraction, 46 of the 53 participants with type 2 diabetes (86.8%) were hyperglycemic according to the results of the nonfasting blood glucose test, and 40 (75.5%) had HbA_{1c} levels greater than 6.5%. Median nonfasting blood glucose levels were 135 mg/dL (range, 78-367 mg/dL), and the median HbA_{1c} level was 7.6% (range, 5.4-12.4%).

We detected no statistically significant differences between the 2 groups for complete blood cell count data, and we observed no critical values. In most patients with type 2 diabetes, we found that the serum levels of IgA, IgG, and IgM, as well as the numbers of $CD3^+$, $CD4^+$, and $CD8^+$ T cells, together with serum levels of C3 and C4, were within the normal range, with no significant differences between the group of patients with diabetes and the control group. Table 4 summarizes the immunologic profiles of all participants.

DISCUSSION

The study results confirm our hypothesis that clinical alveolar healing is satisfactory in patients with type 2 diabetes who are undergoing single, erupted tooth

CHARACTERISTIC	PATIENTS WITH TYPE 2 DIABETE	S (N = 53)	CONTROLS (N = 29)	Р		
	Estimative	95% CI*	Estimative	95% CI	VALUET	
Tooth Extracted,	27 (50.9), 1 maxillary tooth	37-64.7	17 (58.6), 1 maxillary tooth	39.1-75.9	.134	
No. (%)	26 (49.1), 1 mandibular tooth	35.3-63.0	12 (41.4), 1 mandibular tooth	24.1-60.9		
	11 (20.8), 1 anterior tooth	11.3-34.5	2 (7.0), 1 anterior tooth	1.2-24.2		
	42 (79.2), posterior tooth extraction	65.5-88.7	27 (93.0), posterior tooth extraction.	75.8-98.8		
Duration of Surgery	20 min, median (range,10-60 min) 20.6-25.5 [‡] 20 min, median (range,10-45 min) 20.0		20.0-25.9 [‡]	.879‡		
Surgical Technique	6 required tooth sectioning	4.7-23.7	4 required tooth sectioning	4.5-32.6		
Applied	3 required osteotomy	1.5-16.6	1 required osteotomy	0.2-19.6	.632	
	2 required tooth sectioning and osteotomy	0.7-14.1	3 required tooth sectioning and osteotomy	2.7-28.5		
Postoperative			3 (10.3), unpleasant taste	2.7-28.5		
Complications on Day 3, No. (%)	1 (1 0) upploacant tacto	01114	2 (6.9), malaise	1.2-24.2	005 [§]	
	r (1.9), unpreasant taste	0.1-11.4	1 (3.4), trismus	0.2-19.6		
			1 (3.4), loss of appetite	0.2-19.6		
Postoperative Complications on Day 7, No. (%)	53 (100), alveolus is filled with granulation tissue	91.6-100.0	29 (100), alveolus is filled with granulation tissue	85.4-100.0	.999	
Postoperative	44 (83), complete epithelialized	69.7-91.5	29 (100), complete epithelialized	85.4-100.0	.023 [§]	
Complications on Day 21, No. (%)	9 (17), incomplete epithelialized	8.5-30.3	0 incomplete epithelialized	85.4-100.0		
Postoperative Complications on Day 60, No. (%)	53 (100), alveolar sockets completed epithelialized and asymptomatic	91.6-100.0	29 (100), alveolar sockets completed epithelialized and asymptomatic	85.4-100.0	.999	

§ Statistically significant finding.

extractions, even in the presence of slowed epithelialization. Furthermore, glycemic control, neutrophil dysfunction, or other immunologic abnormalities are not associated with postoperative complications or slowed epithelialization.

Compared with previous studies,^{6,7} we ensured a high level of methodological care with our study participants; for example, the same calibrated dentist (M.S.S.) performed all of the dental extractions in a standardized manner. In addition, we followed patients for 60 days (that is, until alveolar bone healing was complete), and the same calibrated dentist (K.S.F.), who was not the dentist who performed the dental extractions (M.S.S.), performed all of the follow-up evaluations. Finally, we performed all laboratory tests, which included complete blood count; HbA_{1c} level; nonfasting blood glucose level; determination of serum IgA, IgG, and IgM levels; lymphocyte immunophenotyping (CD3⁺ T cells, CD4⁺ T cells, and CD8⁺ T cells); determination of serum C3 and C4 levels; and neutrophil function tests (including dihydrorhodamine oxidation test, phagocytic index determination, and neutrophil chemotaxis assay), on blood samples collected at the same dental visit, shortly before the tooth extraction.

In our study, patients with type 2 diabetes exhibited almost no postoperative complications. Only 1 participant complained about having an unpleasant taste on postoperative day 3. Furthermore, we did not document any postoperative infections. Although the evaluation of many of the complications was subjective, the fact that the same calibrated observer (K.S.F.) evaluated all of the complications minimized subjectivity. Of the 53 patients with type 2 diabetes, 36 (67.9%) showed poor glycemic control and 39 (73.6%) showed impaired neutrophil chemotaxis at the time of dental extraction.

Delayed wound epithelialization was more common in the patients with type 2 diabetes than those patients who did not have diabetes. Delayed wound healing was not associated with the development of an infection, discomfort, or pain. Furthermore, it did not compromise postoperative wound healing 60 days after surgery. In our study, we could not identify any laboratory or clinical indicators that could predict a delay in epithelialization or other postoperative complications. Some hypotheses that may explain impaired wound epithelialization in patients with diabetes include excessive production of reactive oxygen species, decreased TARIE 3

nitric oxide production, decreased response to growth factors, reduced expression of insulin-signaling pathway proteins, impaired macrophage activation, and reduced angiogenesis.^{12,19,20}

Dental clinicians are familiar with the empirical recommendation that glycemic control should be achieved before a patient undergoes a tooth extraction. This recommendation was an extrapolation of clinical and scientific evidence taken from the results of studies of major surgery, principally thoracic and abdominal surgery. Although 36 (67.9%) of the 53 patients with type 2 diabetes in our study were hyperglycemic at the time of dental extraction and 40 (75.5%) had HbA_{1c} levels greater than 6.5%, we noted no alveolar infections after tooth extraction or delays in complete wound healing.

Investigators have conducted a limited number of studies on the effect of dia-

betes on wound healing after tooth extraction. In 2010, Aronovich and colleagues⁶ compared healing after tooth extractions among patients with well-controlled diabetes and patients with poorly controlled diabetes. These investigators did not find statistically significant differences in the rate of postextraction epithelialization between patients with well-controlled diabetes and patients with poorly controlled diabetes. Similarly, in our study, we did not find a correlation between epithelialization delay and glycemic control as related to the tooth extraction. When analyzing the details, we noted some methodological differences between Aronovich and colleagues'^b study and our study. Aronovich and colleagues^o combined patients with both type 1 and type 2 diabetes and they did not have a control group of patients who did not have diabetes. Furthermore, different surgeons conducted the extraction procedures, which may have introduced variations in technique and likely may have influenced healing. Study participants' follow-up period lasted only 2 weeks, with patients making follow-up visits at 7 and 14 days postoperatively. In addition, the investigators had complete follow-up data for only 68% of the patients. In our study, we noticed the delay in epithelialization on day 21 after extraction.

Demographic and baseline characteristics of 9 patien
with type 2 diabetes who had delayed wound healing
epithelialization.

CHARACTERISTIC	DELAYED EPITHELIA (N =	WOUND LIZATION 9)	NO DELAYED EPITHELIALI (N = 4	WOUND ZATION 4)	P VALUE		
	Estimative 95% CI*		Estimative	95% CI			
Age, y, Mean (Interquartile Range)	67 (44-75)	53.0-68.4	57.5 (39.0-82.0)	51.5-56.9	.401†		
Female Sex, No. (%)	5 (55.5)	22.7-84.7	22 (50.0)	35.8-64.2	.999 [‡]		
White Race, No. (%)	7 (77.8)	40.2-96.1	27 (61.4)	45.5-75.3	.463 [‡]		
HbA _{1c} Level, %, Mean (Interquartile Range)	8.1 (5.6-10.3)	7.0-9.5	7.4 (5.4-12.4)	6.5-7.4	.586†		
Nonfasting Blood Glucose Levels, Mean (Interquartile Range)	127 (78-182)	80.9-170.5	147.5 (81.0-367.0)	123.2-154.6	.152†		
Participants Showing Reduced Oxidative Burst, No. (%)	2 (22.2)	3.9-59.8	11 (25)	13.7-40.6	.999 [‡]		
Participants Showing Reduced Neutrophil Phagocytosis, No. (%)	2 (22.2)	3.9-59.8	7 (15.9)	7.2-30.7	.640‡		
Participants Showing Reduced Monocyte Phagocytosis, No. (%)	0 (0.0)	0-37.1	1 (2.3)	0.1-13.5	.999 [‡]		
Participants Showing Reduced Neutrophil Chemotaxis, No. (%)	6 (66.7)	30.9-91.0	33 (75.0)	59.4-86.3	.684‡		
* CI: Confidence interval (for mean or proportions).							

† No statistical significance obtained using the Mann-Whitney test.
 ‡ No statistical significance obtained using the Fisher exact test.

Huang and colleagues⁷ conducted a study to determine whether there was a difference in delayed healing after undergoing dental extractions for patients with type 2 diabeties taking oral hypoglycemics and patients who did not have diabetes. The investigators found similar rates of healing between the 2 groups. Our results showed more delayed healing in the group of patients with diabetes; however, similar to Huang and colleagues,⁷ we did not observe any cases of postoperative infections, osteomyelitis, or osteonecrosis of the jaws.

The major limitation of our study was the small sample size. Nevertheless, this sample was able to identify a 20% absolute difference between the 2 groups, with 80% power and 5% level of significance, assuming a 2% complication rate in the control group (Fisher exact test). We hope our results will encourage others to conduct further research in this important and relevant clinical area, particularly studies that assess multiple extractions and extraction of impacted teeth. Furthermore, in addition to our study that used multiple exclusion criteria (for example, being a smoker, using antibiotics, having a tooth with periodontal disease), we believe that investigators also should conduct studies that use no or minimal exclusion criteria so that

TABLE 4

Immunologic profile of the participants, including serum immunoglobulin levels, lymphocyte immunophenotyping, and serum levels of complement components 3 and 4.

REFERENCE VALUES		PARTICIPANTS WIT RANGE VAI	TH NORMAL LUES	PARTICIPANTS WIT ABOVE THE NORM	H VALUES AL RANGE	PARTICIPANTS WIT BELOW THE NORM	ANTS WITH VALUES	
		Participants With Type 2 Diabetes (n = 53)	Controls (n = 29)	Participants With Type 2 Diabetes (n = 53)	Controls (n = 29)	Participants With Type 2 Diabetes (n = 29)	Controls (n = 29)	
Immunoglobulin A,	No. (%)	34 (64.1)	21 (72.4)	17 (32.1)	8 (27.6)	2 (3.8)	0 (0.0)	.494
99-354 mg/dL [†]	95% Cl [‡]	49.7-76.5	52.5-86.6	20.3-46.4	13.4-47.5	0.7-14.1	0-14.6	
Immunoglobulin G,	No. (%)	27 (50.9)	18 (62.1)	23 (43.4)	11 (37.9)	3 (5.7)	0 (0.0)	.333
739-1,390 mg/dL	95% Cl	37.0-64.7	42.4-78.7	30.1-57.6	21.3-57.6	1.5-16.6	0-14.6	
Immunoglobulin M,	No. (%)	27 (50.9)	18 (62.1)	3 (5.7)	1 (3.4)	23 (43.4)	10 (34.5)	.612
81-167 mg/dL	95% Cl	37.0-64.7	42.4-78.7	1.5-16.6	0.2-19.6	30.1-57.6	18.6-54.3	
CD3 ⁺ T cells,	No. (%)	43 (81.2)	27 (93.2)	5 (9.4)	1 (3.4)	5 (9.4)	1 (3.4)	.341
812-2,318 cells/mm ^{3§}	95% Cl	67.6-90.1	75.8-98.8	3.5-21.4	0.21-9.6	3.5-21.4	0.2-19.6	
CD4 ⁺ T cells,	No. (%)	50 (94.3)	29 (100)	0 (0.0)	0 (0.0)	3 (5.7)	0 (0.0)	.49
535-2,480 cells/mm ³	95% Cl	83.4-98.5	85.4-100.0	0-8.4	0-14.6	1.5-16.6	0-14.6	
CD8 ⁺ T cells,	No. (%)	47 (88.7)	28 (96.6)	1 (1.9)	0 (0.0)	5 (9.4)	1 (3.4)	.451
255-1,720 cells/mm ³	95% Cl	76.3-95.3	80.4-99.8	0.1-11.4	0-14.6	3.5-21.4	0.2-19.6	
C3,	No. (%)	50 (94.3)	28 (96.6)	0 (0.0)	3 (5.7)	0 (0.0)	1 (1.9)	.176
90-180 mg/dL	95% Cl	83.4-98.5	80.4-99.8	0-8.4	2.7-28.5	0-8.4	0.20-19.6	
C4,	No. (%)	49 (92.5)	29 (100)	4 (7.5)	0 (0.0)	0 (0.0)	0 (0.0)	.327
10-40 mg/dL	95% Cl	80.9-97.6	85.4-100.0	2.4-19.1	0-14.6	0-8.4	0-14.6	
* P values obtained using the Fisher exact test.								

† mg/dL: Milligrams per deciliter.

‡ CI: Confidence interval (for mean or proportions).

§ cells/mm³: Cells per cubic millimeter.

postextraction wound healing research can be generalized more accurately to a larger population of people with diabetes.

The results of our study allow us to infer that dental patients with type 2 diabetes undergoing extractions of erupted teeth (that are not associated with an acute odontogenic infection) should not be given antibiotic prophylaxis simply because of their diabetic status or level of glycemic control.

CONCLUSION

Our results show that type 2 diabetes per se or glycemic control is not a risk factor for postoperative complications in dental patients undergoing extractions of erupted teeth. Our results suggest that although patients with type 2 diabetes are at an increased risk of experiencing delayed epithelialization of the surgical wounds, this observation was not associated with having an increased risk of experiencing infection or other postoperative complications. Additional research studies using larger sample sizes of patients with diabetes are needed to confirm our findings.

Dr. Fernandes is a postdoctoral researcher, Department of Stomatology, School of Dentistry, University of São Paulo, São Paulo, Brazil.

Dr. Glick is a professor, Department of Oral Diagnostic Sciences, and the dean, School of Dental Medicine, University at Buffalo, The State University

of New York, Buffalo, NY. He also is the editor of the Journal of the American Dental Association.

Dr. de Souza is a dentist, Special Care Dentistry Center, Department of Stomatology, School of Dentistry, University of São Paulo, São Paulo, Brazil.

Dr. Kokron is a professor, Department of Immunology, School of Medicine, University of São Paulo, São Paulo, Brazil.

Dr. Gallottini is a professor and chair, Department of Stomatology, School of Dentistry, University of São Paulo, Av. Prof. Lineu Prestes, 2227, São Paulo, SP, Brazil, e-mail mhcgmaga@usp.br. Address correspondence to Dr. Gallottini.

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1. Organisation for Economic Co-operation and Development. Health at a glance 2013: OECD indicators. Available at: http://www.oecd.org/health/ health-at-a-glance.htm. Accessed March 11, 2015.

2. Vernillo AT. Dental considerations for the treatment of patients with diabetes mellitus. *JADA*. 2003;134(suppl):24S-33S.

3. Camargo GA, Lima MA, Fortes TV, de Souza CS, de Jesus AM, de Almeida RP. Effect of periodontal therapy on metabolic control and levels of IL-6 in the gingival crevicular fluid in type 2 diabetes mellitus. *Indian J Dent Res.* 2013;24(1):110-116.

4. Bergman SA. Perioperative management of the diabetic patient. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103(6):731-737.

5. Alserius T, Anderson RE, Hammar N, Nordqvist T, Ivert T. Elevated glycosylated haemoglobin (HbA1c) is a risk marker in coronary artery bypass surgery. *Scand Cardiovasc J.* 2008;42(6):392-398.

6. Aronovich S, Skope LW, Kelly JP, Kyriakides TC. The relationship of glycemic control to the outcomes of dental extractions. *J Oral Maxillofac Surg.* 2010;68(12):2955-2961.

7. Huang S, Dang H, Huynh W, Sambrook PJ, Goss AN. The healing of dental extraction sockets in patients with Type 2 diabetes on oral hypoglycaemics: a prospective cohort. *Aust Dent J.* 2013;58(1): 89-93.

8. Lockhart PB, Brennan MT, Fox PC, Norton HJ, Jernigan DB, Strausbaugh LJ. Decision-making on the use of antimicrobial prophylaxis for dental procedures: a survey of infectious disease consultants and review. *Clin Infect Dis.* 2002;34(12):1621-1626.

9. Lockhart PB, Loven B, Brennan MT, Fox PC. The evidence base for the efficacy of antibiotic prophylaxis in dental practice. *JADA*. 2007;138(4): 458-474.

10. Barasch A, Safford MM, Litaker MS, Gilbert GH. Risk factors for oral postoperative infection in patients with diabetes. *Spec Care Dentist.* 2008; 28(4):159-166.

11. Vernillo AT. Diabetes mellitus: relevance to dental treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001;91(3):263-270.

12. Ship JA. Diabetes and oral health: an overview. *JADA*. 2003; 134(suppl):4S-10S.

13. Liberatore RR Jr, Barbosa SF, Alkimin M, et al. Is immunity in diabetic patients influencing the susceptibility to infections? Immunoglobulins, complement and phagocytic function in children and adolescents with type 1 diabetes mellitus. *Pediatr Diabetes*. 2005;6(4): 206-212. 14. Cutler CW, Eke P, Arnold RR, Van Dyke TE. Defective neutrophil function in an insulin-dependent diabetes mellitus patient: a case report. *J Periodontol*. 1991;62(6):394-401.

15. Ramaraj PN, Cariappa KM. Is there a need for antibiotic prophylaxis after routine dental extraction in diabetic patients? *Br J Oral Maxillofac Surg.* 2006;44(5):421.

16. Jakelić J, Kokić S, Hozo I, Maras J, Fabijanić D. Nonspecific immunity in diabetes: hyperglycemia decreases phagocytic activity of leukocytes in diabetic patients. *Med Arh.* 1995;49(1-2):9-12.

17. Alba-Loureiro TC, Munhoz CD, Martins JO, et al. Neutrophil function and metabolism in individuals with diabetes mellitus. *Braz J Med Biol Res.* 2007;40(8):1037-1044.

18. Peterson LJ, Ellis E, Hupp JR, Tucker MR. *Contemporary Oral and Maxillofacial Surgery*. 4th ed. St. Louis: Mosby; 2003:126.

19. Brem H, Tomic-Canic M. Cellular and molecular basis of wound healing in diabetes. J Clin Invest. 2007;117(5):1219-1222.

20. Kim HS, Yoo HS. In vitro and in vivo epidermal growth factor gene therapy for diabetic ulcers with electrospun fibrous meshes. *Acta Biomater*. 2013;9(7):7371-7380.