Factors associated with the clinical response to nonsurgical periodontal therapy in people with type 2 diabetes mellitus

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ABSTRACT

Background. Type 2 diabetes mellitus (T2DM) is a growing health problem worldwide. People with T2DM are at risk of experiencing periodontitis and likely require treatment. Using data from the national multicenter Diabetes and Periodontal Therapy Trial (DPTT), the authors assessed patient-based characteristics associated with the clinical response to nonsurgical therapy.

Methods. The DPTT investigators randomly assigned adults with T2DM (hemoglobin A_{1c} [HbA_{1c}] ≥ 7 percent and < 9 percent) and moderate to advanced periodontitis to receive immediate or delayed therapy (scaling and root planing, oral hygiene instruction, chlorhexidine rinse). The investigators assessed probing depth (PD), clinical attachment level (CAL), bleeding on probing (BOP), and medical conditions at baseline, three months and six months. Six-month changes in mean PD, CAL and BOP defined the treatment response. Complete data were available for 473 of 514 DPTT participants. The authors used multiple regression models to evaluate participant-level factors associated with the response.

Results. More severe baseline PD, CAL and BOP were associated with greater improvements in these same measurements ($P < .0001$). Hispanic participants experienced greater improvements in PD and CAL than did non-Hispanic participants ($P < .0001$). Obese participants (those with a body mass index > 30 kilograms per square meter) experienced greater reductions in PD and BOP than did participants who were not obese ($P < .001$). Age, sex, HbA_{1c} values, diabetes duration, and smoking were not associated with change in any outcome ($P > .1$).

Conclusions. In patients with T2DM, baseline disease severity was associated with the clinical response to nonsurgical periodontal therapy. Body mass index and Hispanic ethnicity—but not glycemic control, diabetes duration or smoking—also may be useful in predicting clinical changes in this population.

Practical Implications. These findings could help clinicians identify patients with T2DM who may or may not respond well to initial periodontal treatment.

Key Words. Diabetes mellitus; periodontitis; treatment.

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Nonsurgical periodontal therapy is an effective means of reducing signs of periodontitis.[1] Many reports have documented the range of treatment responses, and it is well established that sites with initially more severe disease experience greater clinical improvements after treatment when compared with less severely affected sites.[2-4] In contrast, less is known about the utility of patient-based characteristics in predicting the clinical response to nonsurgical therapy. One exception is smoking, which is known to affect treatment response adversely.[5]

Haffajee and colleagues[6] compared baseline clinical characteristics between people who responded well and poorly to scaling and root planing and found no significant differences between the groups in any baseline clinical parameter. Several bacteria, however, including *Actinomyces viscosus* and *Treponema denticola*, were more prevalent and at higher levels at baseline in those who responded well versus those who responded poorly. In patients with aggressive periodontitis, smoking and higher initial attachment loss, but not bleeding and probing depth (PD), have been associated with a poor response to scaling and root planing.[7]

Little is known about treatment response predictors in patients with type 2 diabetes mellitus (T2DM). In fact, intervention trials frequently exclude patients with medical conditions, including diabetes, that are known to affect a person's risk of experiencing periodontitis. Yet T2DM is a substantial and growing health problem in the United States and worldwide. An estimated 29 million Americans have diabetes.[8] Because they are at increased risk of experiencing periodontitis,[9] people with T2DM may have more periodontal treatment needs than do otherwise healthy people.

Although diabetes is believed to affect response to periodontal treatment adversely,[10] there is sparse evidence to support this. Investigators in several small trials found comparable clinical responses after scaling and root planing in patients with and without diabetes.[11-13] To the best of our knowledge, no investigators

have published studies in which they have explored predictors of periodontal treatment response in patients with T2DM. We explored associations between baseline characteristics and the periodontal treatment response in people with T2DM who participated in the Diabetes and Periodontal Therapy Trial (DPTT). This report focuses on patient-level, and not tooth-level, factors that could be used by a clinician to assess a person's likelihood of responding to treatment.

METHODS

Design and setting. DPTT was a multicenter, six-month, single-masked,randomized controlled trial designed to test whether periodontal therapy improves glycemic control in participants with T2DM and moderate to advanced periodontitis. A prespecified secondary aim of the trial was to assess the clinical efficacy of periodontal therapy in participants in terms of the periodontal status or condition being evaluated, which is a focus of this report. The study protocol was approved by the institutional review board at each participating center: University of Alabama at Birmingham; University of Minnesota, Minneapolis; Stony Brook University, State University of New York; University of Texas at Houston; and University of Texas at San Antonio. All participants provided written informed consent.

The trial's primary outcome was change in hemoglobin A_{1c} (HbA_{1c}) six months after random assignment to study group. The trial's design and primary results have been described elsewhere.[14,15] Briefly, DPTT investigators randomly assigned 514 participants (recruited as described elsewhere[14]) to groups receiving either immediate or delayed periodontal treatment between November 2009 and March 2012. Treatment group participants received at least 160 minutes of scaling and root planing in two to four visits, used a daily chlorhexidine mouthrinse for at least one month, and received supportive periodontal therapy at three and six months after study group assignment. Therapists used powered scalers and hand curettes. Local anesthetic (applied topically or injected) was used as needed. Completeness of therapy was assessed by the study therapist and confirmed by a study periodontist. Both treatment and control groups received oral hygiene instructions and information on healthy living at the baseline visit. All participants were monitored by the same group of trained examiners using calibrated technique for periodontal disease progression three and six months after study group assignment. Participants with progressive disease received localized or full-mouth scaling and root planing, depending on the extent of disease progression. Control participants were offered full-mouth scaling and root planing after six months.

Data collection. Examiners using calibrated technique obtained clinical periodontal measurements by using manual probes (University of North Carolina–15). They examined participants at baseline and three and six months after study group assignment. They assessed PD, the distance from the cementoenamel junction to the gingival margin (CEJ-GM) and bleeding on probing (BOP) at six sites on all teeth except third molars. They computed clinical attachment level (CAL) for each site from the PD and CEJ-GM measurements. They scored dental plaque at each tooth site as detectable (1) or undetectable (0, with a probe or visually) and computed it as a full-mouth percentage.

Outcome assessment. We assessed change in clinical periodontal status by using three outcomes: six-month change from baseline in full-mouth mean PD, full-mouth mean CAL and the percentage of tooth sites with BOP. Our study included data from 473 participants (240 treatment group participants and 233 control participants) of the 514 participants for whom complete baseline and six-month periodontal data were available.

Statistical analysis. We used individual analysis of variance or Pearson product moment correlations initially to explore bivariate associations between change in full-mouth mean PD, CAL and BOP and the following baseline factors: baseline disease severity (quartile split), treatment group (immediate treatment or delayed treatment [control]), age (in years), sex, race (African American, white or other), ethnicity (Hispanic or non-Hispanic), smoking history (current, former, or never), HbA_{1c} level (percentage), duration of diabetes (self-reported, in years), body mass index ([BMI] in kilograms per square meter, ≤ 30 versus > 30), full-mouth average clinical measurements, dental plaque, diastolic blood pressure (in millimeters of mercury), self-reported overall health and brushing and flossing frequency, and clinical site.

We constructed multiple regression models to evaluate associations between changes in periodontal measurements with various baseline factors simultaneously. We considered factors with P values < 0.1 in bivariate associations with the outcome of interest (change in PD, CAL or BOP) for inclusion in the regression models. We also evaluated all two-way interactions between these factors. We used backward selection to determine the final model. We removed nonsignificant interactions and factors ($P > .05$), and the final models included only factors significantly associated with the outcome. We selected factors by using an F test based on a type 3 sum of squares. We reported both unadjusted P values and P values with Bonferroni adjustment for multiple tests.

The clinical enrollment site was statistically significant in each model. Because our goal was to explore predictors useful to a clinician, in this article we do not report the clinical site effect, although it was adjusted in

ABBREVIATION KEY. **BMI:** Body mass index. **BOP:** Bleeding on probing. **CAL:** Clinical attachment level. **CEJ-GM:** Cementoenamel junction to the gingival margin. **DPTT:** Diabetes and Periodontal Therapy Trial. **HbA_{1c}:** Glycated hemoglobinA_{1c}. **PD:** Probing depth. **T2DM:** Type 2 diabetes mellitus.

TABLE 1

General baseline characteristics of participants in the Diabetes and Periodontal Therapy Trial, according to study arm.

PARTICIPANT CHARACTERISTIC	PARTICIPANT GROUP		*P* VALUE*
	Treatment (n = 240)	Control (n = 233)	
Age, in Years			
Mean (standard deviation [SD])	56.8 (10.6)	58.1 (9.4)	.16
Range	35.0-85.0	35.0-85.0	
≤ 57, no. (%)	130 (54.2)	109 (46.8)	.11
> 57, no. (%)	110 (45.8)	124 (53.2)	
Sex, No. (%)			
Male	133 (55.4)	120 (51.5)	.39
Female	107 (44.6)	113 (48.5)	
Race, No. (%)			
African American	73 (30.4)	63 (27.0)	
White	129 (53.8)	130 (55.8)	.71
Other	38 (15.8)	40 (17.2)	
Hispanic Ethnicity			
Yes	79 (32.9)	75 (32.2)	.87
No	161 (67.1)	158 (67.8)	
Smoking History, No. (%)			
Never	119 (49.6)	132 (56.7)	
Former	84 (35.0)	77 (33.0)	.16
Current	37 (15.4)	24 (10.3)	
Hemoglobin A_{1c} Level			
Mean (SD)	7.84 (0.65)	7.77 (0.60)	.24
Range	6.6-9.9	6.1-9.5	
< 7.7, no. (%)	136 (56.7)	118 (50.6)	.19
≥ 7.7, no. (%)	104 (43.3)	115 (49.4)	
Clinical Site, No. (%)			.95
University of Alabama at Birmingham	47 (19.6)	49 (21.0)	
University of Minnesota, Minneapolis	80 (33.3)	74 (31.8)	
Stony Brook University, State University of New York	35 (14.6)	38 (16.3)	
University of Texas at Houston	8 (3.3)	6 (2.6)	
University of Texas at San Antonio	70 (29.2)	66 (28.3)	
Duration of Diabetes, in Years†			
Mean (SD)	12.5 (8.2)	11.5 (8.7)	.20
Range	0.0-39.0	0.0-55.0	
≤ 5, no. (%)	53 (22.2)	69 (29.7)	
5.1-10, no. (%)	58 (24.3)	49 (21.1)	.17
> 10, no. (%)	128 (53.6)	114 (49.1)	
Diastolic Blood Pressure, in Millimeters of Mercury			
Mean (SD)	78.7 (12.5)	78.7 (10.8)	1.00
Range	50.0-126.0	48.0-114.0	
≤ 78, no. (%)	125 (52.1)	118 (50.6)	.75
> 78, no. (%)	115 (47.9)	115 (49.4)	
Body Mass Index (Weight/Height^2), in Kilograms per Square Meter‡			
Mean (SD)	34.5 (7.2)	34.2 (6.6)	.69
Range	20.2-73.7	20.8-57.8	
≤ 30, no. (%)	64 (26.9)	65 (28.0)	.78
> 30, no. (%)	174 (73.1)	167 (72.0)	
Periodontal Measurements			
No. of teeth			.04
Mean (SD)	25.4 (3.7)	24.7 (3.6)	
Range	16.0-32.0	16.0-32.0	
Probing depth (PD), in mm			
Overall			.67
Mean (SD)	3.3 (0.6)	3.3 (0.7)	
Range	2.2-5.7	2.0-6.6	
No. of sites with PD ≥ 5 mm			.80
Mean (SD)	28.5 (21.1)	28.0 (22.4)	
Range	3-109	3-140	
No. of sites with PD ≥ 7 mm			.69
Mean (SD)	3.3 (6.0)	3.5 (8.3)	
Range	0-50.0	0-77.0	
Clinical attachment loss (CAL), in mm			.98
Overall			
Mean (SD)	3.49 (0.81)	3.48 (0.89)	
Range	1.5-6.4	1.6-7.4	
No. of sites with CAL ≥ 5 mm			.43
Mean (SD)	35.3 (24.9)	33.4 (25.7)	
Range	3.0-118.0	3.0-131.0	
No. of sites with CAL ≥ 7 mm			.65
Mean (SD)	6.4 (9.4)	6.9 (12.0)	
Range	0-61.0	0-89.0	

* Corresponds to a *t* test for continuous variables or χ^2 test of association (categorical).
† Data regarding duration of diabetes were missing for one participant in the treatment group and one participant in the control group.
‡ Data regarding body mass index were missing for two participants in the treatment group and one participant in the control group.

TABLE 1 (CONTINUED)

PARTICIPANT CHARACTERISTIC	PARTICIPANT GROUP		*P* VALUE*
	Treatment (n = 240)	Control (n = 233)	
Bleeding on probing, percentage of sites per person			.53
Mean (SD)	60.6 (24.0)	59.1 (25.9)	
Range	5.7-100	2.8-100	
Plaque, percentage of sites per person			.50
Mean (SD)	0.86 (0.18)	0.84 (0.21)	
Range	0.3-1.0	0.0-1.0	
Self-reported overall health, no. (%)			
Excellent to very good	47 (19.6)	53 (22.7)	
Good	117 (48.8)	129 (55.4)	.06
Fair to poor	76 (31.7)	51 (21.9)	
Frequency of brushing teeth, no. (%)			
More than once per day	152 (63.3)	158 (67.8)	
Once per day	81 (33.8)	62 (26.6)	.14
A few times per week	3 (1.3)	9 (3.9)	
Rarely or never	4 (1.7)	4 (1.7)	
Frequency of flossing teeth, no. (%)			
Daily	59 (24.6)	57 (24.5)	
4-6 times per week	17 (7.1)	21 (9.0)	.84
1-3 times per week	56 (23.3)	57 (24.5)	
Less than once per week	108 (45.0)	98 (42.1)	

all models. Although the primary analysis included all trial participants and included "treatment" in the model, we also studied associations in the treatment group alone and developed multivariate models as described previously. For these analyses, we grouped change in PD, CAL and BOP according to tertiles, and we explored the relationship between baseline characteristics and change (categorized by tertile) by using generalized logistic regression. Results from the two sets of analyses were qualitatively similar, and in this article we report only results regarding the mean change in each clinical measurement that include all participants.

In addition to calculating mean full-mouth PD, CAL and BOP changes, we also computed changes in these clinical measures stratified according to baseline disease severity to compare the clinical response among DPTT participants with summaries of patients' clinical responses typically reported in the literature. To determine this, we averaged changes at sites with baseline probing depths of 3 mm or less, 4 to 6 mm, and 7 mm or more within, then across, participants. For each participant, we used only changes at qualifying sites to calculate mean change. We used linear mixed-effect models, which accounted for intraparticipant correlations, to compute group means, standard deviations (SDs), and *P* values used to compare treatment groups. We performed all data analyses by using statistical software (SAS 9.3, SAS Institute, Cary, N.C.).

RESULTS

Periodontal treatment response. Table 1 summarizes baseline characteristics in the treatment and control groups. The majority of participants were white and non-Hispanic. Although not shown in the table, overall, the most prevalent self-reported ethnic groups according to race (data not shown) were non-Hispanic white (n = 154), non-Hispanic black (n = 135), Hispanic white (n = 105) and Hispanic Native American (n = 35). Only one participant reported being Hispanic and black. Sixty-one of 473 participants (12.9 percent) were current smokers. Participants had relatively long-standing diabetes (mean duration, > 10 years) and more than 70 percent were obese (BMI > 30 kg/m^2). Participants had widespread periodontitis, although relatively few sites per participant had advanced PD and CAL (that is, ≥ 7 mm for both PD and CAL).

Table 2 presents the mean changes in PD, CAL and BOP according to treatment group and baseline PD severity. The treatment group experienced significantly greater changes in these measures than did the control group. Full-mouth mean changes in control participants were small and clinically insignificant. Within the treatment group, mean PD reduction ranged from 0.16 mm in sites with baseline PDs of 3 mm or lower to 1.92 mm in sites with baseline PDs of 7 mm or greater. In untreated control participants, mean PD increased (that is, deepened) slightly in initially shallow sites and improved in initially deep sites. Changes in CAL after treatment followed the same pattern as noted for PD. In contrast, the magnitude of change in BOP was similar across the baseline PD categories—about 20 percent. Findings of the linear trend test, which gauged whether the change in each clinical measure steadily increased (or decreased) across categories, were significant ($P < .01$) for PD and CAL but not for BOP.

Variables associated with change in PD, CAL and BOP. Tables 3 through 5 (pages 1232-1236) summarize the results of the multivariate analyses. For each outcome, we first present the main effects between periodontal change and each factor and then summarize the significant two-way interactions. Hispanic ethnicity was not significantly associated with change in any measure, but we retained it in the models for PD and CAL change because of the significant treatment-according-to-ethnicity interaction for these outcomes (see below). In bivariate analyses, baseline plaque was associated significantly with change in each periodontal measure ($P < .0001$), but we excluded it from the final models because of its

TABLE 2

Baseline and six-month change* in periodontal measurements, stratified according to baseline probing depth (PD) severity and study group.

FULL MOUTH AND SITE WITH LEVEL OF BASELINE PD SEVERITY	STUDY GROUP						TREATMENT EFFECT (95% CONFIDENCE INTERVAL), *P* VALUE†
	Treatment			Control			
	No.‡	Baseline, Mean (SD§)	Six-Month Change (Δ), Mean (SD)	No.‡	Baseline, Mean (SD)	Six-Month Change, Mean (SD)	
Mean PD per Site per Participant, in Millimeters							
Full mouth	240	3.25 (0.56)	−0.47 (0.44)	233	3.28 (0.66)	−0.14 (0.31)	0.33 (0.29-0.37), < .0001
Baseline PD ≤ 3 mm¶	240	2.47 (0.17)	−0.16 (0.29)	233	2.48 (0.19)	0.07 (0.28)	0.22 (0.10-0.35), .0004
Baseline PD 4-6 mm#	240	4.61 (0.23)	−1.02 (0.53)	233	4.62 (0.24)	−0.52 (0.45)	0.50 (0.38-0.63), < .0001
Baseline PD ≥ 7 mm**	143	7.43 (0.71)	−1.92 (1.32)	126	7.55 (0.68)	−1.28 (1.15)	0.62 (0.46-0.78), < .0001
Mean Clinical Attachment Loss (CAL) per Site per Participant, in mm							
Full mouth	240	3.48 (0.80)	−0.36 (0.48)	233	3.47 (0.89)	−0.04 (0.43)	0.32 (0.27-0.37), < .0001
Baseline PD ≤ 3 mm¶	240	2.79 (0.59)	−0.09 (0.41)	233	2.79 (0.60)	0.13 (0.41)	0.22 (0.09-0.36), .002
Baseline PD 4-6 mm#	240	4.68 (0.66)	−0.86 (0.56)	233	4.67 (0.73)	−0.39 (0.60)	0.47 (0.33-0.60), < .0001
Baseline PD ≥ 7 mm**	143	7.44 (1.41)	−1.53 (1.38)	126	7.39 (1.27)	−1.00 (1.29)	0.49 (0.31-0.66), < .0001
Percentage of Sites With Bleeding on Probing per Participant, in Percentages							
Full mouth	240	61 (24)	−20 (21)	232††	59 (26)	−4 (18)	17 (15-19), < .0001
Baseline PD ≤ 3 mm¶	240	52 (24)	−21 (23)	232††	51 (26)	−4 (19)	17 (12-21), < .0001
Baseline PD 4-6 mm#	240	81 (20)	−23 (26)	232††	79 (22)	−5 (21)	18 (14-23), < .0001
Baseline PD ≥ 7 mm**	143	93 (21)	−18 (38)	125††	90 (25)	−6 (32)	11 (6-17), .0001

* Analyses were based on linear mixed-effect models to account for intraparticipant correlations. Six-month changes in periodontal measurements were included as dependent variables and the treatment group status as an independent factor. For each participant, only changes at qualifying sites were used to calculate full-mouth mean change. For example, for the category "Baseline PD ≥ 7 mm," only changes at sites initially 7 mm or greater in depth were included in calculating the mean change for that person. Thus, although a participant could have contributed sites to each of the categories, each tooth site was included in only one category. The number of qualifying sites per person, however, could vary by category.

† Treatment effect: Difference in average change in periodontal measurements (six months – baseline) between the treatment groups (control group – treatment group). Negative values for change indicate improvements from baseline. Treatment effects and 95 percent confidence intervals (CIs) were determined from linear mixed-effect models and P values testing for treatment effects involved the use of t tests based on mixed-effect models. Changes were averaged within participants and then within groups.

‡ Number of participants having at least one site in the baseline PD severity category.

§ SD: Standard deviation.

¶ Mean (SD) numbers of sites with baseline PD of ≤ 3 mm were 100.75 (29.96) and 98.03 (32.13) for the treatment and control groups, respectively.

\# Mean (SD) numbers of sites with baseline PD of 4-6 mm were 47.25 (23.38) and 45.57 (23.82) for the treatment and control groups, respectively.

** Mean (SD) numbers of sites with baseline PD of ≥ 7 mm were 3.25 (6.03) and 3.52 (8.34) for the treatment and control groups, respectively.

†† Data regarding bleeding on probing at six months were missing for one participant.

collinear relationships with the baseline disease severity measures ($P < .0001$ for all correlations between baseline plaque and baseline disease measures).

For PD change, treatment group, BMI and baseline PD remained significant in the multivariate model (Table 3). Participants in the treatment group, those with higher mean baseline PD, and those who were obese experienced greater mean PD reductions than did control group participants and those with lower initial PD and BMI values. When we controlled for all other factors in the model, participants who were obese experienced a 0.10-mm greater reduction in PD than did their counterparts who were not obese ($P = .0007$). Two interactions (Hispanic ethnicity according to treatment group and

TABLE 3

Baseline factors associated with six-month probing depth (PD) change: adjusted values based on final regression model.

BASELINE FACTOR	MEAN (SD*) BASELINE PD, IN MILLIMETERS	ADJUSTED† SIX-MONTH CHANGE AND DIFFERENCE, IN mm		DIFFERENCE (95% CI‡) BETWEEN TREATMENT AND CONTROL GROUPS FOR INTERACTIONS (CONTROL − TREATMENT), *P* VALUE†
		Mean Change (95% CI)	Difference (95% CI), *P* Value†	
Main Effects				
Study group				Not applicable (NA)
Treatment	3.26 (0.57)	−0.47 (−0.52 to −0.42)	−0.38 (−0.44 to −0.33), < .0001§	
Control	3.28 (0.66)	−0.08 (−0.14 to −0.03)	Reference	
Hispanic ethnicity				NA
Yes	3.25 (0.53)	−0.29 (−0.36 to −0.22)	−0.03 (−0.10 to 0.05), .50	
No	3.28 (0.65)	−0.26 (−0.31 to −0.22)	Reference	
Body mass index, in kilograms per square meter				NA
≤ 30	3.27 (0.55)	−0.22 (−0.29 to −0.16)	0.10 (0.05-0.17), .0007§	
> 30	3.27 (0.64)	−0.33 (−0.38 to −0.28)	Reference	
Baseline PD level, in mm				NA
≤ 2.84	2.64 (0.16)	−0.07 (−0.13 to 0.00)	0.45 (0.37-0.53), < .0001§	
> 2.84-3.15	3.00 (0.09)	−0.18 (−0.24 to −0.11)	0.34 (0.26-0.42), < .0001§	
> 3.15-3.59	3.34 (0.13)	−0.34 (−0.41 to −0.28)	0.18 (0.10-0.25), < .0001§	
> 3.59	4.12 (0.53)	−0.52 (−0.59 to −0.45)	Reference	
Interactions				
Study group and Hispanic ethnicity				
Treatment group, Hispanic				NA
Yes	3.25 (0.60)	−0.56 (−0.64 to −0.48)	−0.18 (−0.27 to −0.09), .0002§	0.54 (0.44-0.63), < .0001§a¶
No	3.27 (0.60)	−0.38 (−0.44 to −0.32)	Reference	0.23 (0.16-0.30), < .0001§b
Control group, Hispanic				NA
Yes	3.27 (0.53)	−0.02 (−0.11 to 0.07)	0.13 (0.03-0.23), .01	a
No	3.28 (0.70)	−0.15 (−0.21 to −0.09)	Reference	b

* SD: Standard deviation.
† Based on the final regression with treatment group, Hispanic ethnicity, baseline PD, clinical site (data not shown), interaction between treatment and Hispanic ethnicity, and interaction between treatment and baseline PD as covariates. Age, race, baseline body mass index, diastolic blood pressure, self-reported overall health, gingival health and frequency of flossing also were evaluated but were removed from the final model because they were not associated significantly with six-month PD change. The plaque score was excluded from the final model because it was associated collinearly with baseline PD.
‡ CI: Confidence interval.
§ *P* value remained significant after Bonferroni adjustment ($P < .05/20 = .0025$).
¶ Superscript lowercase letters ($^{a, b, c, d, e, f}$) denote differences in six-month periodontal changes between the treatment and control groups within each Hispanic ethnicity group (Yes/No) and within each baseline PD level (≤ 2.84, 2.84-3.15, 3.15-3.59 and > 3.59). The same letter is used to represent the difference in the six-month change in periodontal outcome between the treatment and control groups for each Hispanic ethnicity and baseline PD category.

baseline PD according to treatment group) also remained significant in the model. PD changes were associated more strongly with baseline PD in the treatment group than in the control group (Table 3). For example, mean PD reductions in the treatment group increased from 0.22 mm in those with a mean baseline PD of 2.84 mm or less to 0.83 mm in those with baseline PD greater than 3.59 mm. The respective values in the control group ranged from a 0.08-mm increase to a 0.20-mm reduction. Finally, the difference in PD change between test

TABLE 3 (CONTINUED)

BASELINE FACTOR	MEAN (SD*) BASELINE PD, IN MILLIMETERS	ADJUSTED† 6-MONTH CHANGE AND DIFFERENCE, IN mm		DIFFERENCE (95% CI‡) BETWEEN TREATMENT AND CONTROL GROUPS FOR INTERACTIONS (CONTROL – TREATMENT), *P* VALUE†
		Mean Change (95% CI)	Difference (95% CI), *P* Value†	
Study group and baseline PD level, in mm				
Treatment group, baseline PD level				
≤ 2.84	2.66 (0.16)	−0.22 (−0.30 to −0.13)	0.62 (0.51-0.73), < .0001§	0.30 (0.18-0.41), < .0001§c
> 2.84-3.15	3.00 (0.09)	−0.30 (−0.38 to −0.22)	0.53 (0.42-0.64), < .0001§	0.24 (0.13-0.35), < .0001§d
> 3.15-3.59	3.34 (0.12)	−0.53 (−0.62 to −0.45)	0.30 (0.19-0.41), < .0001§	0.38 (0.27-0.48), < .0001§e
> 3.59	4.08 (0.42)	−0.83 (−0.92 to −0.74)	Reference	0.63 (0.51-0.74), < .0001§f
Control group, baseline PD level				
≤ 2.84	2.61 (0.17)	0.08 (−0.01 to 0.17)	0.28 (0.17-0.40), < .0001§	c
> 2.84-3.15	3.00 (0.10)	−0.06 (−0.15 to 0.03)	0.14 (0.03-0.26), .01	d
> 3.15-3.59	3.35 (0.14)	−0.15 (−0.24 to −0.07)	0.05 (−0.06 to 0.16), .37	e
> 3.59	4.15 (0.60)	−0.20 (−0.29 to −0.12)	Reference	f

and control groups was significantly greater in Hispanic participants than in non-Hispanic participants. To further explore the effect of ethnicity on PD change, we compared the mean change between non-Hispanic white participants (75 treatment and 79 control) and black participants (73 treatment and 62 control) and between Hispanic white participants (54 treatment and 51 control) and non-Hispanic white participants (75 treatment and 79 control) (data not shown). The mean (standard error of the mean) change did not differ between non-Hispanic white participants and black participants (0.07 [0.08] mm; $P = .35$) but was significantly greater in Hispanic white participants than in non-Hispanic white participants (0.38 [0.09] mm; $P < .0001$).

For CAL change (Table 4), treatment group, baseline CAL, and the treatment-group-according-to-baseline-CAL and treatment-group-according-to-Hispanic-ethnicity interactions remained significant in the model. Again, treatment group participants and those with higher baseline CAL values experienced greater improvements in CAL than did control group participants and those with lower initial mean CAL. As with PD change, the difference in CAL change between test and control groups was significantly greater in Hispanic participants than in non-Hispanic participants. The change in CAL increased monotonically with increasing baseline CAL in the treatment group but not the control group.

Treatment group, BMI and baseline BOP were associated significantly with change in BOP (Table 5). As with PD change, participants who were obese experienced a greater reduction in BOP than did participants who were not obese (adjusted mean difference = 7.6 percent; $P < .0001$). Only one interaction, treatment group according to baseline BOP, remained significant. Within the treatment group, BOP decreased steadily with increasing baseline BOP, from 2.7 percent in those with the least extensive baseline BOP (< 39.9 percent) to 36.3 percent in those with the most extensive BOP (> 81.9 percent).

Interestingly, baseline HbA_{1c} level, diabetes duration and smoking status were not associated significantly with treatment response. To further explore the effect of diabetes measures on periodontal response, we calculated Pearson product moment correlations between change in PD, CAL and BOP and baseline HbA_{1c} level and diabetes duration (in years). For both the combined groups and the treatment group alone, all of the correlations were weak and statistically nonsignificant ($r = -0.11$ to 0.03; all P values > .10).

Finally, because at baseline and at each follow-up visit all participants received information regarding a healthy lifestyle, which is not a routine component of periodontal therapy, we examined the effects of weight loss on the periodontal outcomes. Overall, mean (SD) changes from baseline in BMI were nominal and did not differ significantly between groups (treatment group = −0.10 [1.33] kg/m^2; control group = −0.08 [1.40] kg/m^2;

TABLE 4

Baseline factors associated with six-month clinical attachment loss (CAL) change: adjusted values based on final regression model.

BASELINE FACTOR	MEAN (SD*) BASELINE CAL, IN MILLIMETERS	ADJUSTED† SIX-MONTH CHANGE AND DIFFERENCE, IN mm		DIFFERENCE (95% CI‡) BETWEEN TREATMENT AND CONTROL GROUPS FOR INTERACTIONS (CONTROL − TREATMENT), *P* VALUE
		Mean Change (95% CI)	Difference (95% CI), *P* Value	
Main Effects				
Study group				Not applicable (NA)
Treatment	3.49 (0.81)	−0.38 (−0.45 to −0.31)	−0.34 (−0.42 to −0.27), < .0001§	
Control	3.48 (0.89)	−0.04 (−0.11 to 0.03)	Reference	
Hispanic ethnicity				NA
Yes	3.52 (0.70)	−0.24 (−0.32 to −0.15)	−0.06 (−0.15 to 0.04), 0.27	
No	3.47 (0.91)	−0.18 (−0.24 to −0.12)	Reference	
Baseline CAL level, in mm				NA
≤ 2.94	2.58 (0.33)	0.00 (−0.09 to 0.08)	0.38 (0.28-0.49), < .0001§	
> 2.94-3.33	3.12 (0.12)	−0.16 (−0.24 to −0.08)	0.22 (0.12-0.33) < .0001§	
> 3.33-3.93	3.57 (0.17)	−0.28 (−0.36 to −0.20)	0.10 (0.00-0.20), 0.05	
> 3.93	4.65 (0.65)	−0.39 (−0.47 to −0.30)	Reference	

* SD: Standard deviation.
† Based on the final regression with treatment group, Hispanic ethnicity, baseline CAL, clinical site (data not shown), interaction between treatment and Hispanic ethnicity, and interaction between treatment and baseline CAL as covariates. Age, race, baseline body mass index, diastolic blood pressure, self-reported overall health, gingival health and frequency of flossing also were evaluated but were removed from the final model because they were not associated significantly with six-month CAL change. The plaque score was excluded from the final model because it was associated collinearly with baseline CAL.
‡ CI: Confidence interval.
§ *P* value remained significant after Bonferroni adjustment ($P < .05/19 = .003$).
¶ Superscript lowercase letters ($^{a, b, c, d, e, f}$) denote differences in six-month periodontal changes between the treatment and control groups within each Hispanic ethnicity group (Yes/No) and within each baseline CAL level (≤ 2.94, 2.94-3.33, 3.33-3.93 and > 3.93). The same letter is used to represent the difference in the six-month change in periodontal outcome between the treatment and control groups for each Hispanic ethnicity and baseline CAL category.

P = .85). Correlations between change in BMI and change in PD, CAL and BOP also were low and statistically nonsignificant (*r* = 0.02 to 0.04; all *P* values > 0.1), suggesting that change in BMI was not associated with change in the clinical periodontal measures.

DISCUSSION

We used data from a randomized controlled trial to study predictors of the response to nonsurgical periodontal therapy in patients with T2DM and moderate to advanced periodontitis. As expected, treatment (versus no treatment) was associated with the largest average change in all clinical measures. Baseline disease severity was the only other variable consistently associated with changes in these measures. Obesity (BMI > 30) was associated with a small but more favorable response in terms of change in PD and BOP, but not in CAL. We also found that Hispanic participants responded more favorably than did non-Hispanic participants to treatment in terms of PD and CAL changes.

Interestingly, baseline glycemic control (measured as HbA_{1c} level), duration of diabetes, and smoking were not associated significantly with treatment response. In other words, participants with long-standing diabetes or higher baseline HbA_{1c} values did not respond less favorably than did those with more recent diabetes diagnoses or better glycemic control. This finding contradicts a commonly held notion that hyperglycemia, through its effects on immune functions and the microvasculature,[16] adversely affects a person's response to periodontal treatment. For example, Santos and colleagues[17] treated a small number of people who had diabetes with scaling and root planing and maintenance care and found that participants with baseline HbA_{1c} values ranging from 4.8 to 8.7 percent had significantly greater gains in CAL than did those with baseline values between 9 and 12 percent. The absolute difference between groups in the Santos and colleagues study, however, was slight, and the groups did not differ in terms of PD and BOP changes after receiving treatment. The lack of a similar CAL finding

TABLE 4 (CONTINUED)

BASELINE FACTOR	MEAN (SD*) BASELINE CAL, IN MILLIMETERS	ADJUSTED† SIX-MONTH CHANGE AND DIFFERENCE, IN mm		DIFFERENCE (95% CI‡) BETWEEN TREATMENT AND CONTROL GROUPS FOR INTERACTIONS (CONTROL − TREATMENT), *P* VALUE
		Mean Change (95% CI)	Difference (95% CI), *P* Value	
Interactions				
Study group and Hispanic ethnicity				
Treatment group, Hispanic				
Yes	3.57 (0.69)	−0.47 (−0.58 to −0.37)	−0.19 (−0.31 to −0.06), .003§	0.47 (0.35-0.60) < .0001‡a§
No	3.44 (0.89)	−0.29 (−0.36 to −0.21)	Reference	0.21 (0.12, 0.30), < .0001‡b
Control group, Hispanic				
Yes	3.49 (0.70)	0.00 (−0.11 to 0.11)	0.08 (−0.05 to 0.20), .25	a
No	3.46 (0.95)	−0.07 (−0.15 to 0.00)	Reference	b
Study group and baseline CAL level, in mm				
Treatment group, baseline CAL level				
≤ 2.94	2.54 (0.37)	−0.12 (−0.23 to 0.00)	0.58 (0.44-0.72), < .0001§	0.23 (0.08-0.37), .003§c
> 2.94-3.33	3.13 (0.12)	−0.27 (−0.38 to −0.16)	0.43 (0.29-0.57), < .0001§	0.21 (0.06-0.35), .0052d
> 3.33-3.93	3.53 (0.17)	−0.44 (−0.55 to −0.33)	0.25 (0.11-0.40), .0004§	0.32 (0.17-0.46), < .0001§e
> 3.93	4.54 (0.55)	−0.70 (−0.80 to −0.59)	Reference	0.62 (0.47-0.77), < .0001§f
Control group, baseline CAL level				
≤ 2.94	2.58 (0.34)	0.11 (0.00 to 0.22)	0.18 (0.03-0.34), .02	c
> 2.94-3.33	3.12 (0.12)	−0.06 (−0.17 to 0.05)	0.02 (−0.13 to 0.17), .82	d
> 3.33-3.93	3.59 (0.18)	−0.12 (−0.23 to −0.02)	−0.05 (−0.20 to 0.10), 0.50	e
> 3.93	4.79 (0.71)	−0.07 (−0.20 to 0.05)	Reference	f

in our study may be because DPTT enrolled participants whose HbA_{1c} values were within a relatively narrow range (≥ 7 percent and < 9 percent).

Smoking also was not associated with change in any clinical response measure. The deleterious effects of cigarette smoking on periodontal treatment response are well established in the general population,[18] although we are not aware of any study in which researchers examined smoking's effects exclusively in people with T2DM. Less than 13 percent of participants in DPTT were current smokers, which limited the power of our sample to help detect differences in responses between smokers and nonsmokers. Nonetheless, we found no evidence to suggest that the treatment response was associated with smoking status (current, former or never). Although we did not show results for the bivariate analyses, *P* values used to compare change in the clinical measurements among smoking groups all were greater than .30.

When one considers this study's findings, it is important to consider the magnitude of the clinical response. Investigators in periodontal treatment studies often report PD changes stratified either according to baseline PD or at qualifying teeth or sites only. The full-mouth mean reduction in PD after scaling and root planing in the present our study was 0.47 mm, which included initially healthy and diseased sites. Haffajee and colleagues[19] reported similar mean full-mouth PD reductions six months after scaling and root planing alone or with adjunctive antibiotics. Findings in other studies of patients with chronic periodontitis[20-22] indicated that whereas those patients had greater full-mouth mean PD reductions (0.6-1.0 mm) than did the participants in our study, they also had higher initial mean PDs (3.6-4.4 mm) than did our participants (3.3 mm) (Table 1).

When stratified according to baseline PD, changes in PD and CAL after treatment in DPTT participants were similar to those described by others. For example, in pockets initially 4 to 6 mm in depth, Cobb[1] reported

TABLE 5

Baseline factors associated with six-month bleeding on probing (BOP) change: adjusted values based on final regression model.

BASELINE FACTOR	MEAN (SD*) BASELINE BOP, IN PERCENTAGES	ADJUSTED† SIX-MONTH CHANGE AND DIFFERENCE, IN PERCENTAGES		DIFFERENCE (95% CI‡) BETWEEN TREATMENT AND CONTROL GROUPS FOR INTERACTIONS (CONTROL − TREATMENT), *P* VALUE
		Mean Change (95% CI)	Difference (95% CI), *P* Value	
Main Effects				
Study group				Not applicable (NA)
Treatment	60.6 (24.0)	−19.0 (−21.9 to −16.1)	−14.1 (−18.4 to −9.8), < .0001§	
Control	59.1 (25.9)	−4.9 (−8.2 to −1.6)	Reference	
Body mass index, in kilograms per square meter				NA
≤ 30	60.2 (26.1)	−8.2 (−11.3 to −5.0)	7.6 (4.4-10.9), < .0001§	
> 30	59.8 (24.5)	−15.8 (−18.1 to −13.5)	Reference	
Baseline BOP level, percentage				NA
≤ 39.9	26.5 (9.5)	2.9 (−0.5 to 6.2)	26.6 (22.4-30.8), < .0001§	
> 39.9-62.8	51.2 (6.6)	−8.8 (−12.1 to −5.5)	15.0 (10.7-19.2), < .0001§	
> 62.8-81.9	72.8 (6.1)	−18.2 (−21.6 to −14.8)	5.5 (1.4-9.6), .008	
> 81.9	90.7 (5.2)	−23.7 (−27.3 to −20.2)	Reference	
Interactions				
Study group and baseline BOP level, percentage				
Treatment group, baseline BOP level				
≤ 39.9	28.2 (9.5)	−2.7 (−7.2 to 1.8)	33.6 (27.7-39.5), < .0001§	11.1 (4.6-17.6), .0008§a¶
> 39.9-62.8	51.3 (6.3)	−14.4 (−18.6 to −10.2)	21.9 (16.1-27.7), < .0001§	11.3 (4.9-17.7), .0006§b
> 62.8-81.9	71.6 (6.0)	−22.6 (−27.4 to −17.9)	13.7 (7.9-19.5), .0004§	8.9 (2.2-15.5), .0091c
> 81.9	90.8 (5.5)	−36.3 (−41.1 to −31.4)	Reference	25.1 (18.1-32.1), < .0001§d
Control group, baseline BOP level				
≤ 39.9	25.3 (9.4)	8.5 (3.6-13.3)	19.6 (13.6-25.6), < .0001§	a
> 39.9-62.8	51.7 (7.1)	−3.1 (−8.1 to 1.8)	8.0 (1.9-14.2), .01	b
> 62.8-81.9	73.6 (6.2)	−13.8 (−18.5 to −9.0)	−2.6 (−8.4 to 3.2), .38	c
> 81.9	90.9 (5.2)	−11.2 (−16.3 to −6.1)	Reference	d

* SD: Standard deviation.
† Based on the final regression with treatment group, body mass index, baseline BOP, clinical site (data not shown) and interaction between treatment and baseline BOP (data not shown) as covariates. Age, race, Hispanic ethnicity, diastolic blood pressure, self-reported overall health, gingival health and frequency of flossing also were evaluated but were removed from the final model because they were not associated significantly with six-month BOP change. The plaque score was excluded from the final model because it was associated collinearly with baseline BOP.
‡ CI: Confidence interval.
§ *P* value remained significant after Bonferroni adjustment ($P < 05/15 = .003$).
¶ Superscript lowercase letters ($^{a, b, c, d}$) denote differences in six-month periodontal changes between the treatment and control groups within each baseline BOP level (≤ 39.86, 39.86-62.80, > 62.80-81.88 and > 81.88). The same letter is used to represent the difference in the six-month change in periodontal outcome between the treatment and control groups for each baseline BOP category.

average PD reductions and CAL gains of 1.29 mm and 0.55 mm, respectively. The corresponding amounts for DPTT participants were 1.02 mm and 0.86 mm. For sites initially 7 mm or greater in depth, Cobb reported average PD reductions and CAL gains of 2.16 mm and 1.19 mm, respectively. The respective DPTT amounts were 1.92 mm and 1.53 mm. Thus, the treatment response among DPTT participants could be judged as typical in terms of PD and CAL improvements, even when compared with that in mostly nondiabetic populations. The improvements in PD and CAL in the control group could be attributed to the Hawthorne effect, regression toward the mean, or the effect of oral hygiene instruction and reinforcement provided to all study participants, including control participants.[23,24]

Despite the typical improvements in PD and CAL, DPTT participants experienced only modest improvements in BOP. Compared with baseline, BOP was reduced an average of 19 percent. Cobb[1] reported six-month BOP reductions ranging from 12 to 87 percent in published trials. Although more pronounced reductions in BOP have been reported after nonsurgical periodontal therapy, other studies of people with[25] and without[19] diabetes have shown percentage point reductions similar to ours. Nonetheless, the apparent disassociation between changes in PD, CAL and BOP in our study is difficult to reconcile. The relatively modest reductions may be attributed to the fact that all participants had T2DM, which itself is associated with increased gingival bleeding[26] or may be a consequence of widespread aspirin use among study participants. Regular aspirin use has been associated with increased gingival bleeding.[27,28] About 50 percent of DPTT participants were taking aspirin (up to 325 mg) on a daily basis at baseline; the amount increased to 56 percent at the six-month examination. The theory that prevalent aspirin use in DPTT participants may have contributed to residual bleeding, however, is speculative. We did not include aspirin use, or change in aspirin use, in our prediction models. Investigators in other intervention studies in people with T2DM reported greater BOP reductions after treatment than we observed, although the prevalence of aspirin use was not reported in these trials.[17,29-31] Residual BOP in our treatment participants also may be attributed to levels of residual detectable plaque in participants.[15] Despite the provision of repeated oral hygiene instructions, most tooth surfaces in treatment participants had detectable (not necessarily visible) plaque at the six-month visit. The omission of plaque scores from the final statistical models, however, does not mitigate the importance of plaque control in periodontal treatment, but rather was based on its collinear relationship with baseline disease severity measures—that is, baseline plaque scores and disease severity scores were similarly associated with changes in the disease measures, and we included only the baseline disease severity measures in the final models.

We found that participants who were obese experienced slightly but significantly greater reductions in PD and BOP than those among people who were not obese, which is in contrast to recent findings in people without diabetes. For example, Suvan and colleagues[32] reported that increasing BMI and obesity were associated with smaller short-term reductions in PD after scaling and root planing. Obesity was not associated significantly with changes in bleeding, and only 21 percent of their sample was obese. Previous studies regarding the association between obesity and periodontitis have yielded inconsistent results, highlighting the need for additional intervention trials to increase our understanding of the role of obesity in defining the risk of experiencing periodontitis and periodontal treatment responses.[33]

In our study, all participants had T2DM, and 72 percent were obese (BMI > 30 kg/m^2). Only a small number of participants (N = 20) were of normal weight (BMI < 25), which precluded us from exploring associations with treatment response across all BMI categories (that is, underweight, normal, overweight, obese). In terms of BMI measures, however, our sample appears highly representative of U.S. adults with T2DM. In 2005 and 2006, 62.4 percent of U.S. adults with T2DM were obese,[34] and this proportion continues to increase steadily over time. In this same national report, the mean BMI was 34.2 kg/m^2, which is nearly identical to the mean for DPTT participants.[15] In terms of the relationship between obesity and periodontal treatment response, however, our findings likely are not generalizable to patients who do not have T2DM, most of whom are not obese.

Our study has several limitations. DPTT's enrollment criteria may limit the generalizability of our findings, even among those with T2DM. For example, participants were required to have moderate to poorly controlled T2DM and moderate to advanced periodontitis; fewer than one in three screened people with diabetes were eligible for the trial.[15] Thus, our findings may not apply to people with HbA_{1c} values outside the study range or with less severe or extensive periodontitis. We also evaluated only the short-term (six-month) response to therapy. Factors such as smoking and baseline HbA_{1c} level may be important predictors of longer-term outcomes, such as clinical changes over 12 or more months. Finally, although participants responded well to therapy in terms of PD and CAL changes, overall the changes in BOP were modest. A different set of characteristics may have been associated with change in BOP had these changes been more pronounced.

Finally, a significant clinical-center effect on treatment response remained after adjustment for race, ethnicity and baseline disease severity, all of which differed significantly among the centers. The source of participants also varied among centers (results not shown), with some centers recruiting a greater proportion of participants from diabetes clinics or dental clinics or by

means of study advertisements. We know of no biological reasons why the periodontal treatment response should vary according to recruitment source, and we did not include this variable in the models. In sum, we could not account for the clinical-center effect, which may have been caused by center differences in unmeasured confounding variables or examiner and therapist practices. Rather than ignore this effect, however, we included clinical center in the model but did not report it, for the reasons stated earlier.

Despite these limitations, the study has several strengths. To our knowledge, DPTT is the largest periodontal intervention trial of people with T2DM to date. The sample population was diverse in terms of race, ethnicity and geographic location.[15] Finally, although we analyzed the data on a per-protocol basis (that is, included participants had complete baseline and six-month data), the loss-to-follow-up rate in the parent study was low (about 7 percent). Thus, participants included in this study were representative of the larger trial sample.

CONCLUSIONS

This study demonstrated that baseline disease severity is associated with the magnitude of clinical response after nonsurgical therapy in people with T2DM. Obesity and Hispanic ethnicity also may be useful indicators of responsiveness. To the best of our knowledge, this is the first study in which investigators have assessed prognostic factors for response to periodontal therapy in patients with T2DM. Thus, these findings need to be corroborated by others before this information is incorporated into the treatment planning processes or prognostic assessments for this population. ■

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