

Research Article
Periodontal Science



HbA1c changes in patients with diabetes following periodontal therapy

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ABSTRACT

Purpose: This retrospective cohort study aimed to assess the effect of nonsurgical periodontal therapy on glycated hemoglobin (HbA1c) levels in patients with both type 2 diabetes and chronic periodontitis.

Methods: The intervention cohort (IC) comprised 133 patients with type 2 diabetes who received nonsurgical periodontal treatment, while the matching cohort (MC) included 4787 patients with type 2 diabetes who visited the Department of Endocrinology and Metabolism of Asan Medical Center. The patients in each cohort were divided into 3 groups according to their baseline HbA1c level: subgroup 1, HbA1c <7%; subgroup 2, 7% ≤ HbA1c <9%; and subgroup 3, HbA1c ≥9%. Changes in HbA1c levels from baseline to 6 and 12 months were analyzed. In addition, the association between changes in HbA1c levels and the number of periodontal maintenance visits was investigated.

Results: There were no statistically significant changes in HbA1c levels in the IC and MC or their subgroups when evaluated with repeated-measures analysis of variance. However, the IC showed maintenance of baseline HbA1c levels, while the MC had a trend for HbA1c levels to steadily increase as shown by pairwise comparisons (baseline to 6 months and baseline to 12 months). IC subgroup 1 also maintained steady HbA1c levels from 6 months to 12 months, whereas MC subgroup 1 presented a steady increase during the same period. The number of periodontal maintenance visits had no association with changes in HbA1c levels during the 1-year study duration.

Conclusions: For patients with both type 2 diabetes and periodontitis, nonsurgical periodontal treatment and periodontal maintenance may help to control HbA1c levels.

Keywords: Diabetes mellitus; Glycated hemoglobin A; Periodontal debridement; Periodontitis

INTRODUCTION

Periodontitis and diabetes are common, complex, and chronic diseases with an established bidirectional relationship. Diabetes is associated with an increased prevalence and severity of periodontitis, and severe periodontitis is also associated with compromised glycemic control [1,2]. Glycated hemoglobin (HbA1c) levels are used to monitor overall glycemic control in patients with diabetes. HbA1c levels reflect the average glycemia of the preceding 3 months

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

and have a strong predictive value for diabetes complications [3]. According to the American Diabetes Association (ADA) Standards of Medical Care in Diabetes 2016, diabetes is a state where the HbA1c level exceeds 6.5%, and an HbA1c level of less than 7% is recommended as the treatment goal for adults [4].

Studies have investigated the effects of periodontal treatment on glycemic control in individuals with diabetes. According to systematic reviews and meta-analyses, an additional reduction in HbA1c levels of around 0.4%p was found following periodontal treatment [5-8]. In a recent prospective cohort study, individuals with higher baseline HbA1c levels or poor glycemic control showed a greater reduction in HbA1c levels than those with controlled diabetes after long-term periodontal maintenance [9]. This finding has significant clinical implications, as it is accepted that every 1%p reduction in the HbA1c level could reduce diabetes complications by up to 21% over 10 years [10]. Although previous studies successfully showed the effect of periodontal treatment on changes in HbA1c levels, most of them compared the HbA1c levels for only a 6-month duration because periodontal treatment for participants in the untreated control group could not be delayed longer for ethical reasons. Thus, reports concerning the effects of the periodontal maintenance interval on glycemic control are hard to find.

Recently, the use of big data from electronic health records in biomedical research has progressively increased because of the large volume and diversity of data types and efficient management [11]. Big data investigations can provide more accurate insights into trends regarding a certain topic for a group (or groups) of interest. At Asan Medical Center (AMC) in Seoul, Korea, a research information system named Asan Biomedical research Environment (ABLE) has been developed to support researchers of the institution in utilizing clinical big data belonging to the center [12].

The aim of this study was to assess the effect of nonsurgical periodontal therapy (NPT) on HbA1c levels in patients with type 2 diabetes and chronic periodontitis for 1 year. To compare changes in HbA1c levels for a longer period, a large matching cohort (MC) was used as a control group to make it possible to analyze the effects of the periodontal maintenance interval.

MATERIALS AND METHODS

The present study was a retrospective cohort study, and the study protocol was approved by the Ethics Committee of AMC (Seoul, Korea; 2016-0384). Two cohorts of patients with type 2 diabetes who made follow-up visits to the Department of Endocrinology and Metabolism of AMC from 2010 to 2011 were chosen. The first cohort was the intervention cohort (IC), which included patients who received NPT at the Department of Periodontics of AMC and the second one was a large MC for the IC. NPT in the present study was defined as full mouth scaling and root planing (SRP).

Participants

Intervention cohort

The IC was a set of patients who were diagnosed as having both type 2 diabetes and moderate to severe chronic periodontitis according to the criterion of the 1999 International Workshop for the Classification of Periodontal Disease and Conditions [13]. In addition, the IC patients were required to have a history of NPT and at least 3 HbA1c level assessments, including

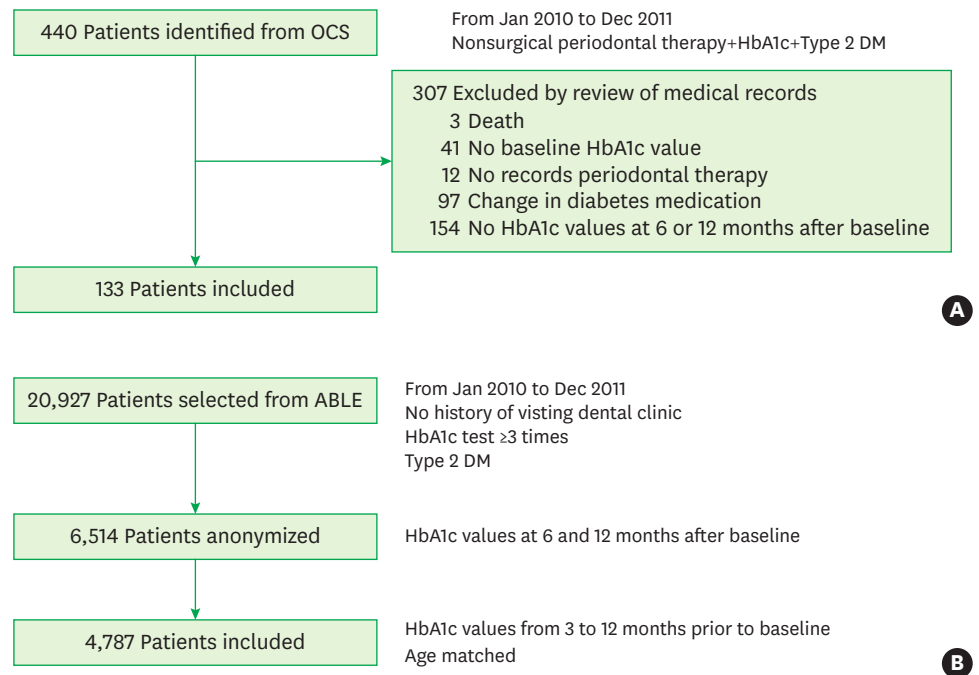


Figure 1. Study flow. (A) Intervention cohort. (B) matching cohort.

OCS: Order Communication System, ABLE: Asan Biomedical research Environment, HbA1c: glycosylated hemoglobin A, DM: diabetes mellitus.

an assessment within 3 months from and to NPT to determine their baseline HbA1c level. Patients who received surgical treatment following NPT were excluded.

The Order Communication System (OCS) was used to obtain a list of patients who received NPT only from 2010 to 2011, and a total of 440 patients were identified. Through a review of the medical records of the selected patients, 307 were excluded for reasons such as the absence of critical clinical data, periodontal treatment that was performed only in some regions of the mouth, changes in anti-diabetic medications, or death (Figure 1A).

Matching cohort

The MC was a set of patients with type 2 diabetes who had both made follow-up visits to the Department of Endocrinology and Metabolism of AMC from 2010 to 2011 and had at least three HbA1c level assessments during the study period. Patients included in the IC were excluded.

An anonymized list of 20,927 patients was obtained from ABLE. After matching by age with the IC and screening for the required HbA1c level assessment data, 4,847 patients were included in the MC (Figure 1B).

Outcome measures

HbA1c

HbA1c values from 3 time points (baseline and 6 and 12 months after the baseline assessment) were collected and compared. The HbA1c value of each patient in the IC within 3 months from and to NPT was referred as the baseline HbA1c, while the first HbA1c value during the study period was regarded as the baseline HbA1c for MC patients.

The patients in each cohort were grouped respectively according to their baseline HbA1c levels based on the ADA standards: <7% (subgroup 1); ≥7% and <9% (subgroup 2); and ≥9% (subgroup 3).

Number of periodontal maintenance visits

For IC patients, the number of periodontal maintenance visits following NPT was gathered and the patients were divided into 2 groups according to whether they had made at least 3 visits or fewer than 3 visits during the study period.

Statistical analysis

Statistical analyses were done with PASW Statistics for Windows version 18.0 (SPSS Inc., Chicago, IL, USA). Demographic data were descriptively presented as mean±standard deviation. The age and sex distributions of both groups were evaluated with the Student's *t*-test and χ^2 test, respectively. The significance level was set to 0.05.

HbA1c

The effects of NPT and periodontal maintenance on HbA1c levels over time were evaluated with repeated-measures (RM) analysis of variance (ANOVA). For intragroup comparisons, changes in HbA1c levels at 6 and 12 months from baseline were compared with the paired *t*-test for each time point. Intergroup comparisons were performed with the Student's *t*-test at each time point.

Number of periodontal maintenance visits

To evaluate the effect of the number of periodontal maintenance visits, HbA1c levels at baseline and 12 months were used. The differences between the group with at least 3 visits and the group with fewer than 3 visits were compared with the Student's *t*-test.

RESULTS

HbA1c

At baseline, the HbA1c levels, age distribution, and sex distribution between the IC and MC were not significantly different ($P>0.05$; by the Student's *t*-test for the baseline HbA1c levels and age distribution, and by the χ^2 test for the sex distribution) (Table 1).

Most patients had HbA1c levels less than 9%, and the distributions were similar for both cohorts at all time points. The HbA1c levels showed a tendency to slightly increase in subgroup 1, to remain stable in subgroup 2, and to decrease in subgroup 3 (Figure 2).

Table 1. Baseline characteristics of the intervention and matching cohorts

Characteristics	Intervention cohort (n=133)	Matching cohort (n=4,787)	P value ^{a)}
Age (yr)	59.78 ± 9.59	60.46 ± 10.79	0.080
Sex			0.928
Male	79 (59.4)	2,862 (59.8)	
Female	54 (40.6)	1,925 (40.2)	
Baseline HbA1c (%)	7.23 ± 1.22	7.25 ± 1.14	0.882

Values are presented as number (%) or mean±standard deviation.

HbA1c: glycated hemoglobin.

^{a)}P-value obtained with either the Student's *t*-test for age and baseline HbA1c or the χ^2 test for sex.

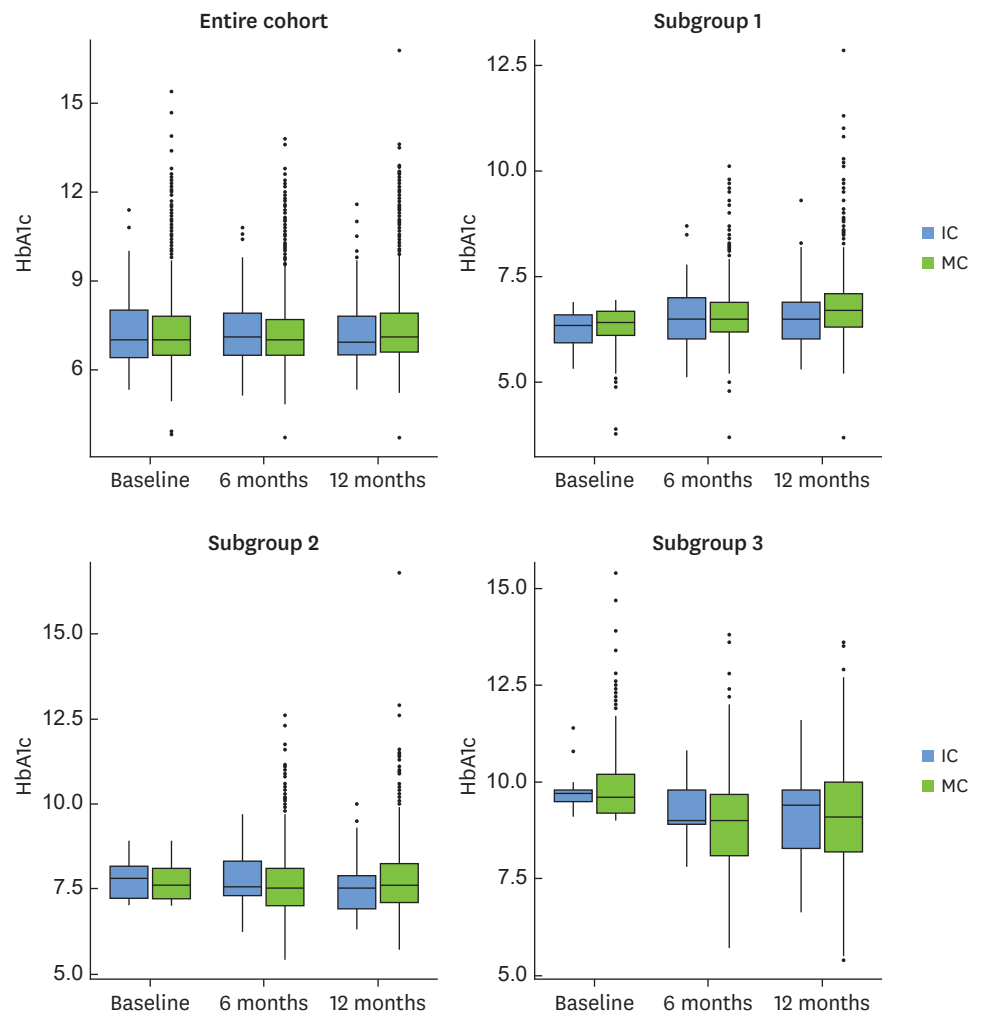


Figure 2. Boxplots for HbA1c levels of the IC and MC and their subgroups. The patients in each cohort were divided into 3 groups according to their baseline HbA1c level: Subgroup 1, baseline HbA1c <7%; subgroup 2, 7%≤ baseline HbA1c <9%; Subgroup 3, baseline HbA1c ≥9%. HbA1c: glycated hemoglobin; IC: intervention cohort, MC: matching cohort.

The entire cohort, as well as all the subgroups, showed no significant differences between the IC and MC over time ($P=0.702$ for the entire cohort, $P=0.090$ for subgroup 1, $P=0.978$ for subgroup 2, and $P=0.703$ for subgroup 3 by RM ANOVA). Similarly, no intergroup difference was found at each time point for the entire cohorts and all subgroups. However, significant changes in HbA1c levels from baseline were found for certain time-group combinations (for the entire cohort of the MC, subgroup 1 of the IC and MC, subgroup 2 of the MC, and subgroup 3 of the MC at 6 months, and for the entire cohort of the MC, subgroup 1 of the IC and MC, subgroup 2 of the IC and MC, and subgroup 3 of the MC at 12 months by the paired t -test). The mean HbA1c levels of subgroup 1 of the IC increased at 6 months and maintained that level at 12 months (6.28% at baseline, 6.56% at 6 months, and 6.59% at 12 months) while subgroup 1 of the MC showed a steady increase in mean HbA1c levels (6.39% at baseline, 6.57% at 6 months, and 6.76% at 12 months) (Table 2).

Table 2. HbA1c levels of the entire cohorts and subgroups at baseline, 6 months, and 12 months

Group	No.	HbA1c level (%)					
		Baseline	6 months	<i>P</i> value ^{a)}	12 months	<i>P</i> value ^{a)}	<i>P</i> value ^{b)}
Entire cohort							
IC	133	7.23 ± 1.22	7.29 ± 1.13	0.406	7.23 ± 1.16	0.992	0.702
MC	4,787	7.25 ± 1.14	7.21 ± 1.06	<u>0.002</u>	7.40 ± 1.12	<u>0.000</u>	
<i>P</i> value ^{c)}		0.889	0.447		0.111		
Subgroup 1							
IC	66	6.28 ± 0.42	6.56 ± 0.69	<u>0.000</u>	6.59 ± 0.76	<u>0.000</u>	0.090
MC	2,320	6.39 ± 0.38	6.57 ± 0.57	<u>0.000</u>	6.76 ± 0.65	<u>0.000</u>	
<i>P</i> value ^{c)}		0.050	0.880		0.079		
Subgroup 2							
IC	54	7.77 ± 0.55	7.71 ± 0.79	0.530	7.56 ± 0.79	<u>0.037</u>	0.978
MC	2,050	7.70 ± 0.54	7.58 ± 0.86	<u>0.000</u>	7.76 ± 0.93	<u>0.002</u>	
<i>P</i> value ^{c)}		0.332	0.259		0.067		
Subgroup 3							
IC	13	9.83 ± 0.62	9.26 ± 0.93	0.117	9.15 ± 1.43	0.202	0.703
MC	417	9.83 ± 0.88	8.97 ± 1.25	<u>0.000</u>	9.14 ± 1.38	<u>0.000</u>	
<i>P</i> value ^{c)}		0.987	0.284		0.977		

Values are presented as mean±standard deviation. The patients in each cohort were divided into 3 groups according to their baseline HbA1c level: Subgroup 1, baseline HbA1c <7%; Subgroup 2: 7%≤ baseline HbA1c <9%; Subgroup 3, baseline HbA1c ≥9%. *P* values less than 0.05 are underlined.

HbA1c: glycated hemoglobin, IC: intervention cohort, MC: matching cohort.

^{a)}*P* value obtained with the one-sample paired *t*-test for intragroup changes from baseline. ^{b)}*P* value obtained with repeated-measures analysis of variance for the overall intergroup changes. ^{c)}*P* value obtained with the Student's *t*-test for the intergroup comparison at the same time point.

Table 3. HbA1c levels of the intervention cohort according to the number of periodontal maintenance visits for 1 year

Number of maintenance visits	No.	HbA1c level (%)			
		Baseline	12 months	Differences	<i>P</i> value ^{a)}
≤3	73	7.34±1.33	7.27±1.29	-0.07±1.01	0.933
≥4	60	7.10±1.07	7.19±0.98	0.08±0.73	

Values are presented as mean±standard deviation.

HbA1c: glycated hemoglobin.

^{a)}*P* value obtained with the Student's *t*-test for the comparison of intergroup differences.

Number of periodontal maintenance visits

The mean HbA1c level from baseline to 12 months of patients with at least 3 maintenance visits for 1 year after the completion of periodontal therapy increased by 0.08%p, whereas that of patients with fewer than 3 maintenance visits decreased by 0.07%p. The results were not statistically significant (*P*=0.933) (Table 3).

DISCUSSION

In this retrospective study, we analyzed the mean changes in HbA1c levels from baseline to 6 months or 12 months between the IC and MC to assess the effect of NPT on HbA1c levels in patients with both type 2 diabetes and chronic periodontitis. There were no statistically significant differences in changes of HbA1c levels in the entire cohorts and all subgroups. Moreover, having at least 3 periodontal maintenance visits per year was found to have no statistically significant effect on HbA1c levels.

However, there were some noteworthy outcomes. For the entire cohorts, the HbA1c levels in the IC at 6 and 12 months were not significantly different from those at baseline when compared by respective pairs (*P*=0.406 for 6 months vs. baseline, *P*=0.992 for 12 months vs. baseline) while the HbA1c levels of the MC at 6 and 12 months were significantly different from those at baseline (*P*=0.002 for 6 months vs. baseline, *P*=0.000 for 12 months vs. baseline). Furthermore, in patients with baseline HbA1c levels less than 7%, the difference

in the change of HbA1c levels between the IC and MC nearly reached statistical significance, with a P value of 0.09, which did not meet the selected alpha level (0.05). These results may be interpreted as indicating that NPT could be helpful in maintaining the HbA1c levels of patients with both periodontitis and controlled glycemia of less than 7% of HbA1c.

To the authors' knowledge, this study is the first to use a big data sample as a control cohort. In previous studies on type 2 diabetes and periodontitis, the study duration was 6 months or less. One reason for this may be ethical problems, such as it not being ethically acceptable to allow patients to remain untreated for a long time. If a certain intervention is effective, the outcome measures from the subjects who received the intervention should be different from those obtained with whole population. Extending this thought, a representative sample of the population could be an effective control for statistical analyses. As the size of the MC was sufficiently large, the MC in the present study could be used as a control for the statistical analysis. Specifically, the size of the MC was 4,847, which was sufficient to calculate statistics on the population of patients with diabetes with a margin of error of 2% at a 99% confidence level. Even the smallest sample (subgroup 3 of the MC, which contained 417 patients) was sufficient for statistical estimates of the population with a 95% confidence level with an error range of 5%.

In the comparison of the entire IC and MC, baseline HbA1c levels were maintained in the IC and increased in the MC during the 12-month study period. However, the difference between cohorts was not statistically significant ($P=0.702$). The results of this retrospective cohort cannot be directly compared with the results of previous systematic reviews of randomized clinical trials; nevertheless, they demonstrated a different pattern. Recent meta-analyses showed a significant reduction in HbA1c levels, ranging from -0.40% to -0.36% , following periodontal therapy [7,8,14-16]. The studies included in the meta-analyses had some factors contributing to heterogeneity, including differences in the sample sizes, follow-up periods, and types of intervention (with or without additional antibiotics). In addition, the criteria of some randomized clinical trials excluded individuals with higher initial HbA1c levels.

The effectiveness of periodontal treatment for improving glycemic control in individuals with type 2 diabetes remains controversial. A large multicenter randomized controlled trial of over 500 patients failed to demonstrate a beneficial effect of periodontal therapy on glycemic control [14], and a cohort study including over 120,000 Veterans Administration participants did not show any positive effect of periodontal therapy on glycemic control, except among individuals with higher initial HbA1c levels ($>9\%$) [9]. Moreover, a recent clinical trial conducted by the DIAbetes and PERIOdontitis (DIAPERIO) group showed no clinical effect on glycemic control and only indicated that periodontal treatment is safe and improves the oral health-related quality of life of patients living with diabetes [17].

Despite the contradictory results and weak evidence of previous studies [18-21], a recent clinical study conducted by D'Aiuto et al. [22] may explain the underlying causes. They noted that many small trials and meta-analyses investigating the potential beneficial effect of periodontal therapy on glycemic control have shown inconclusive findings because most of them had a small sample size and short follow-up period with uncontrolled major confounders when evaluating the association between the 2 disorders, such as the ineffectiveness of NPT in patients with diabetes. In their study, the intensive periodontal treatment (IPT) group was specifically used to remove the effects of the confounding factor (ineffectiveness of NPT). By maximizing the effects of periodontal therapy through the control of periodontal inflammation, the HbA1c level was 0.6% lower in the test group than

in the control group after 12 months, and the test group reported better diabetes-related quality of life. The findings are partially consistent with the results of the present study. Although the difference found in this study was smaller than that reported for the IPT group, a mean difference of 0.2%p between cohorts was confirmed for the subgroup with baseline HbA1c levels of 7% or more and less than 9% after 12 months. The differences between studies in the effect of periodontal therapy on glycemic control are thought to be caused by the failure to control for confounding factors such as differences in individual effects after periodontal treatment. In addition, it is possible that other uncontrolled systemic factors and confounders had a greater effect on glycemic control than the effect of periodontal treatment in patients with well-controlled diabetes (HbA1c levels of less than 7%) and those with severely non-controlled diabetes (HbA1c levels of 9% or more).

Periodontal maintenance (also known as supportive periodontal therapy) after active therapy is routinely considered to be a part of periodontal treatment and performed at selected intervals to assist periodontal patients in maintaining oral health [23]. According to the American Academy of Periodontology's position paper, for most patients with a history of periodontitis, visits at 3-month intervals may be required initially, which will result in a lower likelihood of disease progression when compared with that in patients who receive periodontal maintenance on a less frequent basis [24-27]. However, there are no standardized criteria regarding the interval between maintenance visits; thus, a wide range of periods have been reported in previous studies [28]. Some cohort studies reported that regular compliers had an average maintenance interval of 5.5 months [29] or 4.4 months [30]. A retrospective study noted that patients who were not adherent to periodontal maintenance at an interval of 3-4 months were 5.6 times more likely to lose teeth [31]. Based on these studies, patients with at least 3 maintenance visits for 1 year after the completion of NPT were classified as adherent, and others were classified as non-adherent. To the best of our knowledge, the present study is the first to assess the effect of patient adherence after active periodontal therapy on HbA1c levels. Unexpectedly, the number of maintenance visits, which reflects patient adherence, did not affect HbA1c changes. There is a need to observe the results of periodontal treatment and its effects over a longer period in the future.

This study has the advantage of being able to examine data that reflect an actual clinical setting through the analysis of big data from a general hospital. However, this study also has some critical limitations. First, although we attempted to evaluate a large number of subjects by big data analysis, a sufficient number of samples could not be secured to overcome the limitations of potential confounders. Second, baseline data for the main outcome variable (HbA1c) of the IC were registered up to 3 months following NPT, which could have influenced the results. Since HbA1c levels reflect the average blood glucose level for the past 2 to 3 months, we assumed that the HbA1c levels would not be affected in the first 3 months after periodontal treatment, as reported in previous studies [6,32]. Third, due to the inherent weakness of the retrospective cohort study design, some important confounders such as initial periodontal status, clinical outcomes of periodontal therapy, medical history other than diabetes, the use of other medications affecting glycemic control, duration of diabetes, and different anti-diabetic interventions were not considered in the analysis. In particular, the importance of evaluating the clinical outcomes of periodontal therapy has been emphasized in recent studies. The effect of periodontal therapy on the control of diabetes would be more accurately understood by properly controlling for periodontal inflammation. A prospective cohort study with the analysis of big data through collaboration between medical doctors and dentists should be conducted in the future.

Within the limitations of the present study, treatment of periodontal disease through NPT and periodontal maintenance may help to control HbA1c levels in patients with type 2 diabetes, but this possibility could not be confirmed through statistical analyses. In addition, it seemed that the number of periodontal maintenance visits after periodontal therapy may not be associated with HbA1c level changes during a 1-year period.

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