A Natural Experiment for Inferring Causal Association between Smoking and Tooth Loss: A Study of a Workplace Contemporary Cohort

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Abstract: *Background*: Natural experiments in former smokers are an important criterion for inferring causality between smoking and tooth loss. We examined how former smoking influenced risk estimate of tooth loss incidence.

Methods: Records of dental check-ups of the work cohort were examined. The sample consisted of data from 1,724 workers recorded at the ages of 40 years and 50 years, and this was analyzed for tooth loss incidence during a 10-year period. Former smokers were categorized into two groups based on whether they quit smoking before or during the observational period. Variables used for adjustment were age, sex, oral and overall health behavior, dental visit, and number of existing teeth immediately prior to observation.

Results: The prevalence of tooth loss incidence and number of teeth lost during the observational period were both higher in current smokers than in never smokers (33.7% vs. 23.9% and 0.83 vs. 0.42, respectively). Incident odds ratio of tooth loss in long-term quitters relative to never smokers was not significant and less than one (incident odds ratio 0.85, 95% confidence interval 0.56–1.29). Incident odds ratios of short-term quitters and current smokers were both significant, though short-term quitters exhibited higher values (1.72, 1.15–2.55) than current smokers (1.48, 1.10–2.00).

Conclusions: The causal interpretation is strengthened by attenuation of the risk in long-term quitters. However, additional factors may influence the risk estimates of former smokers, suggesting potential limitations of a natural experiment for inferring causal association between smoking and tooth loss.

Keywords: Natural experiment, Smoking, Tooth loss, Cohort study, Causal inference.

INTRODUCTION

Tobacco smoking is an important environmental risk factor of oral diseases. Dental societies have strengthened the prevention of oral cancer, periodontal disease, and poor wound healing by promoting smoking cessation [1, 2]. Recently, a causal association was suggested between dental caries and active [3] and passive smoking [4]. Since periodontal disease and dental caries are the most frequent reasons for tooth extraction, tooth loss may also be considered as a health consequence of exposure to smoking [5]. A systematic review of high-quality methodology [6] and a meta-analysis of population-based studies [7] reported that smoking is an independent risk factor for tooth loss. Four cohort studies also reported an independent association between smoking and tooth loss incidence [8-11].

Causal interpretation may be strengthened if risk estimate for tooth loss is statistically shown to decrease after smoking cessation [12]. Although a randomized controlled trial may be the ideal study design to exhibit the effects of smoking cessation on tooth loss, it is difficult to implement because of ethical issues. Hence, evidence of a potential reduction in the risk of tooth loss in former smokers may be considered an adequate substitute. The risk estimate in former smokers reported by previous cohort studies is conflicting, with three studies reporting a decrease in the risk estimate [9-11] and one study reporting an increase in the risk estimate [8].

Usually, differences in patient characteristics between groups are generally controlled by using cohort study designs and multivariate analytical methods [12]. Therefore, efforts to minimize potential bias caused by unknown confounders are essential for causal interpretation. Utilizing birth-cohorts may be one way to overcome this problem. However, unknown factors such as patient–dentist interaction may hinder the accurate estimation of the reduction in risk of tooth loss. Difference in the recognition of receiving tooth

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extraction may cause bias between smoking groups. Dental check-up records of contemporary work cohorts may serve as a substitute for birth-cohorts. The aim of this study was to examine how a natural experiment of former smoking influenced risk estimate of tooth loss incidence in a contemporary cohort of workers.

SUBJECTS AND METHODS

Electronic records of civil service officers who underwent two dental check-ups were collected for this study with the permission of the mutual aid association of the local government. The study protocol was approved by the Ethics Committee of Fukuoka Dental College (Ethics Approval No. 144). Figure **1** summarizes the records of potentially eligible participants and strategies for analysis. The occupational dental clinic conducted dental check-ups at the ages of 40 years and 50 years. A dental examination (first check-up) was conducted in 1992–1997 in patients aged 40 years. Follow-up examinations were performed in 2002–2008 and included information on health behavior and frequency of dental visits. Information on smoking status was collected at both check-ups. An anonymous dataset of the workplace cohort was created for statistical analyses.

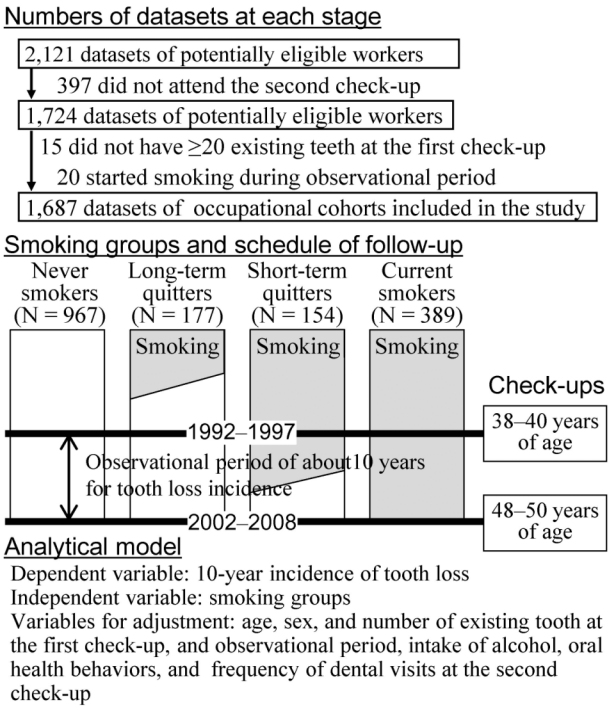

Figure 1: Records of potentially eligible participants and strategy for analysis.

Data from the second check-up was available for only 1,724 (81.3%) workers out of the 2,121 participants who attended the first check-up. The participation rate for the first check-up was not available. Since masticatory function can only be sustained in subjects with 20 or more teeth [13], those who had 19 or fewer teeth may have exerted excessive burden during mastication which could profoundly influence risk estimate of tooth loss. Therefore, 15 subjects who had 19 or fewer teeth at the first check-up were excluded from the analysis. An additional 22 subjects were excluded as they started smoking during the observational period. The final cohort consisted of 1,687 (79.5%) workers.

The outcome variable of tooth loss incidence, which was enumerated from tooth number recorded at the time of the first and second check-ups, was dichotomized into yes and no, and the mean number of teeth lost was considered as secondary outcome. Ever smokers were categorized into three groups: current smokers, those who currently smoke; short-term quitters, those who had quit smoking during the observational period; and long-term quitters, those who had quit smoking prior to the observation period.

Adjusting for potential confounders reduces the influence of bias in smoking groups, as smokers tend to exhibit poor health habits including high intake of alcohol, poor oral health behaviors, and infrequent dental visits that may mask the risk of tooth loss associated with smoking. Therefore, variables of oral and overall health behaviors were also included in this study. Data collected included sex (male or female), age (38 years-39 years or 40 years), observational period (10 years or 11 years), weekly intake of alcohol (yes or no), frequency of daily tooth brushing (less than once or twice or more), use of an interdental brush (yes or no), use of dental floss (yes or no), periodic visits to the dentist for removal of dental calculus (yes or no), and receipt of tooth brushing instruction (yes or no). All of these variables were dichotomized for adjustment. The number of existing teeth (20–26, or 27–28) immediately prior to the observational period was also included to account for the potential effects of previous damage in the mouth on future tooth loss.

The χ^2-test was used to examine the distribution of subjects by smoking group, sex, and incidence of tooth loss by smoking group. Analysis of variance was used to test differences in the number of cigarettes per day, years of smoking, and years of abstinence among the ever-smoking group, whereas analysis of covariance was used to test differences in the number of existing and lost teeth among the smoking group, which

controlled for potential confounders. Furthermore, the ad-hoc Dunnett test was conducted to test differences in the number of cigarettes per day, years of smoking, and the number of existing and lost teeth using current smokers as a reference group.

Incident odds ratios (IORs) and 95% confidence intervals (CIs) were calculated as a measure of risk estimate associated with smoking and tooth loss incidence. Never smokers were considered as the reference group in multivariate logistic regression analysis, controlling for potential confounders. All analyses were conducted using SPSS statistical software (PASW statistics 18.0.0; SPSS Inc., Chicago, IL, USA), and significance level was set at 0.05.

RESULTS

The study sample primarily consisted of male workers (67.7%) and individuals aged between 38 years and 39 years (69.7%). Table **1** shows the distribution of workers by smoking group and sex. Current smokers formed 23.1% and former smokers accounted for 19.6% of the cohort. The smoking rate amongst males (31.7%) was significantly higher than that of females (5.0%). Proportions of short-term (9.1%) and long-term (10.5%) quitters were similar.

Table **2** shows smoking related variables by smoking group. The mean number of cigarettes per day varied from 20.8 to 23.4, but no significant differences were observed among the smoking groups. Current smokers exhibited the longest duration of smoking, while short-term quitters exhibited a duration that was shorter by 5 years. Long-term quitters smoked for approximately half the duration of short-term quitters. Duration of abstinence in long-term quitters was more than four times that of short-term quitters. Intake of alcohol was reported by 70.1% (data not shown) of the cohort. Although only 29.1% and 23.8% of the cohort reported use of interdental brushes and dental floss, respectively, the majority (77.2%) reported tooth brushing two times or more daily. The majority (89.3%) visited a dentist for periodic check-ups, removal of dental calculus, and receipt of tooth brushing instructions, and 22.9% reported dental visits in the previous 12 months for the purpose of dental treatment.

Table **3** compares the number of existing teeth at both check-ups and the number of teeth lost during the observational period. Never smokers and long-term quitters showed significantly greater number of existing teeth in the first and second check-ups when compared to current smokers. Never smokers lost 0.42 tooth on average during the 10-year follow-up period, while the number was nearly double (0.83 tooth) in current smokers. Significant differences in the number of teeth lost were observed when comparing never smokers and long-term quitters to current smokers. Long-term quitters lost 26% fewer teeth (0.31 tooth) than never smokers (0.42 tooth). Short-term quitters lost 23% fewer teeth (0.64 tooth) than current smokers (0.83 tooth), though this difference was not statistically significant.

Table 1: Number of Subjects (%) by Smoking Group and Sex

Smoking group	Male	Female	Total
Never smokers	469 (41.1)	498 (91.4)	967 (57.3)
Long-term quitters	165 (14.4)	12 (2.2)	177 (10.5)
Short-term quitters	146 (12.8)	8 (1.5)	154 (9.1)
Current smokers	362 (31.7)	27 (5.0)	389 (23.1)
Total	1142 (100)	545 (100)	1687 (100)

Table 2: Comparison of Smoking-Related Variables by Smoking Group

Smoking group	Number of cigarettes per day	Years of smoking	Years of abstinence
Long-term quitters	20.8 (19.3–22.4)[a]	11.6 (10.8–12.4)[b]	17.5 (16.7–18.3)
Short-term quitters	23.4 (21.4–25.4)	22.4 (21.3–23.5)[b]	3.6 (3.2–4.0)
Current smokers	22.3 (21.3–23.2)	27.2 (26.6–27.7)	Not applicable

[a]Mean value (95% confident interval).
[b]Significantly different from current smokers ($P < 0.05$).

Table 3: Comparison of the number of existing teeth and lost teeth by smoking group

Smoking group	Mean number (95% confident interval)[a]		
	Existing tooth		Lost tooth during 10 years
	First check-up	Second check-up	
Never smokers	27.1 (27.0–27.2)[b]	26.7 (26.5–26.8)[b]	0.42 (0.32–0.52)[b]
Long-term quitters	27.0 (26.8–27.2)[b]	26.7 (26.4–27.1)[b]	0.31 (0.09–0.53)[b]
Short-term quitters	26.8 (26.6–27.0)	26.2 (25.8–26.5)	0.64 (0.40–0.88)
Current smokers	26.5 (26.4–26.7)	25.7 (25.5–25.9)	0.83 (0.67–0.98)

[a]Adjusting for sex, age, duration of observation, and health behavior.
[b]Significantly different from current smokers (P < 0.05).

Table 4: Prevalence, Adjusted Incident Odds Ratio (IOR), and 95% Confidence Interval (CI) of 10-Year Incidence of Tooth Loss by Smoking Group

Smoking group	Incidence of tooth loss		
	Prevalence (%)[a]	Adjusted IOR (95% CI)[b]	P
Never smokers	23.9 (231/967)	1.00 (Reference)	
Long-term quitters	20.9 (037/177)	0.85 (0.56–1.29)	0.444
Short-term quitters	34.4 (053/154)	1.72 (1.15–2.55)	0.008
Current smokers	33.7 (131/389)	1.48 (1.10–2.00)	0.010

[a]Significantly associated with smoking group.
[b]Based on multivariate regression controlling for age, sex, observation period, oral health behaviors, weekly intake of alcohol, and number of existing teeth at the first check-up.

Table **4** compares the prevalence of tooth loss incidence by smoking group. This was higher in short-term quitters (34.4%) and current smokers (33.7%) than never smokers (23.9%) and long-term smokers (20.9%), and the differences were statistically significant. The prevalence was also lower in long-term quitters than never smokers (20.9% vs. 23.9%), while this rate was higher in short-term quitters compared to current smokers (34.4% vs. 33.7%). Adjusted IOR of long-term quitters relative to never smokers was less than one (0.85, 95% CI: 0.56–1.29), while the adjusted IORs of current smokers and short-term quitters were significant at 1.48 (95% CI: 1.10–2.00) and 1.72 (95% CI: 1.15–2.55), respectively. The IOR of short-term quitters was higher than that of current smokers (1.72 vs. 1.48).

DISCUSSION

In the current study, the increasing risk of tooth loss incidence in current smokers reinforces consistency in the association between smoking and tooth loss [7]. When interpreting the association between smoking and tooth loss, evidence of causality can be strengthened in the criterion of a natural experiment by observed attenuation of significant differences in tooth loss incidence between long-term quitters and never smokers.

The risk estimate for tooth loss incidence in long-term quitters is lower than that of never smokers (0.86 vs. 1.00). This trend was seen in the number of teeth lost during the observational period. Since long-term quitters smoked for 11.6 years on average, the risk estimate should have declined to a level between current and never smokers. A similar trend was observed in previous cross-sectional studies that utilized Japanese national databases [14, 15]. They reported risk estimates for prevalence of tooth loss equal to 0.86 (95% CI: 0.46–1.60) and 0.52 (95% CI: 0.23–1.18) in female former smokers aged 40 years or more and less than 39 years, respectively. However, the risk estimates in male former smokers were more than 1 [7]. In the present study, former smokers quit smoking at the age of 32 years, an average of 17.5 years before the second check-up. In 1987, the smoking rate amongst males was 61.6% when the participants of this study first quit smoking, and this rate was double that of 2014 (30.3%). The corresponding rates in females were 13.4% and 9.8%. The civil officers who quit smoking early at a time when three in five adult men smoked may have been more health-conscious compared to never smokers, reflecting the lower value of risk estimate for tooth loss incidence. These results call for further investigation, adjusting for health consciousness if possible.

Risk estimate of tooth loss incidence was also likely to increase more in short-term quitters than current smokers (1.74 vs. 1.63). Since short-term quitters had abstained for 3.6 years on average, the risk estimate should have declined from the level of current smokers. Indeed, this trend was reflected in the number of teeth lost during the observational period. Short-term quitters were seen to give up smoking around 2000 when the national health movement began in Japan. The public health recommendations included information on the association between smoking and tooth loss. Therefore, civil officers who quit during the observational period may have experienced tooth loss more frequently than current smokers and may have been informed about the risk of smoking more intensively by the dentist. This detailed information was not included in the analytical model, although frequency of dental visits was adjusted for. In this study, potential confounders were adjusted for in the multivariate analysis, and an occupational cohort who had spent the same era working in similar circumstances was selected to minimize bias between smoking groups. However, awareness of health consequences of smoking and/or willingness to quit smoking may have influenced the risk estimates in former smokers. These findings suggest potential limitations of a natural experiment as a criterion for inferring a causal association between smoking and tooth loss.

Years of smoking and abstinence in the smoking groups should be additionally taken into consideration when interpreting risk associated with smoking cessation. To the best of the authors' knowledge, this is the first study to address the limitations of natural experiments examining the relationship between smoking and tooth loss. The strength of this study is that it examined a workplace cohort, which reduced potential bias caused by demographic or behavioral differences between generations to a greater extent than studies that analyze data collected from various generations. Therefore, characteristics that were not adjusted for in the statistical model could be reflected in the risk estimates of smoking groups. Limitations of this study include the lack of information on socioeconomic status (SES), which may influence poor health behaviors including less frequent dental visits. However, SES in this occupational cohort may have been relatively high as civil workers are generally well paid and have stable employment.

It has been shown that loss of teeth results in poor dietary intake amongst the elderly [13]. Information on the relationship between smoking and tooth loss distinctively promoted motivation at the population and individual levels [16]. Hence, accumulation of evidence in support of a causal association will help clinicians and policy makers. Since tooth loss is dependent on multifactorial diseases such as dental caries and destructive periodontal disease and also on the interaction between patients and dentists, various factors play a role in its incidence in the later life of smokers. Three studies that reported a decrease in the risk estimate [9-11] were conducted in the United States, whereas one Australian study reported an increase in the risk estimate [8] and was published about 10 years prior to these studies. Given the discrepancy of the risk estimates in former smokers in the present study, social norm to the health consequence of smoking might influence the results of these populations. This limitation for the criterion of a natural experiment may be extended to any health events with similar background characteristics as tooth loss [16].

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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