Abstract: There have been few prospective studies on the relationship between oral health conditions and the development of metabolic syndrome (MetS). This prospective cohort study was performed at a Japanese company over one year. Routine medical health examinations, oral health examinations, and a questionnaire pertaining to education, job type, and health behaviors was administered. Participants aged ≥35 years who had no MetS components at baseline were re-examined after one year. Modified Poisson regression analyses were performed to calculate the relative risks (RRs) associated with oral health variables, including periodontitis, decayed and missing teeth, and decayed, missing, and filled teeth (DMFT) in relation to the development of MetS. Of 152 eligible participants, 136 were re-examined after one year; 30 exhibited one or more newly developed MetS components upon re-examination. Decayed teeth at baseline were significantly associated with development of at least one MetS component (adjusted RR 3.25, 95% confidence interval 1.59-6.63). There were no associations between periodontitis, missing teeth, or DMFT and the development of MetS. The association between decayed teeth and MetS was independent of other risk factors, including age and body mass index; therefore, decayed teeth may be associated with the development of MetS.

Keywords: dental caries, DMFT, metabolic syndrome, oral health, periodontitis, tooth loss

Introduction

The prevalence of metabolic syndrome (MetS) is increasing worldwide [1]. It is known that MetS consists of four components, namely glucose intolerance, abdominal obesity, as measured via waist circumference (WC), hypertension, and dyslipidemia. Combined, these components increase the risks of arteriosclerosis, heart disease, cerebrovascular disease, and diabetes [2-4]. Risk factors for MetS include age [5], body mass index (BMI) [5], physical inactivity [3,5], atherogenic and diabetogenic diets [3,5], smoking [3,5], and stress [6]. The prevention of MetS is a substantial global public health concern.

Recently, associations between MetS and poor oral health, as indicated by periodontitis [7-10] or the presence of decayed [7,11-13] or missing [7,14-16] teeth, have been investigated. Most previous investigations have been cross-sectional or case-control studies; however, one longitudinal study investigated whether poor oral health affects the incidence of MetS [7] in Japanese workers who were monitored over four years. The results revealed that periodontal disease at baseline was significantly associated with the development of one or more MetS component. However, the study used BMI, rather than WC, to measure abdominal obesity, and details pertaining to medication status and patients’ medical histories were not included in the analysis. Given this relative paucity of data, further investigations are required to elucidate the potential causal relationships between poor oral health and MetS.

The purpose of the present study was to examine the relationships between oral health conditions and the development of MetS over one year, using data from routine medical health examinations, oral health examinations, and a self-reported survey of Japanese workers. Periodontitis, decayed and missing teeth, and decayed, missing, and filled teeth (DMFT) were investigated as independent variables, and their relationships with the development of MetS were analyzed.

Materials and Methods

Participants

The present prospective cohort study was performed at a Japanese dental and medical device manufacturing company. The study size was not decided by statistical sample size calculation, but decided in consideration of feasibility; the participants of this study were recruited from those who were all employed by, and working at, the company in 2015. In 2015, 712 workers underwent oral health examinations and completed a questionnaire pertaining to their educational backgrounds and job classifications. The workers were followed up after one year. Subjects <35 years of age were excluded since WC data were unavailable for these subjects, and any subjects positive for any MetS components at baseline and/or taking medication for hypertension, diabetes, or dyslipidemia were also excluded.

The present study was conducted in accordance with the Declaration of Helsinki, and the Institutional Review Board of The University of Tokyo (approval no.10589) and the Ethics Committee of Faculty of Dentistry, Tokyo Medical and Dental University (approval no. D2018-014) approved the study.

Oral health examinations

Oral health examinations were performed at the manufacturing worksite. Twenty well-trained dentists performed the baseline examinations of patients, who were sitting in dental chairs equipped with overhead lights. Periodontal disease was evaluated in accordance with the 1997 version of the community periodontal index of treatment needs (CPI) proposed by the World Health Organization (WHO) [17]. The updated guidelines (updated in 2013; http://www.who.int/oral_health/publications/9789241548649/en/) were not used due to the time constraints associated with performing oral health examinations at the worksite. Periodontal disease was defined as a CPI code of ≥3 (periodontal pocket ≥4 mm). The DMFT number was recorded. Although the WHO criteria were not followed exactly, the DMFT was calculated as follows: A decayed tooth was recorded if it had an unmistakable cavity, undermined enamel, or a detectably softened floor or wall. In addition, a missing tooth comprised a missing tooth, due to caries or for any other reason, since all study participants were >30 years old. The DMFT was divided into two groups, using the median value as a cut-off (DMFT ≥ 15 vs. ≤ 14), since the DMFT criteria had not been standardized.

Medical health examinations

Data from routine health examinations were used to derive information pertaining to the overall health of each employee in 2015 and 2016. The data included age, sex, BMI, WC, systolic blood pressure (SBP), diastolic blood pressure (DBP), high-density lipoprotein cholesterol (HDL-C) level, triglyceride (TG) level, fasting plasma glucose (FPG) level, medical history (i.e., hypertension, diabetes, and dyslipidemia), current medication usage, current smoking status, daily alcohol consumption, and sleep patterns. “Insufficient sleep” was recorded if participants self-reported that they did not feel rested upon waking. When blood pressure measurements
were elevated (SBP ≥ 140 mmHg or DBP ≥ 95 mmHg), blood pressure was measured twice and the average values were used.

Study participants were instructed not to eat after 8 p.m. on the day before the health examinations and not to drink any fluids on the day of the examination. Eating habits were also evaluated. “Late-evening meal” was defined as eating within 2 h before sleep onset three or more times weekly. “Nighttime meal after evening meal” was defined as eating a meal following their evening meal three or more times weekly. “Without breakfast” was defined as not eating breakfast three or more times weekly. Finally, exercise habits were surveyed. The subjects were asked to report whether they undertook exercise of at least 30 min per day on 2 or more days per week on average throughout the year and whether they walked for at least 1 h per day on a regular basis.

Survey data
The participants were asked to confirm the information obtained from their routine medical health examinations (i.e., smoking status, alcohol consumption, sleep patterns, eating habits, and exercise habits). Additionally, the questionnaire asked participants to provide information pertaining to their educational backgrounds and job types. Educational background was classified as ≥13 years or ≤12 years. Job type was also categorized into two groups, blue-collar (processing or assembly work) and white-collar (design, management, clerk, sales, and “other”).

Outcomes
The primary outcome measure was development of one or more components of MetS. Since the definition of MetS is not globally standardized [18], the criteria provided by the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) for Asian populations [5,19,20] and the International Diabetes Federation (IDF) criteria for Japanese individuals (https://www.idf.org/e-library/consensus-statements/60-idf-consensus-worldwide-definition-of-the-metabolic-syndrome) were used. The criteria in the NCEP-ATP III and IDF guidelines are the same, and are as follows: 1) WC ≥ 90 cm (male), ≥ 80 cm (female) (2) TG ≥ 150 mg/dL (3) HDL-C < 40 mg/dL (male), < 50 mg/dL (female) (4) BP ≥ 130/85 mmHg (5) FPG ≥ 100 mg/dL (6) Medication usage or history of hypertension, diabetes, dyslipidemia.

Statistical analysis
The Student’s t-tests or Mann-Whitney U test was used to compare the continuous variables, and the Chi-squared test or Fisher’s exact test were used to investigate associations between categorical variables and outcomes. Adjusted relative risks (RRs) and 95% confidence intervals (CIs) for developing one or more MetS components in individuals with various oral health conditions (CPI ≥ 3, decayed teeth ≥ 1, missing teeth ≥ 1, and
DMFT ≥ 15) were calculated using modified Poisson regression analyses (Poisson regression with robust standard errors). In accordance with analyses performed in previous studies [3,5,21-23], the following factors were considered covariates: sex, age, BMI, current smoking status, daily alcohol intake, late-evening meal, nighttime meal after evening meal, without breakfast, exercise habits, walking habits, insufficient sleep, job types, and educational backgrounds. The threshold for significance was $P < 0.05$. All statistical analyses were conducted using Stata 11.1 (StataCorp, College Station, TX, USA). The study conformed to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for human observational studies.

Results

Of the 152 participants who were ≥35 years of age and who had no MetS components at baseline, 136 were followed up after one year, yielding a follow-up rate of 89.5% (Fig. 1). Of these individuals, 30 were identified as having developed one or more MetS components during that time. The incidence rate of each MetS component was as follows: glucose intolerance 2.9%, abdominal obesity 3.7%, hypertension 10.3%, and dyslipidemia 8.1%. The baseline characteristics of participants included in the 1-year follow-up are shown in Table 1. Factors associated with a significantly increased risk of developing one or more MetS components were decayed teeth, age, and BMI.

The results of the modified Poisson regression analyses used to predict the incidence of MetS components, using four oral health variables, are shown in Table 2. Job type was excluded in this analysis due to collinearity with educational background. Decayed teeth were significantly associated with developing at least one MetS component (adjusted RR 3.25, 95% CI 1.59-6.63). By contrast, there were no statistically significant associations between CPI, missing teeth, or DMFT and development of one or more MetS components. Among covariates, age and BMI were significantly associated with development of one or more MetS components.

Discussion

In this one-year follow-up study, after adjusting for known risk factors, including sex, age, BMI, health behaviors, and educational background, the presence of decayed teeth at baseline was associated with an increased risk of developing at least one MetS component. To date, few longitudinal studies have investigated whether decayed teeth or periodontitis are associated with MetS. The previously described longitudinal study, with a four-year follow-up period, concluded that individuals with periodontitis at baseline had an increased likelihood of developing a MetS component within four years [7]. However, in this previous longitudinal study, decayed or missing teeth showed no statistically significant association with the development of a MetS component. Since patients with tooth decay, accompanied by tooth pain or sensitivity, are likely to seek and receive dental care, tooth decay’s influence may change according to treatment. However, relatively few (39.7%) participants in the present study who had...
Table 2  Poisson regression analyses of associations between baseline characteristics and the presence of at least one MetS component at the 1-year follow-up (n = 136)

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Unadjusted RR (95% CI)</th>
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<th>Adjusted RR (95% CI)</th>
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<tbody>
<tr>
<td>CPI ≥ 3</td>
<td>0.74 (0.35-1.52)</td>
<td>0.64 (0.31-1.34)</td>
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<td>Decayed teeth ≥ 1</td>
<td>2.70 (1.33-5.48)</td>
<td>3.25 (1.59-6.63)</td>
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<td>Missing teeth ≥ 1</td>
<td>0.95 (0.48-1.86)</td>
<td>0.69 (0.33-1.42)</td>
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<td>DMFT ≥ 15</td>
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<td></td>
<td>1.78 (0.92-3.46)</td>
<td>1.27 (0.56-2.77)</td>
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<tr>
<td>Sex (female)</td>
<td>0.93 (0.34-2.59)</td>
<td>1.21 (0.48-3.02)</td>
<td>0.92 (0.36-2.34)</td>
<td>0.92 (0.36-2.32)</td>
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<tr>
<td>Age</td>
<td>1.07 (1.02-1.12)</td>
<td>1.08 (1.03-1.14)</td>
<td>1.08 (1.03-1.13)</td>
<td>1.06 (1.01-1.13)</td>
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<tr>
<td>BMI</td>
<td>1.17 (0.98-1.39)</td>
<td>1.20 (1.02-1.42)</td>
<td>1.16 (0.99-1.36)</td>
<td>1.18 (1.00-1.38)</td>
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<tr>
<td>Current smoking</td>
<td>1.18 (0.64-2.00)</td>
<td>1.04 (0.50-2.17)</td>
<td>1.51 (0.69-3.35)</td>
<td>1.28 (0.57-2.87)</td>
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<tr>
<td>Daily alcohol intake</td>
<td>1.67 (0.80-3.46)</td>
<td>1.99 (0.98-4.04)</td>
<td>1.62 (0.82-3.21)</td>
<td>1.68 (0.82-3.42)</td>
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<td>Late-evening meal</td>
<td>1.35 (0.64-2.84)</td>
<td>1.43 (0.70-2.92)</td>
<td>1.33 (0.64-2.79)</td>
<td>1.32 (0.63-2.77)</td>
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<td>Nighttime meal after evening meal</td>
<td>0.52 (0.15-1.74)</td>
<td>0.62 (0.26-1.89)</td>
<td>0.61 (0.18-1.99)</td>
<td>0.55 (0.17-1.81)</td>
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<td>Without breakfast</td>
<td>1.26 (0.56-2.84)</td>
<td>1.07 (0.50-2.28)</td>
<td>1.27 (0.55-2.93)</td>
<td>1.22 (0.54-2.77)</td>
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<td>Exercise habits</td>
<td>0.83 (0.37-1.83)</td>
<td>0.70 (0.29-1.69)</td>
<td>0.92 (0.39-2.17)</td>
<td>0.82 (0.36-1.89)</td>
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<td>Walking habits</td>
<td>0.97 (0.46-2.04)</td>
<td>0.90 (0.41-1.95)</td>
<td>0.97 (0.46-2.05)</td>
<td>0.96 (0.45-2.06)</td>
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<td>Insufficient sleep</td>
<td>0.89 (0.47-1.69)</td>
<td>0.96 (0.52-1.76)</td>
<td>0.89 (0.48-1.66)</td>
<td>0.93 (0.48-1.81)</td>
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<tr>
<td>Education ≥ 13 years</td>
<td>1.03 (0.49-2.14)</td>
<td>0.98 (0.45-2.12)</td>
<td>0.91 (0.42-1.94)</td>
<td>0.96 (0.47-1.99)</td>
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MetS, metabolic syndrome; DMFT, decayed, missing, and filled teeth; RR, relative risk; CI, confidence interval; BMI, body mass index. *P < 0.05; **P < 0.01

Decayed teeth at baseline visited a dental clinic during the follow-up year. Therefore, the significant association between tooth decay and MetS in the present study suggested the impact of treatment had little influence in this one-year follow-up. By contrast, in the aforementioned longitudinal study [7], the association may have been obscured by treatments during the four years between the initial and follow-up examinations. Previous cross-sectional studies examining tooth decay and MetS have reported that individuals with decayed teeth were more likely to have MetS than those without decayed teeth [11-13]. The presence of decayed teeth may affect an individual’s chewing ability [24], leading to adverse dietary changes that may contribute to MetS development. Reports investigating the effects of decayed teeth on diet are limited; however, they suggest that individuals with decayed teeth exhibit higher lipid intake [25] and lower vegetable consumption [26] than those without tooth decay. Nutrient intake imbalance and increased eating speed due to decayed teeth have also been suggested as factors contributing to the associations between tooth decay and MetS development [27-28]. Although the prevalence of decayed teeth among the participants in the present study was higher than the oral condition of the Japanese population in national data, it was difficult to determine whether or not participants experienced chewing difficulty due to decayed teeth since the severity of decay and chewing ability were not measured in the present study. Therefore, elucidating the mechanisms linking tooth decay to MetS requires future investigation. Cross-sectional studies have also associated an increased number of missing teeth with a higher prevalence of MetS [14-16]. However, in the present study, no association between missing teeth and the development of MetS was observed, which may be attributable to the relatively small number of missing teeth.

In the present study, DMFT was divided into two groups, using the median value as a cut-off, and observed a trend that participants with a higher DMFT number were more likely to have components of MetS than those with a lower DMFT number. This result did not differ when the mean DMFT values in the Japanese national data by each age group (Survey of Dental Diseases in Japan. 2016. https://www.mhlw.go.jp/toukei/list/62-17b.html) were used as cut-offs. These results were consistent with a previous cross-sectional study [13], indicating that patients with two or more DMFT were more likely to develop MetS, although this association was not statistically significant. A meta-analysis investigating relationships between periodontitis and MetS indicated that individuals with periodontitis were more than twice as likely to develop MetS than those without periodontitis [8]. As a more possible mechanism underlying the impact of periodontitis on MetS development, a chronic inflammatory reaction induced by periodontal pathogens has been suggested [29-32]. The reason why no association between periodontitis and MetS development was observed in this study may be that the prevalence of periodontitis among participants was lower than that in the Japanese national data by each age group (participants vs. Japanese national data: 27% vs. 43% in those 35-44 years old, 49% vs. 50% in those 45-54 years old, and 30% vs. 55% in those 55-64 years old). The present study’s results were not consistent with these previous results [8,13-16], possibly since the participants in the present study were relatively young. The prevalence of MetS, DMFT, missing teeth, and periodontitis tend to increase with age. As individuals with MetS components at baseline were excluded in the present study, the relationships of DMFT, missing teeth, and periodontitis may have been underestimated. Therefore, a one-year follow-up period may be too short with regard to the evaluation of relationships between the longitudinal effects of periodontitis and MetS development. Further investigations with longer follow-up periods are warranted.

In terms of the incidence rate of each MetS component, hypertension and dyslipidemia were relatively high. Since blood pressure tends to vary according to conditions, the misclassification of hypertension may occur. To minimize such misclassification, blood pressure was measured twice in two periods are warranted.
invading cariogenic bacteria, including *Streptococcus mutans* (S. mutans) [33]. This possibility is supported by several previous findings. Clinical studies have demonstrated that *S. mutans* was detected in arteriosclerotic lesions [34,35]. An animal study reported that atherosclerotic plaque formation and inflammatory cell infiltration were promoted in mice infected with *S. mutans* [36]. Additionally, inflammatory cytokines released due to tooth decay have been implicated in MetS development. In a previous study, *S. mutans* reportedly promoted the production of inflammatory cytokines, including interleukin-6 [37].

The covariates associated with outcomes in multivariate analysis were age and BMI. These results are supported by previous studies that age and obesity were major MetS risk factors [5]. Unmeasured confounding factors, such as diet, may have also affected the results. However, dietary habits (i.e., nighttime meal after evening meal) were used as covariates rather than dietary intake. In addition, the present study used various adjustment variables including “without breakfast” (i.e., individuals not eating breakfast in the mornings), which has been associated with an increased blood lipid levels [21] and body weight [22], and “insufficient sleep,” which is reportedly associated with MetS [23]. A certain study used tooth brushing frequency as a covariate since it has been suggested that the prevalence and incidence of MetS are associated with tooth brushing frequency [33]. In the present study, tooth brushing may be regarded as an intermediate variable since its frequency is associated with the presence of decayed teeth (P < 0.01) and MetS components (P < 0.01) in baseline participants (n = 370). Therefore, the frequency of tooth brushing was not included in the analysis.

The present study had several limitations. Since all participants worked in the company and were relatively healthy compared to the general population, caution must be exercised when generalizing the results to different populations. Other limitations were that the study only reflected short-term relationships, and the number of participants was relatively low. Studies with larger samples and longer follow-up periods may be required to elucidate the relationships between periodontitis or missing teeth and MetS. Finally, with regard to the CPI, due to the practical time limitations inherently associated with conducting examinations at a worksite, it was impractical to limit the number of examiners or to calibrate the examiners. Therefore, it is possible that intra-examiner or inter-examiner error existed. However, multilevel analysis performed to adjust for individual examiners’ tendencies did not affect the results.

Despite the above limitations, the present study was unique in terms of both longitudinal design and the performance of oral examinations by dentists. At the one-year follow-up, a significant association was found between decayed teeth and the development of one or more MetS components. Since this association was independent of other major risk factors, decayed teeth may be related to MetS development. Tooth decay and periodontal disease account for 85% of tooth loss [38], and both diseases are preventable. Based on the present and previous findings, prevention and early treatment of oral diseases are important to prevent MetS, and development of a system leading to better oral health behavior is required.

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Conflict of Interest
None.

References