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What's new for the clinician?
- Excerpts from and summaries of recently published papers

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1. Is there an association between stress and periodontitis?

JM Coelho, SS Miranda, SS da Cruz, et al. Is there association between stress and periodontitis? Clinical Oral Investigations. 2020; 24: 2285-94.

INTRODUCTION

The psycho-physiological response of the organism to perceived challenge or threat is referred to as stress.[1] Stress is compatible with good health, being necessary to cope with the challenges of everyday life. Problems start when the stress response is inappropriate to the intensity of the challenge and it has been reported that periodontal disease is more widespread and severe in those with higher levels of stress.[1]

Psychological disturbances can lead patients to neglect oral hygiene with resultant unfavorable effects on the periodontal tissues. Although previous studies have suggested that stress may favour the occurrence of periodontitis, the evidence is still fragile, due to variations in the method and lack of standardization in the definition of exposure and outcome factors, and as a result of a small sample size.[1]

Coelho and colleagues (2020)[1] from Brazil reported on a cross-sectional study that sought to investigate the strength of the association between stress and periodontitis.

MATERIALS AND METHODS

Patient attending for care at dental clinics in Brazil was invited to participate in this cross-sectional comparative study consisting of two groups: the exposed group (individuals with exposure to stress) and non-exposed group. The target sample size was 235 per group with 470 in total.

Participants were included if they had at least four teeth to ensure the validity of periodontal status measurements, were not pregnant, or did not have cancer or HIV-AIDS, were not using anti-inflammatory medication in the 2 months prior to the study, and had no periodontal treatment in the 6 months prior to the survey.

Those with anterior infarction, percutaneous coronary revascularization history within the previous 6 months or surgical revascularization in the 2 months prior to the study were excluded.

Information related to socioeconomic and demographic characteristics, general and oral health condition, habits and lifestyle, medical and dental history, and access to oral health care was obtained through an interview questionnaire. Furthermore, each participant completed a Perceived Stress Scale survey.

Individuals underwent a complete periodontal examination by a single examiner, who had been previously trained. The degree of agreement of the collected clinical periodontal data, through the Kappa coefficient (0.87 with difference of ± 1 mm), showed good agreement.

The following clinical periodontal parameters were evaluated: probing depth, gingival recession, clinical attachment level, bleeding on probing, visible plaque index, and number of teeth.

These were obtained at six sites per tooth except the third molars, corresponding to the mesial buccal, medium-buccal, disto buccal, mesial lingual, mid-lingual, and disto lingual regions, through the use of a Williams periodontal probe. The visible plaque index was evaluated in four regions per tooth (mesial, distal, buccal, palatal/lingual).

The probing depth record was obtained by measuring the gingival margin at the deepest region of penetration of the probe. The measurement of gingival recession was the distance between the cementum-enamel junction and the gingival margin.

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The clinical attachment level was obtained by adding together the probing depth values and the gingival recession measurements of each site. The bleeding index was established by observing its occurrence up to 10 s after the examination of probing depth.

The visible plaque index was evaluated using the probe only to confirm the presence of biofilm on the tooth surface. The data on lipid and glycaemic profile, body mass index (BMI), and blood pressure were later obtained from the medical records of study participants. These data and tests were performed within 30 days of the oral exam.

The participant was considered diagnosed with periodontitis when 4 or more teeth were present, with 1 or more sites with probing depth greater than or equal to 4 mm, with clinical attachment level greater than or equal to 3 mm in the same place, and the presence of bleeding on probing. Furthermore, two clinical parameters were also employed as surrogates for defining the presence of periodontitis: probing depth ≥ 4 mm and clinical attachment level ≥ 5 mm.

Stress was evaluated using the Perceived Stress Scale. This instrument has 14 questions with response options ranging from zero to four (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = always).

The questions with positive connotation (4, 5, 6, 7, 9, 10, and 13) had a punctuation as follows: 0 = 4, 1 = 3, 2 = 2, 3 = 1, and 4 = 0. The remaining questions are negative and were added directly.

Results varied from zero to 56. Finally, an arithmetic average was obtained to observe which individuals had stress greater than the average scores, thus defining the diagnosis of stress. As such, two groups were formed: (1) individuals with perceived stress score ≤ 24 - not exposed to stress group; (2) individuals with perceived stress score > 24 - the group exposed to stress.

RESULTS

The study included 621 individuals, of which 300 were female and 321 male, with a mean age of 59.42 ± 10.91 (± SD) years, median of 59 years and a range of 40-91 years in the group exposed to stress (301 individuals).

In the unexposed group (320 individuals without stress), the mean age was 59.40 ± 10 years (± SD), median of 58.5 years and a range of 40-89 years.

Data for sample characterization, socioeconomic and demographic covariables related to lifestyle habits, oral health, and overall health conditions proved to be homogeneous for most characteristics with statistically significant difference only for the covariables: gender ($P < 0.01$) and schooling level ($P < 0.01$).

The results showed that participants with stress, compared to those not exposed to this condition, were more frequently female (55.15% vs. 41.88%), and those with 4 years or less of study (82.67% vs. 72.84%).

The study individuals were reclassified according to the diagnosis of periodontitis and those with periodontitis (142 individuals) presented a mean age of 58.82 ± 10.90 (± SD), median of 56.5 years and a range of 40-84 years. And, for the group without periodontitis (479 individuals), they presented a mean of 59.67 ± 10.89, median of 59 years and a range of 40-91 years.

The distribution of the investigated covariables showed that the groups were comparable, with only current smoking habit showing a statistical difference between comparison groups, with higher occurrence of individuals with that habit in the group with periodontitis (19.01% vs. 12.32%).

The periodontal condition with greater alteration was observed in the group exposed to stress, with statistically significant differences in the number of teeth ($P = 0.02$), number of sites with clinical attachment level of 3 to 4 mm ($P < 0.01$), number of sites with clinical attachment level of 5 mm ($P = 0.04$), number of sites with a probing depth of 4 and 5 mm ($P < 0.01$), and number of sites with a probing depth ≥ 6 mm ($P = 0.02$).

Unadjusted association measurements between stress and periodontitis showed that there was only association between stress and probing depth ≥ 4 mm. Those patients with a probing depth ≥ 4 mm were 1.26 more likely to be diagnosed with stress than those with a lower probing depth.

After making adjustments for the following confounder covariables, age, sex, schooling level, current smoking habit, pulmonary disease, and body mass index, all models showed a positive association between stress and probing depth ≥ 4 mm, stress and clinical attachment level ≥ 5 mm, and stress and periodontitis. These measurements showed that in individuals exposed to stress the frequency of periodontitis was 15 to 36% higher than those without the condition and this was statistically significant.

CONCLUSION

The findings showed positive association between exposure to stress and the presence of periodontitis, reaffirming the need to prevent and control stress.

Implications for practice

This study with a large sample size provides evidence of an association between stress and periodontitis. However, this does not prove causality. Stress has been identified as a risk factor for both poor general and oral health outcomes.

Reference

1. Coelho JM, Miranda SS, da Cruz SS, et al. Is there association between stress and periodontitis? Clinical Oral Investigations. 2020; 24: 2285-94.

2. Is there an association between periodontitis and all-cause and cancer mortality?

P Chung, T Chan. Association between periodontitis and all-cause and cancer mortality: retrospective elderly community cohort study. BMC Oral Health. 2020; 20: 168.

INTRODUCTION

Periodontal diseases and, in particular, periodontitis is reported to be potentially associated with some systemic diseases and conditions such as cardiovascular disease, the impairment of glycaemic control in patients with diabetes and preterm births or low-birth weight.[1] Such correlation could be due to several mechanisms:

1. The spread of bacteria from the oral cavity could cause tissue damage to various organs.
2. The increase in inflammatory systemic burden that may augment the susceptibility of atheromatous plaque formation.
3. An autoimmune response which could be triggered by bacterial sepitopes from oral bacterial species.[1]

Published studies demonstrated a role of viruses such as Human Papilloma virus (HPV) and Epstein-Barr virus (EBV), that could be detected in periodontal pockets, as suspected agents for oral cancer through the activation of specific oncogenes (such as E6 and E7 for HPV).[1]

Specific pathogens, such as *P. gingivalis*, were demonstrated to prevent, after invading the epithelium, cell apoptosis, thus favouring cancer initiation.[1] These pathogens could be found in carcinomas of the gingiva [18], but could also be associated with distant tumours [21].

Indirect mechanisms for a link between periodontitis and cancer were mainly related to the known association between the inflammatory process itself and cancer. Periodontitis may induce a significant increase in inflammatory markers and molecules that enhances the inflammatory reaction.

This condition causes the release of reactive oxygen species and other metabolites that could promote cancer initiation.[1] Chung and Chan (2020)[2] from Taiwan reported on a retrospective cohort study that sought to assess the association between periodontitis and all-cause mortality, and all-cancer and specific cancers' mortality in a health examination cohort of the elderly in the communities.

MATERIALS AND METHODS

This was a 7-year retrospective cohort study which used a dataset of health examinations for the elderly in Taipei City (Taiwan) with age equal to or above 65 years old.

The study population received an interview, physician consultation and clinical examination. Those aged less than 65 years old (*n* = 853), or with a mis-recorded examination date (*n* = 9) or missing data on periodontal status (*n* = 5257) at the first visit were excluded. Finally, 82,548 study participants were included for further analyses.

The total visits numbered 262,035 as of the end of the study after excluding 26,461 visits with missing data regarding periodontal status (*n* = 26,455) or mis-recorded examination dates (*n* = 6).

For the oral examination, participants with periodontal status reported as "inapplicable" or "refused" were excluded. If participants' periodontal status as diagnosed by dentists showed "no obvious abnormalities" then these participants were classified as having healthy periodontium, while participants with "abnormal periodontal status" diagnosis and periodontal tissues described as "tooth mobility" or "periodontitis" by dentists were classified as having periodontitis.

The primary endpoint was the date of death, especially death from cancer, or the end of the follow-up period (December 31, 2012). The cause of death was recorded according to the International Classification of Diseases, Ninth Revision (ICD-9) or Tenth Revision (ICD-10).

The baseline interview collected age, sex, education level (illiterate, 1-6 years of schooling, 7-14 years of schooling, or above 14 years of schooling), marital status (married and living together, vs. others), self-reported smoking status in the past 6 months (smoked every day, smoked some days or socially, or did not smoke), and self-reported intake of two fruits and three dishes of vegetables daily (yes, no).

If the participant had a history of diabetes or took long-term medication for controlling diabetes, or the fasting blood glucose report revealed abnormality, then the participant was defined as diabetic. In each oral examination, periodontal status was recorded by dentists.

The proportions of participants with different periodontal status at the baseline were calculated separately by demographic characteristics and health behaviors.

Comparisons of baseline characteristics between subgroups according to the periodontal status were made using logistic regression in which the first category in each variable was regarded as the reference group.

Kaplan-Meier curves with the log-rank test were employed to demonstrate the differences in survival curves in subgroups of different periodontal status at the baseline.

At each time point, Kaplan-Meier survival data included the numbers at risk.

A Cox proportional hazards model and Cox frailty model were used for calculating the hazard ratios of all-cause mortality and all-cause cancer mortality under different periodontal status.

After deleting participants who had one or more missing covariates regarding education level ($n = 12{,}592$), marital status ($n = 1347$), and smoking status ($n = 335$) in the baseline data, the Cox proportional hazards model and the Cox frailty model estimated the hazard ratio for all-cause and all-cancer mortality and included age, sex, education level, marital status, smoking status and periodontal status.

Due to the low number of each specific cancer to test the association, besides periodontal status, the Cox frailty models of deaths from cancer were only adjusted for age and sex.

RESULTS

At baseline, 24,806 participants had periodontitis (30.05%). The mean age of the sample at baseline was 73.59 years, and the slight majority was males (52.15%). More participants had 7-14 years of schooling (43.12%), were not married and living together (72.95%), had not smoked in the past 6 months (90.86%), ate fruits and vegetables daily (77.41%) and were not diagnosed with diabetes (65.8%).

When comparing participants with healthy periodontium to participants with periodontitis, the latter were more likely [$p < 0.05$] to be male (32.98%), be illiterate (32.70%), have higher frequency of smoking (smoke daily 39.82%) and have no fruit and vegetable intake daily (33.10%). However, there was no obvious difference ($p > 0.05$) in the percentages between the healthy periodontium group and periodontitis group by marital status and diabetes. At the end of study, the number of deaths was 11,160 participants, among which about 33.15% had periodontitis.

Association between periodontal status and risk of all-cause mortality and all-cancer mortality

At the midpoint of the study (1500 days), the survival probability of the periodontitis group was lower than that of the healthy periodontium group with regard to both all-cause mortality and all-cancer mortality.

Of the 82,548 participants, 7460 of 57,742 (12.9%) in the healthy periodontium group and 3700 of 24,806 (14.9%) in the periodontitis group died by the end of the study. The estimated rate of overall survival at 3000 days in the Kaplan-Meier analysis was 80.9% (95% CI, 80.1 to 81.8) in the periodontitis group and 82.3% (95% CI, 81.3 to 83.3) in the healthy periodontium group. There were significant differences in the rates of survival between the two groups ($P < 0.001$). Of the 82,548 participants, 2362 of 57,742 (4.1%) in the healthy periodontium group and 1153 of 24,806 (4.6%) in the periodontitis group died from cancer. The estimated rate of overall survival at 3000 days in the Kaplan–Meier analysis was 93.5% (95% CI, 92.9 to 94.1) in the periodontitis group and 94.2% (95% CI, 93.7 to 94.7) in the healthy periodontium group. There were significant differences in the rates of survival among the two groups ($P = 0.004$).

After controlling for other covariates, participants with periodontitis had significantly higher hazard ratios (HRs) for all-cause mortality (HR = 1.077, 95% CI:1.027 to 1.130). Being male, being elderly, and smoking were risk factors for all-cause mortality.

Participants with a high education level (above 14 years of schooling) had lower mortality. In regard to all-cancer mortality, after controlling for other covariates, hazard ratios (HRs) of all covariates had the same trend as that this result was not statistically significant for all-cancer mortality.

With regard to all-cause mortality and all-cancer mortality, there were significant associations with periodontitis. Being male, having a low education level and being a smoker were risk factors for both all-cause mortality and all-cancer mortality when considering each visit.

Association between periodontal status and risk of specific cancer mortality

Comparing mortality of lung cancer in the periodontitis group to the healthy periodontium group, the hazard ratio was 1.185 (95% CI: 1.027 to 1.368) which meant that there was significantly fewer deaths of lung cancer in the healthy periodontium group when compared to the periodontitis group. Similar findings were reported for prostate cancer. No statistical significance was found for esophageal cancer, pancreatic cancer, liver and gallbladder cancer, and colorectal cancer.

CONCLUSIONS

Being male, having a low education level, and being a smoker were risk factors for mortality in this retrospective elderly community cohort study. Our study findings showed mixed evidence that periodontal disease is associated with all-cause, all-cancer and specific-cancer mortality.

Implications for practice

Although the population studied was different to our patients, the large sample size highlight risk factors that may be important in our setting.

Reference

1. Corbella S, Veronesi P, Galimberti V, Weinstein R, Del Fabbro M, Francetti L. Is periodontitis a risk indicator for cancer? A meta-analysis. PLoS One. 2018; 13(4): e0195683.
2. Chung P, Chan T. Association between periodontitis and all-cause and cancer mortality: retrospective elderly community cohort study. BMC Oral Health. 2020; 20: 168.