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## Longitudinal relationship between dietary $\omega$ -3 fatty acids and periodontal disease

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### ABSTRACT

**Objective:** Fish oil has anti-inflammatory actions that may benefit periodontal health. We investigated the longitudinal relation between dietary  $\omega$ -3 fatty acids (FAs), docosahexaenoic acid (DHA), and eicosapentaenoic acid (EPA) to periodontal disease in community-dwelling elderly.

**Methods:** Fifty-five participants aged 74 y were randomly selected from a longitudinal interdisciplinary study of aging. Dietary intake data were obtained by a 3-d weighed food intake. The dietary intakes of energy, DHA, and EPA were calculated based on the *Standard Food Composition Tables in Japan*. Dental examinations were carried out at baseline and once a year for 5 y. The number of teeth with periodontal progression over 5 y per person was calculated as "periodontal disease events." Negative binomial regression analysis was conducted, which included DHA, EPA, and other covariates as independent variables to estimate the influence on periodontal disease events. Longitudinal data were analyzed for participants for whom data were available for 5 y ( $n = 36$ ).

**Results:** Low DHA intake was significantly associated with more periodontal disease events. The mean number of periodontal disease events for participants who consumed the lowest tertile of DHA was approximately 1.5 times larger (lowest tertile, incidence rate ratio 1.49, 95% confidence interval 1.01–2.21) than the reference group (highest tertile of DHA consumption), after simultaneously adjusting for possible confounders.

**Conclusion:** The findings suggest there may be an inverse, independent relation of dietary DHA intake to the progression of periodontal disease in older people.

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### Introduction

Periodontal disease is defined as an inflammatory condition of the gingival tissues, characterized by loss of attachment of the periodontal ligament and the bony support of the tooth. Several studies have examined the effects of  $\omega$ -3 fatty acids (FAs) in rodent periodontitis models. Two of these studies demonstrated decreases in gingival tissue levels of prostaglandin E<sub>2</sub>, prostaglandin F<sub>2 $\alpha$</sub> , leukotriene B<sub>4</sub>, and platelet activating factor, which are major inflammatory mediators and contribute to bone destruction in periodontal disease, and suggested that decreased

alveolar bone loss may have been seen with longer periods of  $\omega$ -3 administration [1,2].

Dietary fish or fish oil rich in  $\omega$ -3 FAs, mainly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), can attenuate chronic inflammatory diseases by various mechanisms [3]. DHA has demonstrated anti-inflammatory effects by interference with interleukin-1 signaling pathways leading to cyclooxygenase-2 induction in endothelial cells [4]. A high intake of the DHA has been associated with an important function in the prevention and treatment of inflammatory diseases [5]. In addition, EPA lowers the level of arachidonic acid (AA) available for metabolism and competes against AA for metabolism to form metabolites of the 5-series leukotrienes and 3-series prostaglandins, thereby taming the inflammatory reaction [6].

Periodontal disease is the main risk factor for tooth loss in the elderly [7,8]. Tooth loss has been associated with nutrient

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deficiency and changes in food preference [9,10]. In the relation between the number of teeth present and food group, we previously showed that people with fewer teeth consumed less seafood than people with more teeth [11]. According to a previous report, fish intake was positively associated with intake of  $\omega$ -3 FAs [12].

Investigating the relation between  $\omega$ -3 FAs and periodontal disease is important to understand the potential role of dietary modification in the prevention and treatment of periodontal disease and the ultimate prevention of tooth loss through periodontal disease. The composition of FAs in inflamed gingival tissues has been reported to be significantly different from that in healthy tissues in a previous study [13] and serum FA imbalance has been reported in patients with periodontal bone loss [14]. There are no reports in the literature of the relation between dietary intake of  $\omega$ -3 FAs and change in periodontal condition over time. Consequently, the hypothesis of the present study is that DHA and EPA may prevent periodontal disease, which triggers tooth loss. The study aimed to investigate any longitudinal relation between dietary  $\omega$ -3 FAs and periodontal disease in community-dwelling elderly.

## Materials and methods

### Study population

In 1998, a longitudinal interdisciplinary study of aging was initiated to evaluate the relation between general health status, including nutrient intake and anthropometry, and dental diseases. Initially, 4542 (2099 men and 2443 women) Niigata citizens, aged 70 y, were sent a written request to participate in the survey and were informed of the purpose of this survey. After two requests, 81.4% (3695) responded positively to participate in the survey. Considering the availability of resources, examination appointments could be arranged for 600 subjects. The final study sample was randomly recruited from several areas of Niigata to have an approximately equal number of men (306) and women (294). The participants agreed to undergo medical and dental examinations and signed informed consent forms regarding the protocol, which was approved by the ethics committee of Niigata University School of Dentistry. The study was carried out according to the rules of the Declaration of Helsinki. The participants were recalled and re-examined once a year using the same methods as the baseline survey. A total of 433 people (screened population) participated in the follow-up survey conducted in June 2001.

Of the screened population, 106 individuals who were randomly selected from several areas of Niigata were sent a written request to participate in the detailed nutrient survey and were informed of the purpose of this survey. Sixty-two people (58.5%) agreed to take part in this survey. Complete 3-d food intake data were obtained from 55 of the participants (26 men and 29 women). Seven volunteers did not submit complete data. At the time of this survey, all participants were 74 y old. For the screened population, body height, weight, smoking habits, and the number of teeth present were measured, and body mass index (BMI) was calculated to evaluate the difference between the screened population and the 55 volunteers.

None of the participants was hospitalized or institutionalized. They did not require special care for their daily activities.

### Dietary intake

This nutritional survey was conducted from November 5 to December 5, 2001, to avoid seasonal changes in food intake between the present study and Japan's National Nutrition Survey, which was conducted on November 11. Trained dietitians visited the participants the day before the survey started. The participants were fully instructed on how to record all consumed food. Each type of food consumed by the participants was weighed on 3 consecutive days using the same model of scale (Tanita, Tokyo, Japan). The dietitians checked the records of dietary intake weighed by the participants twice, on the second of the 3 consecutive days and after 3 consecutive days. Food consumption data were obtained at the participant's homes by 12 trained dietitians. Two dietitians checked all the food intake data. After that, nutrient intakes were calculated based on the *Standard Food Composition Tables in Japan* [15]. Items that were unregistered in the food tables were substituted by using the mean of existing items in the same food groups. Special attention was paid to the cooking condition of food for calculation according to the *Standard Food Composition Tables*. In case "the composition value of cooked food" was listed in the standard

tables, these values were used for calculation. Alcohol-derived energy was included in the total energy intake. The total energy intake and the mean dietary DHA and EPA intakes per day were calculated based on the *Standard Food Composition Tables in Japan*.

### Dental condition and smoking habits

Dental examinations were carried out at baseline (2001) and once a year for 5 y. Periodontal conditions were estimated for participants with at least one remaining tooth. Four dentists carried out intraoral examinations under sufficient illumination using artificial light, mouth mirrors, and a specially designed pressure-sensitive Vivacare TPS Probe (Vivacare, Schaun, Liechtenstein).

The periodontal condition, measured as the clinical attachment level, was recorded. Teeth were probed at six sites per tooth for all teeth present, and measurements were recorded approximately to the nearest whole millimeter. In the longitudinal study, a change in the loss of attachment of at least 3 mm in 1 y at any site was counted as a periodontal disease event [16]. Teeth with one disease event were excluded from additional-year assessments. Numbers of teeth with events over 5 y per person were calculated as periodontal disease events.

The examiners were calibrated before and during the survey using 18 volunteer patients in the Niigata University Hospital. As determined by replicate examinations of the attachment level, each percent agreement ( $\pm 1$  mm) ranged from 70.0% to 100% among four examiners. The  $\kappa$  values ranged from 0.62 to 1.00.

Participants were classified as smokers or non-smokers based on an interview conducted to obtain information regarding smoking habits. Individuals who reported any smoking history were considered smokers.

### Statistical analyses

Statistical analyses were performed as follows. Initially, the differences of selected characteristics (height, weight, BMI, and smoking habit) and dental condition (number of teeth present) were estimated between participants and the screened population. Then the number of teeth present was compared between highest and lowest tertiles of each DHA and EPA intake at baseline using Student's *t* test.

Furthermore, separate negative binomial regression analyses were performed including DHA, EPA, gender, BMI, smoking habit, number of present teeth at baseline, and mean clinical attachment level at baseline as independent variables to estimate the influence on periodontal disease events. Data were analyzed in 36 participants (20 men, 16 women) examined as dentate in 2006. They were classified by membership in tertile groups (lowest, middle, and highest) according to the value of DHA and EPA, respectively.

The level of statistical significance was set at  $P < 0.05$ . All calculations and statistical analyses were performed using SAS 9.1 for Windows (SAS Institute, Cary, NC, USA).

## Results

There were no significant differences in body height, weight, BMI, smoking habits, and the number of teeth present between the screened population and the participants (Table 1).

Overall, 19 participants withdrew during this study. Individuals who withdrew were excluded from the following statistical analyses. Dietary DHA mean intakes at baseline were  $947.1 \pm 684.2$  mg for participants and  $760.7 \pm 431.5$  mg for the group who withdrew during the survey. This was not significantly different between the two groups ( $P = 0.29$ , Student's *t* test). In addition, mean dietary EPA intakes at baseline were  $635.2 \pm 467.4$  mg for participants and  $449.0 \pm 243.6$  mg for the group who withdrew during the survey. No significant difference between the two groups was found ( $P = 0.11$ , Student's *t* test).

Participants' characteristics, dental status, and nutrient intake are listed in Table 1. There were significant differences in body height, BMI, smoking habits, total energy intake, and dietary DHA and EPA intakes between men and women. Men consumed more total energy, DHA, and EPA than women.

Significant differences were found in the number of teeth present between the two groups of DHA intake ( $22.3 \pm 6.9$  versus  $15.2 \pm 9.6$  for highest versus lowest tertile of DHA intake, respectively,  $P = 0.013$ , Student's *t* test; Fig. 1). The group with lowest tertile of DHA intake had significantly fewer teeth than

**Table 1**  
Selected characteristics, dental status, and nutrient intake in participants and the screened population\*

| Variables                              | Male  |                                  |                       | Female  |                                  |                       | <i>p</i> <sup>§</sup> |
|--|---|----------------------------------|-----------------------|---|----------------------------------|-----------------------|-----------------------|
|  | Screened population <sup>†</sup><br>( <i>n</i> = 233) | Participants<br>( <i>n</i> = 26) | <i>P</i> <sup>‡</sup> | Screened population <sup>†</sup><br>( <i>n</i> = 200) | Participants<br>( <i>n</i> = 29) | <i>P</i> <sup>‡</sup> |                       |
| Height (cm)                            | 162.2 ± 5.5   | 161.6 ± 5.1                      | NS                    | 149.1 ± 4.9   | 148.5 ± 5.1                      | NS                    | <0.0001               |
| Weight (kg)                            | 58.7 ± 8.4  | 55.8 ± 6.3                       | NS                    | 51.0 ± 7.8  | 52.1 ± 7.3                       | NS                    | NS                    |
| BMI (kg/m <sup>2</sup> )               | 22.3 ± 2.8  | 21.4 ± 2.5                       | NS                    | 22.9 ± 3.3  | 23.6 ± 2.6                       | NS                    | 0.0028                |
| Smoking (%)                            | 84.1  | 89.7                             | NS                    | 7.0   | 7.7                              | NS                    | <0.0001               |
| Dental condition: no. of teeth present | 17.0 ± 9.7  | 19.1 ± 9.6                       | NS                    | 16.6 ± 9.2  | 17.5 ± 9.1                       | NS                    | NS                    |
| Energy (kcal)                          | No data   | 2445.9 ± 421.7                   |                       | No data   | 1949.3 ± 296.3                   |                       | <0.0001               |
| DHA intake (mg)                        | No data   | 1085.9 ± 731.1                   |                       | No data   | 656.0 ± 326.5                    |                       | 0.0079                |
| EPA intake (mg)                        | No data   | 692.5 ± 482.5                    |                       | No data   | 435.2 ± 262.4                    |                       | 0.0191                |

BMI, body mass index; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid

\* Values expressed as average ± SD and percentage.

<sup>†</sup> People who participated in the follow-up survey of a longitudinal interdisciplinary study of aging conducted in June 2001.

<sup>‡</sup> Comparison of selected characteristics and dental condition between the screened population and participants.

<sup>§</sup> For the selected characteristics and dental status between men and women.

the group with the highest tertile of DHA intake. Also, there were significant differences in the number of teeth present between the two groups of EPA intake (22.1 ± 7.5 versus 14.7 ± 9.6 for highest versus lowest tertile of EPA intake, respectively,  $P = 0.013$ , Student's *t* test; Fig. 2). Participants who had lowest tertile of EPA intake had significantly fewer teeth than those with the highest tertile of dietary EPA intake.

The mean number of periodontal disease events in participants was 7.8 ± 5.3.

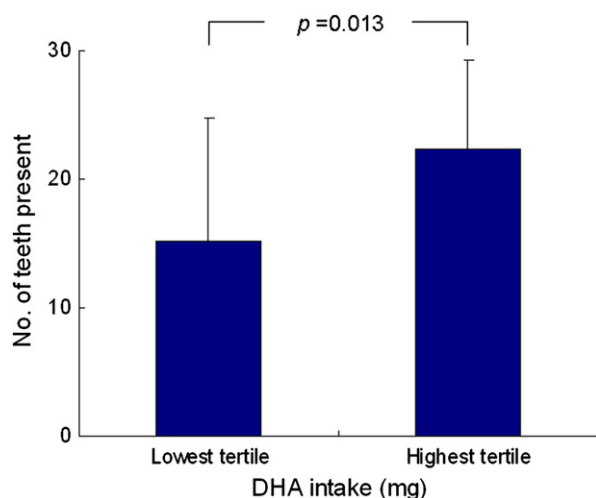
According to the results of negative binomial regression models, low DHA intake was significantly associated with more periodontal disease events. The mean number of the periodontal disease events for participants who consumed the lowest tertile of DHA was approximately 1.5 times larger (lowest tertile, incidence rate ratio 1.49, 95% confidence interval 1.01–2.21) than the reference group (highest tertile of DHA consumption) after simultaneously adjusting for gender, BMI, smoking status, the number of teeth at baseline, and mean clinical attachment level at baseline (Table 2). There was no significant difference between the middle tertile of DHA consumption group and the reference group. Also, there was no significant relation between EPA consumption at baseline and periodontal disease events (Table 2), although there was a tendency for the lowest EPA intake

group to have more periodontal disease events (incidence rate ratio 1.47, 95% confidence interval 0.97–2.21,  $P = 0.067$ ).

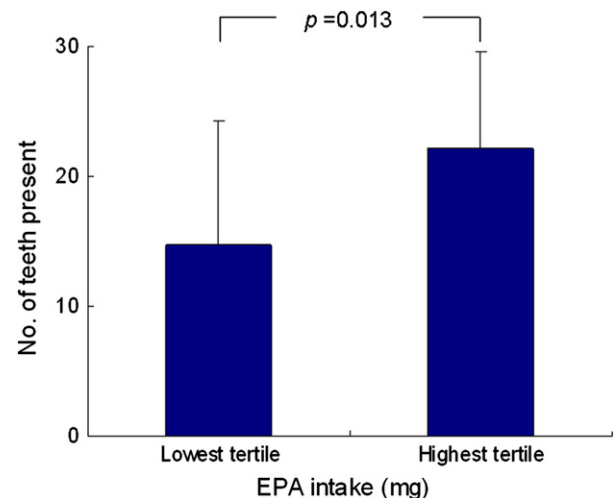
## Discussion

Because diet and tooth loss are influenced by health behavior, socio-behavioral factors may confound the results. We controlled such factors, in part, by using surrogate variables such as gender and smoking habits similar to the previous report [11]. In addition, a homogeneous group restricted to the age of 74 y was selected to exclude the influence of race and age variation in the results. Furthermore, there was no significant difference in general health and dental conditions between the screened population and the participants in the study. There was no significant difference in dietary DHA intake and dietary EPA intake between participants of the longitudinal survey and those who dropped out; therefore, it was believed that the participants in this study were representative of the parent study group.

Because the dietary intakes of DHA and EPA were thought to be influenced by the amount of food consumption, we used the dietary DHA and EPA data divided by the total energy in the final



**Fig. 1.** Relation between DHA intake and number of teeth present at baseline. DHA, docosahexaenoic acid.



**Fig. 2.** Relation between EPA intake and number of teeth present at baseline. EPA, eicosapentaenoic acid.

**Table 2**  
Negative binomial regression analysis for periodontal disease events

|                                  | Periodontal disease events <sup>*</sup> |      |            |                       |                  |           |
|----------------------------------|---|------|------------|-----------------------|------------------|-----------|
|                                  | Estimate                                | SE   | Chi-square | <i>p</i> <sup>†</sup> | IRR <sup>‡</sup> | 95% CI    |
| Intercept                        | -0.52                                   | 0.53 | 0.95       | 0.329                 | 0.60             | 0.21–1.68 |
| DHA intake/energy (mg/kcal)      |   |      |            |                       |                  |           |
| Lowest                           | 0.40                                    | 0.20 | 4.03       | 0.045                 | 1.49             | 1.01–2.21 |
| Middle                           | 0.16                                    | 0.20 | 0.70       | 0.401                 | 1.18             | 0.80–1.73 |
| Highest (reference)              | 0                                       | 0    | 1.00       | 1.00                  |                  |           |
| Gender                           |   |      |            |                       |                  |           |
| Male                             | 0.42                                    | 0.27 | 2.43       | 0.119                 | 1.52             | 0.90–2.58 |
| Female (reference)               | 0                                       | 0    | 1.00       | 1.00                  |                  |           |
| Smoking status                   |   |      |            |                       |                  |           |
| Smoker                           | -0.15                                   | 0.25 | 0.37       | 0.545                 | 0.86             | 0.52–1.41 |
| Non-smoker (reference)           | 0                                       | 0    | 1.00       | 1.00                  |                  |           |
| No. of teeth present at baseline | 0.07                                    | 0.01 | 23.28      | <0.0001               | 1.07             | 1.04–1.10 |
| Mean CAL at baseline             | 0.20                                    | 0.09 | 4.95       | 0.026                 | 1.23             | 1.02–1.47 |
| Intercept                        | -0.53                                   | 0.57 | 0.87       | 0.351                 | 0.59             | 0.19–1.80 |
| EPA intake/energy (mg/kcal)      |   |      |            |                       |                  |           |
| Lowest                           | 0.38                                    | 0.21 | 3.35       | 0.067                 | 1.47             | 0.97–2.21 |
| Middle                           | 0.22                                    | 0.23 | 0.93       | 0.336                 | 1.24             | 0.80–1.94 |
| Highest (reference)              | 0                                       | 0    | 1.00       | 1.00                  |                  |           |
| Gender                           |   |      |            |                       |                  |           |
| Male                             | 0.42                                    | 0.27 | 2.44       | 0.118                 | 1.53             | 0.90–2.60 |
| Female (reference)               | 0                                       | 0    | 1.00       | 1.00                  |                  |           |
| Smoking status                   |   |      |            |                       |                  |           |
| Smoker                           | -0.13                                   | 0.27 | 0.25       | 0.619                 | 0.87             | 0.51–1.49 |
| Non-smoker (reference)           | 0                                       | 0    | 1.00       | 1.00                  |                  |           |
| No. of teeth present at baseline | 0.07                                    | 0.02 | 22.15      | <0.0001               | 1.08             | 1.04–1.11 |
| Mean CAL at baseline             | 0.19                                    | 0.10 | 4.01       | 0.045                 | 1.21             | 1.00–1.46 |

CAL, clinical attachment level; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid

\* Number of teeth with periodontal disease progression during 5 y.

† Probability for chi-square test.

‡ Incidence rate ratio.

model to eliminate such effects, according to the previous report [11].

To our knowledge, this is the first longitudinal study of the relation between periodontal conditions and dietary  $\omega$ -3 FAs intake in older people. In this longitudinal study, an inverse independent relation of dietary DHA intake with periodontal disease events in the elderly was found, after controlling for confounding factors by negative binomial regression analysis. People with low DHA intake had an approximately 1.5 times higher incidence rate ratio of periodontal disease progression. In addition, it was found that participants with low EPA intake had a non-significant trend toward having a larger number of periodontal disease events.

This association between periodontal disease and  $\omega$ -3 FAs is probably explained by the systemic anti-inflammatory effects of  $\omega$ -3 FAs. In periodontal diseases, bacteria trigger inflammatory host responses that cause destruction of the alveolar bone and periodontal connective tissue [17]. Moreover, this local tissue-destructive immuno-inflammatory response produces pro-inflammatory immune mediators, such as interleukin-1, interleukin-6, tumor necrosis factor- $\alpha$ , and prostaglandin E<sub>2</sub>, that are dumped into the systemic circulation and subsequently may exert effects on distant organ systems [18]. DHA and EPA are  $\omega$ -3 FAs found in oily fish and fish oils. According to previous reports, DHA and EPA inhibit AA metabolism to inflammatory eicosanoids. They also give rise to mediators that are less inflammatory than those produced from AA or that are anti-inflammatory [19]. Furthermore, several reports have indicated that the increase in dietary intake of DHA blocks inflammatory cytokine production [20]. Consequently, dietary  $\omega$ -3 FA intake might contribute to the

control of periodontal disease progression through its anti-inflammatory effects. Fish intake was positively associated with intake of  $\omega$ -3 FAs [12]. Fish intake may therefore contribute in protecting against periodontal disease progression in the elderly.

Periodontal disease is one of the main risk factors for tooth loss [21]. Moreover, periodontal disease has been implicated as a risk factor for serious systemic diseases such as cardiovascular disease. Periodontal disease might add to the inflammatory burden of the individual and might increase the levels of cardiovascular risk based on serum C-reactive protein concentrations [22,23]. In contrast, the intake of the two  $\omega$ -3 FAs, DHA and EPA, is recommended for cardiovascular disease prevention, treatment after a myocardial infarction, prevention of sudden death, and secondary prevention of cardiovascular disease [24,25]. These recommendations are based on some prospective cohort studies [26,27]. Furthermore, because blood concentrations of  $\omega$ -3 FAs are a strong reflection of dietary intake, an  $\omega$ -3 FA biomarker might be considered a potential risk factor for coronary heart disease mortality, especially sudden cardiac death [28]. Consistent with these previous studies, our study might indicate another aspect of the association between periodontal diseases, dietary  $\omega$ -3 FAs, and heart diseases. Low dietary DHA and EPA might be a significant risk factor of periodontal disease progression and heart diseases, especially in the elderly.

## Conclusion

In summary, the findings of present study suggest there may be an inverse, independent relation of the dietary DHA intake to the progression of periodontal disease in older people.

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