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A Prospective Study of Green Tea Consumption and Oral Cancer Incidence in Japan

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PURPOSE: To examine the relation of green tea consumption with oral carcinogenesis, we prospectively analyzed data from a nationwide large-scale cohort study in Japan.
METHODS: A total of 20,550 men and 29,671 women aged 40–79 years, without any history of oral and pharyngeal cancer at baseline survey, were included in the present study. During a mean follow-up period of 10.3 years, 37 oral cancer cases were identified. The Cox proportional hazard model was used to estimate the hazard ratio (HR) and 95% confidence interval (95% CI) for oral cancer according to green tea consumption by sex, while adjusting for age, smoking, alcohol drinking, and other dietary factors.
RESULTS: For women, the HRs of oral cancer for green tea consumption of 1–2, 3–4, and 5 or more cups per day were 0.51 (95% CI: 0.10–2.68), 0.60 (95% CI: 0.17–2.10), and 0.31 (95% CI: 0.09–1.07), respectively, compared with those who drank less than one cup per day (*p* for trend, 0.08). For men, no such trends were observed.
CONCLUSIONS: Our findings did not suggest a prominent inverse association of green tea consumption with oral cancer, although there was a tendency for a reduced risk in women.
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KEY WORDS: Oral Cancer, Green Tea, Cohort Study.

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Selected Abbreviations and Acronyms

CI = confidence interval
EGCG = (-)-epigallocatechin-3-gallate
HR = hazard ratio
ICD = *International Classification of Disease*
JACC Study = Japan Collaborative Cohort Study
SAS = Statistical Analysis System

INTRODUCTION

In recent years, tea has attracted attention for its potential for preventing cancer since it contains polyphenols, chemicals that act as antioxidants (1). Green tea is a popular beverage in Japan. It is inexpensive, harmless, and convenient to drink, and thus its use is a valid lifestyle-related strategy for cancer prevention. Although the cancer-preventing effects of green tea have been shown in laboratory studies, few epidemiologic studies have evaluated whether green tea consumption provides protection against oral cancer (2).

A major risk factor for oral cancer is tobacco smoking (3), and alcohol drinking can also increase risk (4). Meanwhile, some studies have indicated that diets high in fruit and vegetables may protect against oral cancer (5–7) A clear relationship has not been found between oral cancer and nonalcoholic beverages (8), except for one particular type of tea (mate) (9).

Some prospective cohort studies have examined the association between green tea consumption and cancer in Japan. However, the results were inconsistent. Two studies found a significant inverse association between green tea consumption and total cancer incidence (10, 11), while a recent study reported that the consumption of green tea was not related to reduced mortality due to cancer (12). To our knowledge, there have been no previous prospective epidemiologic studies of green tea and oral cancer.

Japan has an ethnically homogeneous population with a fairly low incidence of oral cancer involving the tongue, the gums, the floor, and other parts of the mouth (13). In this study, therefore, to examine the relationship between green tea consumption and the risk of oral cancer prospectively, we analyzed data from the Japan Collaborative Cohort Study (JACC Study) for Evaluation of Cancer Risk, a nationwide large-scale cohort study sponsored by the Ministry of Education, Science, Sports and Culture of Japan (Monbusho).

MATERIAL AND METHODS

The JACC Study

The primary purpose of the JACC Study, sponsored by the Ministry of Education, Science, Sports and Culture of Japan, is to evaluate various risks of cancer incidence and mortality. The details have been described previously (14–16). Briefly, baseline registration was carried out between 1988 and 1990 by 24 collaborating institutions, covering 45 areas in various parts of Japan. A comprehensive self-administered questionnaire that included sociodemographic characteristics (e.g., level of education, marriage status), lifestyle-related factors (e.g., smoking, alcohol drinking, diet), and medical history (e.g., cancer, blood transfusion) was conducted at baseline. Of the 110,792 subjects (46,465 male and 64,327 female) aged 40–79 years, 65,184 (26,464 male and 38,720 female) in 24 areas were studied to identify the incidence of cancer (17). This incidence data were coded according to the *International Classification of Disease, Revision 10* (*ICD 10*) (before 1994, *ICD 9*). The status of the participants was confirmed annually based on population registers at each regional research center. Although the tentative end point of observation was in 2001, it was before 2001 in 5 areas.

The research protocol for this study was approved by the Ethics Committee of Medical Care and Research at the University of Occupational and Environmental Health, Japan, and the Ethical Board of the Nagoya University School of Medicine, where the central secretariat of the JACC Study is located.

Study Subjects

We first selected 65,184 subjects who lived in areas where the incidence of cancer was known. Four areas were then excluded from the analysis because the baseline questionnaire did not include the items for green tea, coffee, the above-mentioned foods, and history of cancer. Of the remaining 56,286 subjects, we excluded (1) those with any history of oral or pharyngeal cancer ($n = 31$), (2) those who were followed up for 12 months or less ($n = 556$), and (3) those whose response for green tea consumption was not recorded ($n = 5478$). Data for the remaining 20,550 men and 29,671 women were used in the present study.

Green Tea Consumption and Covariates

The subjects were first categorized into 4 groups according to their green tea consumption: less than 1 cup per day, 1 or 2 cups per day, 3 or 4 cups per day, or 5 or more cups per day. For further analysis, the subjects were recategorized into two groups: 4 or less cups per day and 5 or more cups per day. Covariates used in the multivariate analysis were age (years), sex, smoking (current smoker, past smoker, nonsmoker, unknown), alcohol drinking (current drinker, past drinker, nondrinker, unknown), and daily intake of green and yellow vegetables, salty foods, fruit, and coffee. The frequency of food and beverage consumption was assessed from 5 responses in the questionnaire: every day, 3 to 4 times (or cups) per week, 1 to 2 times (or cups) per week, 1 to 2 times