Null Results in Brief

No Association between Green Tea and the Risk of Gastric Cancer: Pooled Analysis of Two Prospective Studies in Japan

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Introduction

Although green tea shows protective effects against gastric cancer in laboratory experiments and most of eight case-control studies, none of the five prospective studies found a significant inverse association (1–6). Furthermore, no prospective studies have examined the association between green tea and gastric cancer by anatomical subsite or histological subtype. We conducted pooled analysis of two population-based prospective cohort studies in rural northern Japan. We reported null results from one of the two cohorts elsewhere (5).

Materials and Methods

Cohort 1 started in 1984 and included 31,345 subjects ages ≥40 years (93.7% response rate; Ref. 5). Cohort 2 started in 1990 and included 47,605 subjects ages 40–64 years (91.7% response rate). Self-administered questionnaires asked about recent (cohort 1) or usual (cohort 2) consumption of green tea. The two questionnaires used the same five frequency categories ranging from "never" to "≥5 cups/day." We documented the questionnaire assessment of green tea consumption to be sufficiently reproducible and valid (5). After exclusion of subjects with missing response on green tea and prior history of cancer, 26,311 subjects in cohort 1 and 39,604 in cohort 2 remained. We followed up vital and residential status of subjects by population registries. We identified through a population-based cancer registry 419 incident cases of gastric cancer among cohort 1 subjects (9 years of follow-up with 199,748 person-years) and 314 among cohort 2 subjects (7 years of follow-up with 290,599 person-years). We classified gastric cancer cases according to anatomical subsite of the primary lesion (cardia, body, and antrum), as well as histological subtype (differentiated and nondifferentiated). Differentiated and nondifferentiated types correspond to intestinal and diffuse types, respectively.

We used Cox regression to compute from each cohort RR[2] and 95% CI of gastric cancer according to green tea consumption with adjustment for sex, age, and potential confounders. We pooled these estimates to obtain summary measures using the general variance-based method. Because we observed no differential findings between the two cohorts, we present pooled results only. This study has ~85% statistical power, with the two-sided α-error level of 5%, in detecting a true RR of 0.7 among the highest *versus* lowest categories of green tea consumption.

Results

We reported characteristics of cohort 1 subjects according to green tea consumption elsewhere (5). Briefly, subjects with higher intake tended to be older, current smokers (men only), and to consume several food items (such as rice, vegetables, and fruits) more frequently. We observed similar tendency in cohort 2 subjects, except for no differences in the prevalence of current smoking by green tea consumption. We found no inverse association between green tea and gastric cancer (Table 1). We observed no differential results according to the histological subtype or anatomical subsite. Exclusion of gastric cancer cases diagnosed in the first 3 years of follow-up also did not change the findings substantially. Stratified analyses by covariates included in multivariate models did not reveal remarkable effect modifications.

Discussion

This pooled analysis of two prospective cohort studies in northern Japan found no association between consumption of green tea and risk of gastric cancer. The results disagree most of the eight case-control studies but agree with the five prospective studies.

This is the first prospective study examining the association between green tea consumption and the risk of gastric cancer by anatomical subsite or histological subtype. One case-control study in China reported that the protective effects of green tea drinking were similar for cardiac lesions and pyloric lesions (2). We observed no association regardless of anatomical subsite or histological subtype.

We could not specifically examine the effect of very high consumption of green tea because the highest category in our questionnaire was ≥5 cups/day. Among four studies examining the effect of very high consumption (≥7 cups/day), two case-control studies found significant inverse association (1, 3), whereas the smallest of five prospective studies found nonsignificant inverse association (4) and the largest prospective study found no association (6). Therefore, the hypothesis that risk of gastric cancer decreases only with very high consumption of green tea is not supported by the recent prospective studies.

We had no data on subjects' history of infection with *Helicobacter pylori*, an established risk factor for gastric cancer. No previous studies of green tea and gastric cancer had this information. Because green tea is suggested to have antibacterial effects, it is unlikely that the prevalence of *H. pylori*

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[2] The abbreviations used are: RR, relative risk; CI, confidence interval.

Table 1 RRs and 95% CIs of gastric cancer according to green tea consumption[a]

Variable	Green tea consumption (cups/day)				*P* for trend
	<1	1 or 2	3 or 4	≥5	
No. of cases/person-years					
Cohort 1	66/36,572	68/34,129	79/43,748	206/85,299	
Cohort 2	90/83,686	69/68,225	60/62,162	95/74,183	
Sex- and age-adjusted RR	1.0	1.03 (0.82–1.29)	0.91 (0.72–1.14)	1.12 (0.91–1.37)	0.29
Multivariate RR	1.0	1.01 (0.80–1.27)	0.89 (0.70–1.13)	1.06 (0.86–1.30)	0.61
Multivariate RR for histological subtype					
Differentiated (375 cases)	1.0	0.89 (0.63–1.26)	0.81 (0.57–1.14)	1.16 (0.87–1.55)	0.21
Nondifferentiated (154 cases)	1.0	0.75 (0.45–1.23)	0.74 (0.45–1.22)	0.88 (0.57–1.37)	0.67
Multivariate RR for anatomical subsite					
Cardia (95 cases)	1.0	1.21 (0.63–2.30)	0.53 (0.23–1.20)	1.27 (0.71–2.26)	0.55
Body (157 cases)	1.0	0.96 (0.57–1.63)	0.92 (0.55–1.55)	1.27 (0.81–1.99)	0.21
Antrum (197 cases)	1.0	1.02 (0.64–1.61)	1.02 (0.65–1.60)	1.05 (0.70–1.58)	

[a] In the five frequency categories about green-tea consumption, "never" and "occasionally" were collapsed into the single category of <1 cup/day. The multivariate RR has been adjusted for sex; age (in years); type of health insurance (five categories); parental history of gastric cancer; history of peptic ulcer; cigarette smoking (never smoking, smoking in the past, currently smoking 1–19 cigarettes/day, or currently smoking 20 or more cigarettes/day); alcohol consumption (never drinking, drinking in the past, currently drinking less often than daily, or currently drinking daily); consumption of rice (≤2, 3, 4, or ≥5 bowls), black tea, coffee (never, occasionally, 1 or 2 cups/day, or ≥3 cups/day), pickled vegetables, bean-paste soup (<1 day/week, 1 or 2 days/week, 3 or 4 days/week, or daily).
The multivariate RR for cohort 1 has also been adjusted for consumption of meat, green or yellow vegetables, other vegetables, and fruits (<1 day/week, 1 or 2 days/week, 3 or 4 days/week, or daily). The multivariate RR for cohort 2 has also been adjusted for consumption of pork, ham, spinach, carrot, cabbage, Chinese cabbage, orange, and other fruits (<1 day/week, 1 or 2 days/week, 3 or 4 days/week, or daily). Values in parentheses are 95% CI.

infection is substantially higher among subjects with higher green tea consumption and that failure to adjust for this infection had masked the protective effect of green tea.

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