Tea Consumption and Risk of Type 2 Diabetes: A Meta-Analysis of Cohort Studies

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BACKGROUND: Tea consumption has been extensively studied in relation to various diseases, several epidemiologic studies have been performed to investigate the association of tea consumption with type 2 diabetes; however, the results of these studies were not entirely consistent.

OBJECTIVE: To conduct a meta-analysis of studies that assessed the association of tea consumption and the risk of type 2 diabetes.

RESEARCH DESIGN AND METHODS: We performed a systematic literature search through November 2008 in PUBMED, MEDLINE, EMBASE, and Cochrane Database of Systematic Reviews. The search was limited to English-language studies. Studies were excluded if they were type 1 diabetes, animal studies. Nine cohort studies were identified by two authors, and summary relative risks (RRs) were calculated using a random-effects model.

RESULTS: We identified nine cohort studies, including 324,141 participants and 11,400 incident cases of type 2 diabetes with follow-up ranging from 5 to 18 years. The summary adjusted RR did not show that tea consumption was associated with a reduced type 2 diabetes risk (RR, 0.96; 95% confidence interval (CI), 0.92–1.01). Evidence from the results of our stratified analyses revealed that tea consumption ≥ 4 cups per day (RR, 0.8; 95% CI, 0.7–0.93) might play a role in the prevention of type 2 diabetes. However, no statistically significant association was observed for sex and the follow-up durations stratified between tea consumption and type 2 diabetes.

CONCLUSIONS: This meta-analysis indicates that tea consumption ≥ 4 cups per day may lower the risk of type 2 diabetes.

KEY WORDS: type 2 diabetes; tea; meta-analysis.

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INTRODUCTION

Type 2 diabetes as a public health burden has dramatically increased worldwide.¹ It is considered as the fifth leading cause of death in the world. The number of diagnosed type 2 diabetes is predicted to reach approximately 366 million by the year 2030.^{2,3} Increasing physical activity and modifying lifestyle have been proved to prevent or delay the incidence of type 2 diabetes.⁴ It has been proposed that chronic oxidative stress as a underlying mechanism in the development of insulin resistance, impaired glucose tolerance, β -cell dysfunction, and type 2 diabetes.^{5–7} Recent researches have found that green tea has antioxidative, antiinflammatory, and cholesterol-lowering effects.^{8–10}

Tea, next only to water, is the most popular consumed beverage in the world with a per capita consumption of 120 ml per day.¹¹ Therefore, small effects of tea at a population level would have a large impact on public health. Tea, derived from the plant *Camellia sinensis*, can be classified into three major types depending on the level of fermentation: green tea (unfermented), oolong tea (partially fermented), and black tea (fermented).^{12,13} The components of each tea are different, which is due to the different producing process. Green tea comes from steamed fresh leaves, which contain more catechins, including epigallocatechin gallate (EGCG), epicatechin-3-gallate (ECG), epigallocatechin (EGC), and epicatechin (EC).¹⁴ Black tea and oolong tea contain more theaflavins and thearubigins.¹⁵ In recent years, tea consumption has been extensively studied in relation to various diseases, especially cardiovascular disease and cancer.^{16–18}

There is accruing evidence that tea may prevent diabetes. Green tea polyphenols (GTP) have been shown to scavenge free radicals, decrease lipid peroxidation by increasing the activity of superoxide dismutase and glutathione, and also have antidiabetic effects.¹⁹ EGCG has insulin mimetic effect; it controls gluconeogenesis by inhibiting the expression of genes, such as PEPCK (phosphoenolpyruvate carboxykinase) and G6Pase (glucose-6-phosphatase). It also may promote the phosphorylation of insulin-signaling proteins and enhance insulin activity.^{20–22} Wolfram et al.²³ indicated that EGCG beneficially improved glucose and lipid metabolism in H4IIE cells and enhanced glucose tolerance in models of diabetes. Green tea extract also could increase fat metabolism and lipolysis in healthy humans.²² Another study provided evidence that green tea promoted glucose metabolism in healthy humans and produced an antihyperglycemic effect in diabetic mice.²⁴ A population-based, case-control study by

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Polychronopoulos et al.²⁵ reported that tea consumption could reduce levels of fasting blood glucose in nonobese elderly people.

To our knowledge, several epidemiologic studies^{25–34} have been performed to investigate the association of tea consumption with type 2 diabetes; however, the results of these studies were not entirely consistent: some studies showed that tea consumption might reduce the risk of type 2 diabetes,^{25,28,29,32–34} whereas others found nonsignificant relationships between the two.^{26,27,30,31} Because the relationship between tea consumption and risk of type 2 diabetes is still equivocal, we conducted this meta-analysis to further clarify this association based on the studies from the United States, Europe, and Asian countries.

METHODS

Study Selection and Data Extraction

We conducted a systematic literature search of PUBMED, MEDLINE (1966 to November 2008), and EMBASE (1980 to November 2008) to identify relevant studies. The Cochrane Database of Systematic Reviews also was queried. Search terms included tea, coffee, catechin, or flavonoids in combination with diabetes, glucose, and insulin. The search was limited to English-language articles. The titles and abstracts were scanned to exclude studies that were clearly irrelevant. The full texts of the remaining articles were read to determine whether they contained information about our interest. In addition, the electronic searches were supplemented by scanning reference lists from retrieved articles to identify additional studies. All searches were conducted independently by two investigators.

The eligible studies had to fulfill the following criteria: 1) to improve the validity of our results, only cohort studies could be included; 2) there are different types of tea in the world; we only included tea derived from *Camellia sinensis*; 3) the exposure of interest was tea consumption; and 4) the result of each study was expressed as relative risk (RR) or hazard ratio (HR) together with its corresponding 95% confidence interval (CI), or sufficient information to calculate. Because this study focused on tea consumption in relation to type 2 diabetes and related outcomes, we excluded studies concerning type 1 diabetes and animal studies.

The primary literature search identified 451 records; 432 articles were excluded after screening titles and abstracts, because they were laboratory studies, review articles, or irrelevant to the current study. Thus, a total of 19 articles were identified. Seven studies were excluded because they were other design types.^{24,25,35–39} A study by Mackenzie et al.⁴⁰ was excluded because some participants had diabetes at baseline. Two articles were excluded because they did not provide 95% CI or data to calculate (Fig. 1).^{41,42}

The first author's name, year of publication, country where the study was performed, age range of study participants, years of follow-up, sample size, diabetes definition/assessment, measurement of tea consumption, different levels of tea consumption of green tea, black tea, and oolong tea, covariates controlled for in the analysis, risk estimates with corresponding 95% CI, and cohort designation were collected from every included study. If a study provided several risk

Figure 1. Study flow chart.

estimates, the most completely adjusted estimate was extracted independently by two investigators. Discrepancies were resolved by discussion and repeated examination of the articles.

Quality Assessment

For measuring quality of observational studies no universal scale was available, therefore, we followed the guidelines of the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group and assessed the quality of the included studies based on the following criteria: 1) clear description of the population and setting; 2) tea should be derived from *Camellia sinensis* only; 3) appropriate measurement of outcomes; 4) response rate of the original study was higher than 80%; 5) completeness of follow-up; 6) appropriate consideration and adjustment for potential confounders; 7) <20 percent dropout rate; 8) clear reporting of dropouts; 9) provided data on levels of tea consumption; 10) appropriate statistical and analytical methods.⁴³ Throughout this assessment, when information about a specific item was consistent with the criteria, it was scored as “1”; otherwise, it was scored as “0”. Studies that fulfilled more than eight criteria were considered high-quality (i.e., scored ≥ 8).

Statistical Analysis

For meta-analysis, we used RRs as the common risk assessment measurement. We considered hazard ratios as RRs directly.⁴⁴ Study-specific RRs and corresponding 95% CIs of tea consumption levels were extracted. To obtain a pooled RR and its 95% CI, the log RR were weighted by the inverse of their variances. Pooled relative risks with 95% CIs were calculated with the method of DerSimonian and Laird random-effects model.⁴⁵ Overall RR and 95% CI were directly extracted from two studies.^{28,30} In other included studies, we calculated the total RR and 95% CI with the information provided. In addition, we analyzed tea consumption by men and women separately and distinguished three levels: <1 cup per day; 1–3 cups per day; and ≥ 4 cups per day. We defined <1 cup per day as >0 cups per day but <1 cup per day. To improve comparability with other studies, we combined 1 cup per day and 2–3

cups per day into 1–3 cups per day, 1–2 and 2–3 cups per day were considered 1–3 cups per day, and 1–6 cups per week also was considered <1 cup per day.^{26,28,30–32,34}

We evaluated possible heterogeneity of study results using the *Q* test ($P < 0.1$ was considered representative of statistically significant heterogeneity) and the I^2 statistic.⁴⁶ If significant heterogeneity existed, sensitivity analyses were performed. Funnel plot was used to assess the publication bias and Egger regression test to determine funnel plot asymmetry. We considered $P < 0.1$ to indicate a statistically significant publication bias.⁴⁷ All statistical analyses were conducted by using STATA 9.2 software (STATA Corporation, College Station, TX).

RESULTS

We identified nine cohort studies, including 324,141 participants and 11,400 incident cases of type 2 diabetes with the

follow-up ranging from 5 to 18 years (Table 1).^{26–34} Three studies involved women only, and the other six studies included both men and women. Mean age at baseline varied from 26 to 88 years. In our included studies, age, body mass index (BMI), physical activity, diet, inherit education, smoking status, and alcohol intake were considered as potential confounders. Of the nine cohort studies, five^{26–29,33} were performed in the United States, and the remaining four were performed in Finland,³⁰ the United Kingdom,³¹ Japan,³² and Singapore.³⁴ Five studies reported that tea consumption was not statistically significantly associated with risk of type 2 diabetes.^{26,27,30,31} Although Hamer et al.³¹ indicated that intake of >3 cups of tea per day was associated with a lower risk of diabetes after adjustment for age, sex, ethnicity, and social status, it was not robust for further adjustment. Two studies^{29,33} revealed that there was a possible reduction for type 2 diabetes with higher tea intake (≥ 4 cups per day) relative to the lower (<1 cup per day, 1–3 cups per day). A

Table 1. Characteristics of Studies Included in the Meta-Analysis

Source	Sex/ Quality Scores	Age at Baseline (yr)	Total N/ No. of Cases	Mean Follow-up (yr)	Type 2 Diabetes Definition/ Assessment	Method for Adjustment	Cohort Designation
Salazar-Martinez et al., 2004 ²⁷ , USA	M 9	40–75	41,934/ 1,311	12	NDDG diagnostic criteria, self-report, confirmed by medical records	Proportional hazards regression	The Nurses' Health Study and Health Professionals' Follow-up Study
	F 9	30–55	84,276/ 4,079	18	NDDG diagnostic criteria, self-report, confirmed by medical records	Proportional hazards regression	The Nurses' Health Study and Health Professionals' Follow-up Study
Song et al., 2005 ²⁹ , USA	F 9	≥ 45	37,457/ 1,593	8.8	ADA diagnostic criteria, self-report, confirmed from supplemental questionnaire and physician information	Proportional hazards regression	Women's Health Study
Greenberg et al., 2005 ²⁸ , USA	M/F 9	32–88	5,127/ 170	8.4	self-report of doctor's diagnosis	Proportional hazards regression	First National Health and Nutrition Examination Survey Epidemiologic Follow Up Study
van Dam et al., 2006 ²⁶ , USA	F 9	26–46	88,259/ 1,263	10	NDDG diagnostic criteria, self-report, confirmed by medical record review	Proportional hazards regression	Nurses' Health Study II
Hu et al., 2006 ³⁰ , Finland	M/F 9	35–74	21,385/ 964	13.4	WHO criteria, NHDR, NSIHDR	Proportional hazards regression	4 surveys in Finland
Iso et al., 2006 ³² , Japan	M 8	40–65	6,727/ 231	5	FSG ≥ 7.8 mmol/L, or RM ≥ 11.1 mmol/L, or treatment with oral hypoglycemic agents or insulin to indicate new cases of diabetes, self-report	Multiple logistic regression	25 communities across Japan
	F 8	40–65	10,686/ 213	5	FSG ≥ 7.8 mmol/L, or RM ≥ 11.1 mmol/L, or treatment with oral hypoglycemic agents or insulin to indicate new cases of diabetes, self-report	Multiple logistic regression	25 communities across Japan
Pereira et al., 2006 ³³ , USA	F 9	55–69	N/A	11	4 follow-up mailed surveys, self-report	Proportional hazards regression	Iowa Women's Health Study
Hamer et al., 2008 ³¹ , United Kingdom	M/F 9	35–55	5,823/ 387	11.7	OGTT, diabetic medication, self-report of doctor's diagnosis	Proportional hazards regression	Whitehall II cohort
Odegaard Ao et al., 2008 ³⁴ , Singapore	M/F 9	45–74	22,467/ 1,189	5.7	DRICD codes, Telephone interview	Proportional hazards regression	The Singapore Chinese Health Study

Abbreviations: NHDR, National Hospital Discharge Register; NSIHDR, National Social Insurance Institution's Drug Register; OGTT, oral glucose tolerance test; N/A, information not available; ADA, American Diabetes Association; NDDG, National Diabetes Data Group; FSG, fasting serum glucose concentration; RM, randomly measured concentration; WHO, World Health Organization; DRICD, codes, diabetes-related International Classification of Diseases codes

recent study performed in Singapore³⁴ reported that black tea was potentially associated with a lower risk of type 2 diabetes; however, Iso et al.³² reported that only consumption of green tea was associated with a reduced risk for type 2 diabetes. The study by Greenberg et al.²⁸ reported that the inverse association existed in the 60 years and younger age group.

According to the generic quality grading for all included studies, they were evaluated as high quality. The summary relative risk of type 2 diabetes was 0.96 (95% CI, 0.92–1.01), which did not show that tea consumption was associated with decreased risk of type 2 diabetes. There was no statistically significant heterogeneity among studies ($Q=6.37$; $P=0.61$; $I^2=0\%$). However, visualization of the funnel plot (Fig. 2) and Egger's test ($P=0.05$) revealed some publication bias.

We also conducted stratified analyses of sex, follow-up years, and daily tea consumption. Compared with those who never drink tea, the analysis of daily tea consumption revealed that there are statistically significant effects for tea intake ≥ 4 cups per day (RR, 0.8; 95% CI, 0.7–0.93; Fig. 3). For <1 cup per day (RR, 0.99; 95% CI, 0.94–1.05) and 1–3 cups per day (RR, 0.99; 95% CI, 0.93–1.05), we did not find any statistical significance. The distinction among green tea, black tea, and oolong tea might be relevant for risk of type 2 diabetes, so we intended to abstract data from included studies; however, only one study provided information on tea types,³² therefore, we were not able to conduct stratified analysis on tea types. For sex and follow-up duration stratified analyses, no statistically significant association was observed: male (RR, 0.94; 95% CI, 0.86–1.02), female (RR, 0.94; 95% CI, 0.86–1.04); and follow-up durations: <10 years (RR, 0.94; 95% CI, 0.86–1.03), ≥ 10 years (RR, 0.97; 95% CI, 0.92–1.02).

DISCUSSION

To our knowledge, this is the first meta-analysis to evaluate the association between tea consumption and the risk of type 2 diabetes. Our study, based on nine cohort studies, showed that participants who drank four or more cups of tea per day had a 20% lower risk of type 2 diabetes compared with those who drank less or none. However, no statistically significant association was observed for sex and the follow-up durations

Figure 2. Begg's funnel plot of tea consumption and type 2 diabetes risks.

Figure 3. Stratified analysis pooled relative risks of type 2 diabetes on daily tea consumption. All the three levels were compared to those who never drinking tea. The area of the squares reflects the study-specific weight (i.e., inverse of the variance). The diamond represents the pooled relative risk and 95% confidence interval of every subgroup.

stratified between tea consumption and type 2 diabetes. In the absence of larger population-based, long-term, randomized, intervention studies, our study is the best available evidence.

This study showed that relatively high tea intake could lower the risk of type 2 diabetes. This could be a dose-response effect. Many researches have certified that the main extracts of tea have antidiabetes effects. One study reported that green tea extract (300 mg/kg BW/day) could significantly decrease blood glucose in rats.⁴⁸ Wu et al. revealed that ingestion of 0.5 g per day of green tea could significantly reduce fasting hyperglycemia compared with the control group in a fructose-fed rat model. They also found that daily supplementation of 0.5 g of green tea for 12 weeks could reduce fasting plasma glucose levels, insulin, triglyceride, and free fatty acids in Sprague-Dawley rats.^{49,50} Islam et al. reported that green tea intake of 23 g per day could increase serum insulin concentration in rats, and higher consumption of green tea can be beneficial for normal human subjects with hyperlipidemia.⁵¹ Therefore, certain doses of green tea were beneficial for diabetes prevention.

Multiple etiological risk factors for diabetes have been identified, such as family history, genetic alteration, environmental factor, lifestyle, and physical activities. Genetic and lifestyle factors may influence the effect of tea consumption in the process of diabetes, and these factors were not completely controlled in all of our included studies, therefore, it was not easy to make a definitive conclusion. Further epidemiologic studies are required.

Several potential limitations of this meta-analysis must be considered when interpreting the results. First, our search was

restricted to studies published in indexed journals. There lacked more unpublished studies with negative results and we only included papers published in English languages, which would be the source of our publication bias. Moreover, the small sample size of our meta-analysis for evaluating the association between tea consumption with type 2 diabetes risk may reduce the power of any test to detect publication bias. Also, because no universally validated scale of study quality exists, we used a scale of items that were selected based on common sense only. A different scale may have yielded other results. Second, most of our included studies were not originally designed to test the tea/type 2 diabetes hypothesis and methods for measuring tea intake differed across studies, which may influence our results. Third, information from articles was limited: we cannot conduct stratified analysis on green tea, black tea, and oolong tea consumption with type 2 diabetes risk. Finally, our analysis was based on observational studies and we cannot exclude uncontrolled confounders as a potential explanation for the observed association. There was a lack of adjustment for socioeconomic status (only 5 studies adjusted for socioeconomic status or education), which could contribute to a noncausal association between tea consumption and diabetes, because low socioeconomic status is related to depression and other factors, which will increase the risk for type 2 diabetes.^{52–54}

CONCLUSIONS

This study indicates that tea consumption ≥ 4 cups per day may lower the risk of type 2 diabetes. However, the reasons for this remain unclear; therefore, it is too early to recommend that the public drink more tea. Larger, population-based, randomized, controlled trials are required to further clarify the relationship between tea consumption and the risk of type 2 diabetes.

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Conflict of Interest: None disclosed.

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