

Original Article

Association between tea and coffee consumption and risk of laryngeal cancer: a meta-analysis

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Abstract: Objective: Epidemiological studies evaluating the association of tea and coffee consumption and the risk of laryngeal cancer have produced inconsistent results. Thus, we conducted a meta-analysis to assess the relationship between tea and coffee consumption and laryngeal cancer risk. Methods: Pertinent studies were identified by a search in PubMed, Web of Knowledge and Wan Fang Med Online. The random effect model was used based on heterogeneity test. Publication bias was estimated using Egger's regression asymmetry test. As a result, 11 articles were included in this meta-analysis. Results: For tea consumption and laryngeal cancer, data from 8 studies including 2167 laryngeal cancer cases were used, and the pooled results suggested that highest tea consumption versus lowest level wasn't associated with the risk of laryngeal cancer [summary RR = 0.909, 95% CI = 0.674-1.227]. Eight studies comprising 2596 laryngeal cancer cases for coffee consumption and laryngeal cancer risk were included, and no association was found (summary RR = 1.218, 95% CI = 0.915-1.622). Conclusions: Finding from this meta-analysis suggested that tea and coffee consumption weren't associated with the risk of laryngeal cancer. Since the potential biases and confounders could not be ruled out completely in this meta-analysis, further studies are warranted to confirm this result.

Keywords: Tea consumption, coffee consumption, laryngeal cancer, meta-analysis

Introduction

It has reported that cancer continues to be a major public health problem despite of the development in medical technology for its prevention, diagnosis and treatment. Larynx cancer is the fourteenth most common cancer in the world and it is the most common cancer in the head and neck [1]. Tobacco smoking and alcohol drinking are the two major risk factors for the laryngeal carcinoma in the developed countries [2]. For the other factors, dietary factors and life styles have been suggested to have a relevant role. In a case-control study from Italy and Switzerland, fruit and vegetables diversity is related to a decreased risk of laryngeal cancer risk [3].

Tea and coffee are the most commonly consumed beverages in the worldwide. Tea, which has attracted much attention for the potential cancer preventive effect for a long time, is

reported to be inversely associated several cancer. In the Ohsaki Cohort study involving 41,761 Japanese adults, green tea consumption is associated with a reduced risk of liver cancer incidence [4]. Coffee is a rich source of various polyphenols. The polyphenols are known to be important antioxidant properties which are beneficial against several oxidative stress related diseases such as cancer, cardiovascular diseases, and aging [5]. The effect of coffee consumption on the incidence was detected in numerous studies [6] and heterogeneous conclusions were gotten. The association between consumption of tea and coffee and risk of laryngeal cancer was reported, however, no consistent conclusion was obtained. Therefore, we conducted a meta-analysis to (1) first assess the laryngeal cancer risk for the highest vs. lowest categories of tea and coffee consumption; (2) assess the heterogeneity among studies and publication bias.

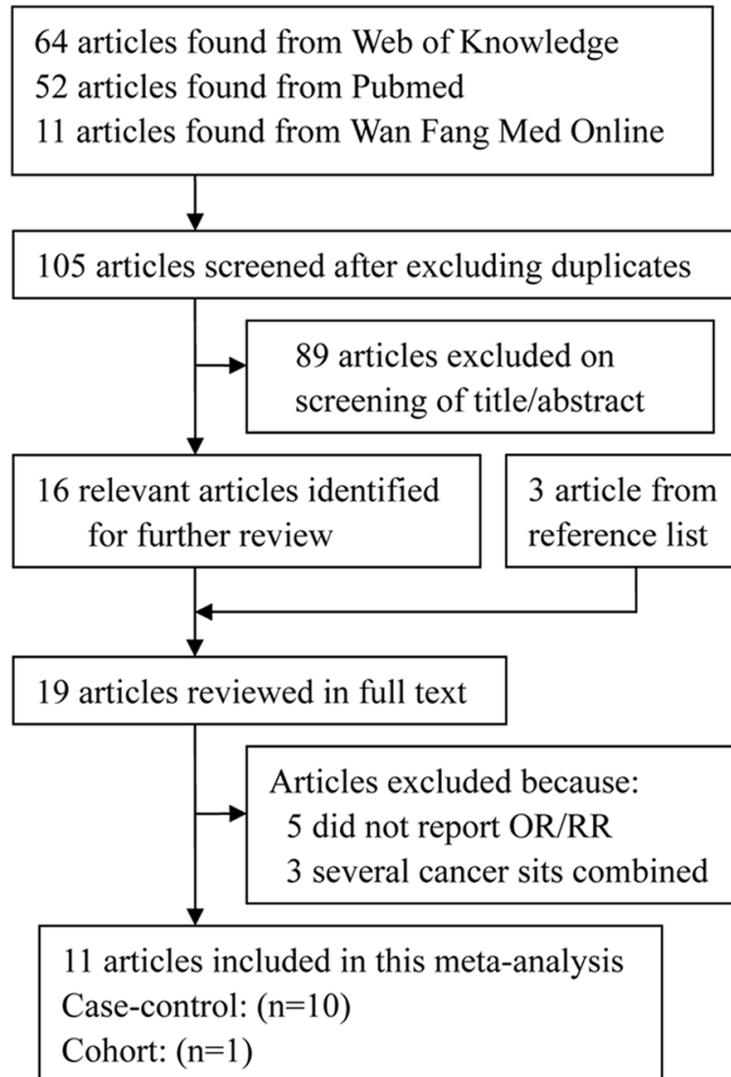


Figure 1. The flow diagram of screened, excluded, and analyzed publications.

Methods

Search strategy

A comprehensive search was conducted for available articles published in English or Chinese using the databases of PubMed, Web of Knowledge and Wan Fang Med Online up to December 2013 and by hand-searching the reference lists of the computer retrieved articles. The following search terms were used: “tea”, “green tea”, “black tea”, “coffee”, “caffeine”, “beverages”, “diet” and “laryngeal cancer”, “laryngeal carcinoma”. Two investigators searched articles and reviewed of all retrieved studies independently. Disagreements between

the two investigators were resolved by consensus with a third reviewer.

Inclusion criteria

All relevant studies reporting the association of tea and coffee consumption and laryngeal cancer risk were considered for inclusion. The inclusion criteria were as follows: (1) use a case-control, nested case-control or cohort design; (2) the exposure of interest were tea or coffee consumption; (3) the outcome of interest was laryngeal cancer; (4) report associations in the form of RR with the 95% confidence intervals (CI) for tea or coffee consumption or providing us with sufficient information to calculate them. Accordingly, the following exclusion criteria were also used: (1) reviews and (2) repeated or overlapped publications.

Data extraction

Two researchers independently extracted the relevant information. The data extraction was conducted via a standardized data extraction form, collecting information on the name of first author, the publication year, study design, number of cases and controls, sample size, study

site, tea drinking definitions, adjustments of the confounding factors, and the OR/RR value with 95% CI. When the tea drinking wasn’t stated, it would be categorized as “ever versus never”. When the OR or RR was not reported in the article, the RR with 95% confidence intervals (CI) with the raw data and no confounding factors were adjusted. If there was disagreement between the two investigators about eligibility of the data, it was resolved by consensus with a third reviewer.

Statistical analysis

The pooled measure was calculated as the inverse variance-weighted mean of the natural

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Table 1. Characteristics of studies in tea and coffee consumption and laryngeal cancer risk

First author, year	Country	Study design	Cases, age	RR (95% CI) for highest versus lowest category	Adjustment or matched for
Vassileiou et al. 2012	Greece	Case-control (HCC)	70, < 80	1.77 (1.36-2.35) for coffee	Age, sex
Ren et al. 2010	USA	Population based cohort	179, 50-71	1.01 (0.71-1.44) for coffee 0.92 (0.63-1.36) for hot tea 0.86 (0.62-1.18) for iced tea	Age, sex, tobacco smoking, alcohol drinking, BMI, education, ethnicity, usual physical activity throughout the day, vigorous physical activity and the daily intake of fruit, vegetables, red meat, white meat and calories
Galeone et al. 2010	Europe	Case-control	1178, 18-80	0.92 (0.34-2.53) for coffee 0.97 (0.80-1.18) for tea	Age, sex, race/ethnicity, education, study, cigarette smoking (pack-years), duration of cigar smoking, duration of pipe smoking, alcohol intake, weight, and vegetable and fruit intake
Zvrko et al. 2008	Montenegro	Case-control (HCC)	108, 35-85	3.32 (1.16-9.49) for coffee	Age, sex, residence, alcohol, smoking and other risk factors not reported
Kapil et al. 2005	India	Case-control (HCC)	305, 41-80	4.20 (1.80-10.09) for tea	Age, sex and place of residence
Bosetti et al. 2002	Italy and Switzerland	Case-control (HCC)	527, 30-79	0.81 (0.55-1.20) for coffee	Age, sex, center, education, smoking, alcohol, nonalcoholic energy
Franceschi et al. 1999	Italy	Case-control (HCC)	327, 32-76	0.9 (0.8-1.1) for coffee	Age, sex, centre, education, smoking habit, alcohol and energy intake
Pintos et al. 1994	Brizil	Case-control (HCC)	97, < 54 - > 75	1.89 (0.7-4.9) for coffee 1.06 (0.4-2.5) for tea	Tobacco, alcohol, income, rural residency, 10 dietary variables and consumption of other nonalcohol beverages
La Vecchia et al. 1992	Italy	Case-control (PCC)	149, < 85	0.4 (0.2-0.8) for tea	Age, sex, area of residence, education, smoking, and coffee consumption
La Vecchia et al. 1990	Italy	Case-control (HCC)	110, < 45-74	1.40 (0.85-1.98) for coffee	Age
Notani et al. 1987	India	Case-control (HCC/PCC)	80, < 40 - > 60	0.5 (0.3-0.9) for tea (HCC) 1.1 (0.6-2.0) for tea (PCC)	Age and tobacco habits

Abbreviations: PCC = population-based case-control study; HCC: hospital-based case-control study; BMI: Body Mass Index.

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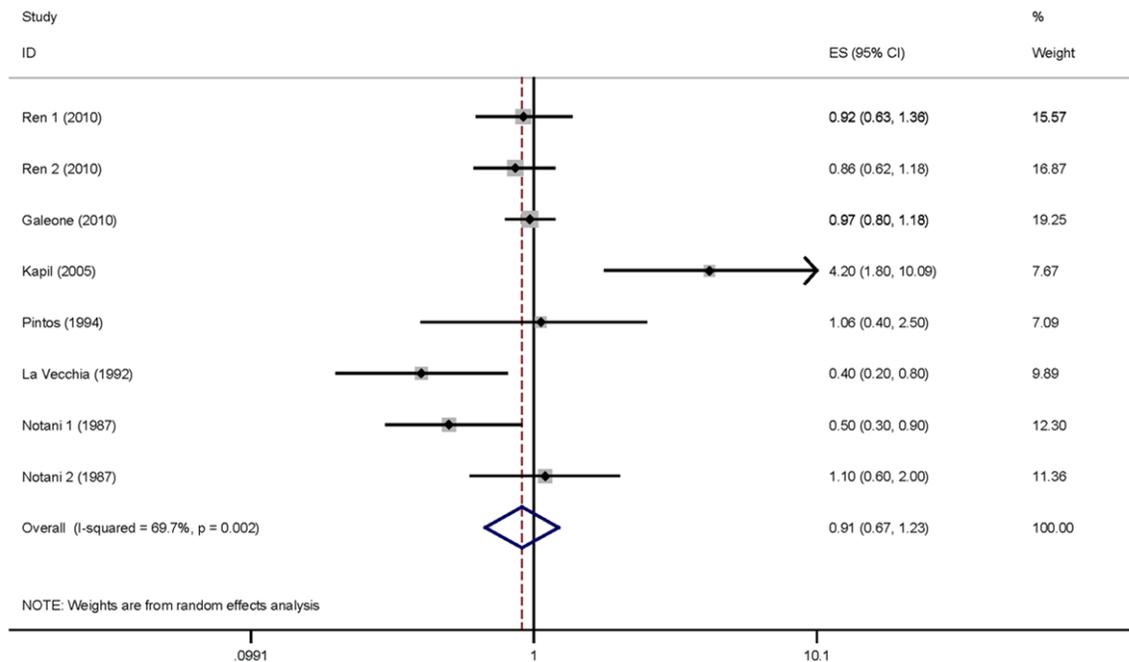


Figure 2. The forest plot between highest versus lowest categories of tea consumption with risk of laryngeal cancer.

logarithm of multivariate adjusted RR with 95% CI for the highest vs. lowest levels to assess the association of tea or coffee consumption with the risk of laryngeal cancer. Random-effects model was used to combine study-specific RR (95% CI), which considers both within-study and between-study variation [7]. The Q test and I^2 of Higgins and Thompson [8] were used to assess heterogeneity among included studies and I^2 values of 0, 25, 50 and 75% represent no, low, moderate and high heterogeneity. Meta-regression with restricted maximum likelihood estimation was performed to describe the potentially important covariates [9]. If no significant covariates were found to be heterogeneous, the “leave-one-out” sensitive analysis [10] was carried out to evaluate the key studies with substantial impact on between-study heterogeneity. Publication bias was estimated using Begg’ funnel plot [11] and Egger’s regression asymmetry test [12]. A study of influence analysis [13] was conducted to describe how robust the pooled estimator is to removal of individual studies. An individual study is suspected of excessive influence if the point estimate of its omitted analysis lies outside the 95% CI of the combined analysis. All analyses were conducted using STATA software, version 10.0 (Stata Corp LP, College Station, Texas). Two-tailed $P \leq 0.05$ was accepted as statistically significant.

Results

Search results and study characteristics

The flowchart of the study selection was presented in **Figure 1**. A total of 127 publications were retrieved from the initial literature search (52 from PubMed, 64 from Web of Knowledge and 11 from Wan Fang Med Online). After excluding 22 duplicated articles, a total of 105 records were detailed evaluated. Among these articles, 19 full-texts were assessed for eligibility after removing 89 articles. At the end, 11 original articles that included data on the association between tea and coffee consumption and laryngeal cancer were ultimately included in our meta-analysis [14-24]. The characteristics of these studies are presented in **Table 1**. The geographical distribution of the articles was 8 were in European, 2 in Americas and 1 in Asia.

Tea consumption

High versus low analyses: For tea consumption and laryngeal cancer, data from 6 articles [15, 16, 18, 21, 22, 24] (2 prospective studies and 6 case-control studies) were used including 2167 laryngeal cancer cases. Inverse association of tea consumption with risk of laryngeal cancer was reported in 2 studies, no significant

association of tea consumption with risk of laryngeal cancer was reported in 5 studies, and 1 study reported that tea consumption could increase the laryngeal cancer risk. Pooled results suggested that highest tea consumption versus lowest level wasn't associated with the risk of laryngeal cancer [summary RR = 0.909, 95% CI = 0.674-1.227, $I^2 = 69.7\%$, $P_{\text{heterogeneity}} = 0.002$] (**Figure 2**).

Sources of heterogeneity and subgroup analyses: As seen in **Figure 2**, evidence of heterogeneity ($I^2 = 69.7\%$, $P_{\text{heterogeneity}} = 0.002$) was found in the pooled results. However, univariate meta-regression analysis, with the covariates of publication year, study region, and sources of controls showed no covariate having a significant impact on between-study heterogeneity, respectively. The key contributor to this high between-study heterogeneity assessed by the leave-one-out analysis was one study conducted by Kapil et al. After excluding this study, heterogeneity was reduced to $I^2 = 44.2\%$, and the summary RR for laryngeal cancer was 0.826 (95% CI = 0.662-1.029; $P_{\text{heterogeneity}} = 0.096$).

In subgroup analyses for geographical, when we restricted the analysis to America and Europe, the pooled RR of laryngeal cancer for the highest category of tea consumption versus the lowest category were 0.895 (95% CI = 0.705-1.136) and 1.125 (95% CI = 0.425-2.981), respectively. When we conducted the subgroup analysis by sources of control, adjustment for smoking or alcohol, the results were also no significant between tea consumption and laryngeal cancer in all strata. The main results are summarized in **Table 2**.

Influence analysis and publication bias: Influence analysis showed that no individual study had excessive influence on the association of tea consumption and laryngeal cancer. Begg's funnel plot and Egger's test showed no evidence of significant publication bias between tea consumption and laryngeal cancer ($P = 0.964$).

Coffee consumption

High versus low analyses: Data from 8 articles [14-17, 19-21, 23] (1 prospective study and 7 case-control studies) including 2596 laryngeal cancer cases for coffee consumption and laryngeal

geal cancer risk were used. Two studies reported that coffee consumption can increase the laryngeal cancer risk, while 6 studies didn't show the significant association between coffee consumption and laryngeal cancer risk. The pooled results showed no significant association between coffee consumption and laryngeal cancer risk (summary RR = 1.218, 95% CI = 0.915-1.622) (**Figure 3**). However, high heterogeneity was found ($I^2 = 74.1\%$, $P_{\text{heterogeneity}} = 0.000$).

Sources of heterogeneity and subgroup analyses: We used univariate meta-regression analysis with the covariates of publication year, study region, number of cases, and sources of controls to find the sources of heterogeneity, however, no covariate having a significant impact on between-study heterogeneity. The key contributor to this high between-study heterogeneity assessed by the leave-one-out analysis was one study conducted by Vassileiou et al [14]. After excluding this study, heterogeneity was reduced to $I^2 = 48.7\%$, and the summary RR for laryngeal cancer was 1.073 (95% CI = 0.845-1.362; $P_{\text{heterogeneity}} = 0.069$).

Seven case-control studies were included in this meta-analysis, and the pooled RR was 1.276 (95% CI = 0.907-1.796) for the highest category of coffee consumption versus the lowest category and laryngeal cancer risk. For the subgroup of ethnicity, no significant associations were found both in America (RR = 1.165, 95% CI = 0.696-1.950) and Europe (RR = 1.234, 95% CI = 0.861-1.767). Furthermore, no associations of coffee consumption with risk of laryngeal cancer were found for the subgroups of sources of control. When combined the results of the studies which adjustment for smoking or alcohol, we found that coffee consumption could increase the laryngeal cancer for the studies not adjustment for smoking and alcohol. The main results are summarized in **Table 2**.

Influence analysis and publication bias: Influence analysis showed that no individual study had excessive influence on the association of coffee consumption and laryngeal cancer. Begg's funnel plot and Egger's test showed no evidence of significant publication bias between coffee consumption and laryngeal cancer ($P = 0.256$).

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Table 2. Summary risk estimates of the association between coffee and tea consumption and laryngeal cancer risk

Sub-groups	Tea				Coffee			
	Studies, n	RR (95% CI)	I ² (%)	P _{heterogeneity}	Studies, n	RR (95% CI)	I ² (%)	P _{heterogeneity}
All	8	0.909 (0.674-1.227)	69.7	0.002	8	1.218 (0.915-1.622)	74.1	0.000
Case-control	6	0.942 (0.579-1.534)	78.2	0.000	7	1.276 (0.907-1.796)	77.7	0.000
Sources of control								
Population-based	4	0.819 (0.599-1.119)	44.5	0.144	1	--	--	--
Hospital-based	3	1.269 (0.353-4.566)	88.0	0.000	6	1.317 (0.913-1.899)	81.3	0.000
Area								
America	3	0.895 (0.705-1.136)	0.0	0.900	2	1.165 (0.696-1.950)	29.0	0.235
Europe	3	1.125 (0.425-2.981)	88.5	0.000	6	1.234 (0.861-1.767)	80.5	0.000
Adjustments								
Smoking, yes	5	0.869 (0.703-1.075)	33.7	0.196	6	1.005 (0.787-1.283)	41.3	0.130
no	3	1.265 (0.420-3.806)	88.1	0.000	2	1.652 (1.313-2.078)	0.0	0.361
Alcohol, yes	4	0.939 (0.808-1.092)	0.0	0.925	6	1.005 (0.787-1.283)	41.3	0.130
no	4	0.946 (0.386-2.317)	86.3	0.000	2	1.652 (1.313-2.078)	0.0	0.361

Discussion

Finding from this meta-analysis suggested that tea and coffee consumption were not significantly associated with the risk of laryngeal cancer. No associations were found between tea and coffee consumption and laryngeal cancer risk when we conducted the subgroups of geographical, sources of control.

Previous meta-analyses have suggested that no associations were found between bladder cancer and overall tea consumption [25-27]. No significant association between tea consumption and esophageal cancer was found, and the pooled RR was 1.09 [95% CI = 0.76-1.55] for greatest vs. non/least green tea consumption [28]. And the results from another meta-analysis showed that no significant association was found between tea consumption and breast cancer [29]. For coffee consumption and cancer risk, finding from a meta-analysis suggested that a favorable effect of coffee consumption and the risk of liver cancer [30], but a linear relationship was found between coffee consumption and increased risk of lung cancer, especially for consumers of ≥ 3 cups per day [31]. However, no significant association was found between breast cancer risk and coffee (RR = 0.97, P = 0.09), decaffeinated coffee (RR = 0.98, P = 0.55) and caffeine (RR = 0.99, P = 0.73), respectively [32]. The association was also no significant between coffee consumption and prostate cancer risk among overall analysis [33].

Tea and coffee are served as hot beverage usually. They might modify the incidence of laryngeal cancer through more than the tea and coffee itself. In a systematic review, the results strongly suggest that high-temperature beverage drinking increases the risk of esophageal cancer [34]. We speculate that the hot temperature would decline the potential protective effects of tea and coffee. Ren et al conducted a prospective study, and the effects of both iced and hot tea on the laryngeal cancer incidence were investigated [15]. Neither the iced tea (RR = 0.86; 95% CI = 0.62-1.18) or hot tea (RR = 0.92; 95% CI: 0.63-1.36) consumption was reported to be associated with the incidence of laryngeal cancer after adjusting the relevant confounding factors, such as age, sex, tobacco smoking, alcohol drinking, BMI, education and ethnicity. The temperature of tea and coffee is a potential important factor in their effects on the laryngeal cancer risk.

As a paper of published study [35], between-study heterogeneity is common in the meta-analysis, and exploring the potential sources of between-study heterogeneity is the essential component. Although high heterogeneities were found in high versus low analysis between tea and coffee consumption and laryngeal cancer risk, after leave-one-out analysis, the result showed consistent association with the previous one, thus strongly identifying the relationship between tea and coffee consumption and laryngeal cancer.

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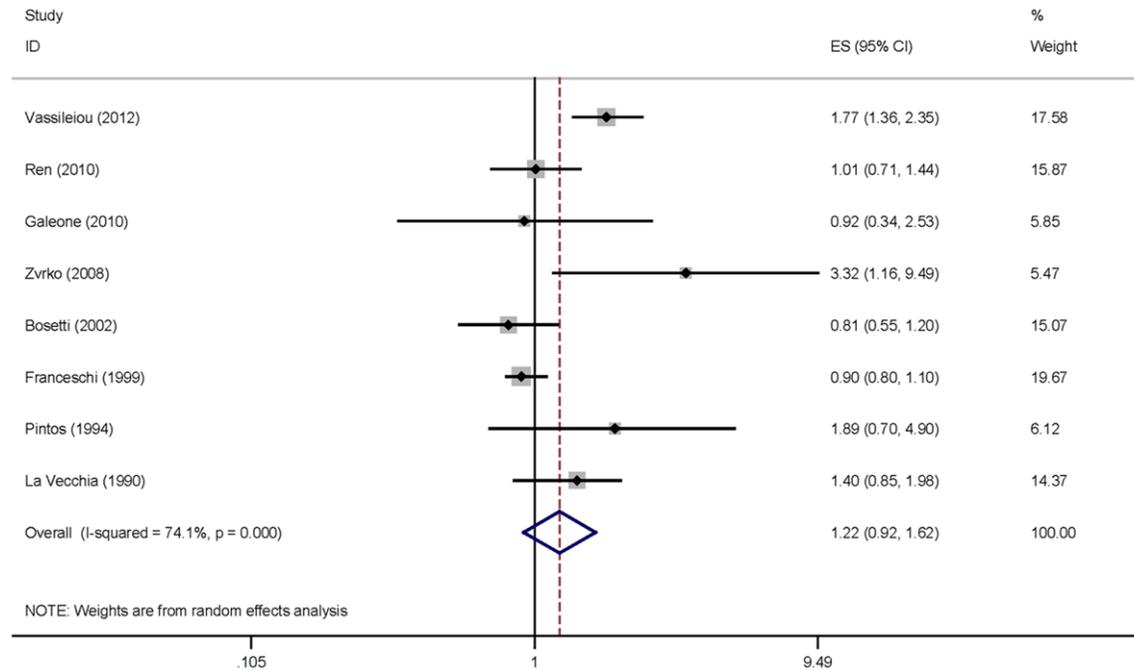


Figure 3. The forest plot between highest versus lowest categories of coffee consumption and laryngeal cancer risk.

To our best knowledge, this is the first meta-analysis investigating the relationship between tea consumption and risk of laryngeal cancer. A comprehensive literature search and advanced detailed consulting the relevant references was conducted to make sure all the potential logical articles included. In this current meta-analysis, the results of the sensitivity analyses suggest that the conclusions of this study were quite robust. The stratified analyses provided abundant knowledge. Despite these strengths mentioned above, some limitations of the current meta-analysis should be noted. Firstly, only 11 articles were included in this meta-analysis and the relative small sample size would make the conclusion unstable. We have tried our best to access all the possible studies. In the quantitative synthesis, the random-effect model might provide a more conservative conclusion. Secondly, the most of our studies followed a case-control study design, and therefore there were recall and selection bias which are inherent to retrospective studies. More relevant cohort studies are required in the future.

In summary, results from this meta-analysis suggested that tea and coffee consumption weren't associated with the risk of laryngeal cancer. Since the potential biases and confounders could not be ruled out completely in

this meta-analysis, further studies are warranted to confirm this result.

Disclosure of conflict of interest

None.

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