Original Article

Coffee consumption and risk of gastric cancer: an updated meta-analysis

Yan Xie MD[1], Shifeng Huang PhD, MD[1], Tongchuan He PhD, MD[2], Yuxi Su PhD, MD[2]

[1]Department of Laboratory Medicine, Chongqing Key Laboratory of Pediatrics, Ministry of Education Key Laboratory of Child Development and Disorders, the Children's Hospital of Chongqing Medical University, Lab medicine of Yubei Maternity and Children Care Hospital, China International Science and Technology Cooperation base of Child development and Critical Disorders, Chongqing, China
[2]Department II of Orthopaedics, Stem Cell Biology and Therapy Laboratory, Chongqing Key Laboratory of Pediatrics, Ministry of Education Key Laboratory of Child Development and Disorders, China International Science and Technology Cooperation base of Child development and Critical Disorders, the Children's Hospital of Chongqing Medical University, Chongqing, China

Background and Objectives: Coffee is one of the most widely consumed beverages worldwide, and many studies have investigated the association between coffee consumption and gastric cancer. However, the results are inconsistent. We conducted a systematic analysis of relevant population studies to derive a more precise estimation. **Methods and Study Design**: Cochrane library, PubMed and Embase databases were searched to identify studies that met predetermined inclusion criterion through July 2014. All epidemiologic studies regarding coffee consumption and gastric cancer risk were selected, and relative risks (RRs) with 95% confidence intervals (CIs) were calculated. **Results:** Twenty two studies (9 cohort and 13 case-control studies) involving 7,631 cases and 1,019,693 controls were included. The summary RR of gastric cancer was 0.94 (95% CI: 0.80-1.10) for the highest category of coffee consumption compared with the lowest category, and 0.93 (95% CI: 0.88-0.99) for coffee drinkers compared with nondrinkers. We stratified the population by coffee consumption. The pooled RR for the population with <1 cup/day, 1-2 cups/day and 3-4 cups/day coffee consumption compared with nondrinkers were 0.95 (95% CI: 0.84-1.08), 0.92 (95% CI: 0.82-1.03) and 0.88 (95% CI: 0.76-1.02), respectively, indicating that an increase in coffee consumption was associated with a decreased risk of gastric cancer. Furthermore, we stratified the studies by design, sex, population and time. A significant association between coffee intake and decreased gastric cancer risk was shown in case-control studies (RR=0.85, 95% CI: 0.77-0.95) and among the studies published over the last ten years (RR=0.88, 95% CI: 0.77-1.00). **Conclusions**: Our meta-analysis suggested that coffee consumption might be associated with a decreased risk of gastric cancer.

Key Words: coffee, gastric cancer, meta-analysis, epidemiologic study, risk factor

INTRODUCTION

Gastric cancer is a commonly diagnosed cancer and is the third-leading and fifth-leading causes of cancer-related deaths in men and women worldwide, respectively.[1] As reported by WHO, the steadily increasing proportion of elderly people in the world will result in an approximately 50% increase in new cancer cases over the next 20 years. Previous reports have suggested that approximately one-third of these common cancers, including lung cancer, breast cancer, liver cancer and gastric cancer, could be prevented.[2,3] Epidemiological studies and systematic analysis showed the intimate association between diet and the risk of gastric cancer. The incidence of gastric cancer is especially high in East Asian populations due in part to a high prevalence of *Helicobacter pylori* (*H. pylori*) infection, and diets rich in salt, rice and fermented foods.[4,5] In contrast, some foods, such as fruits and vegetables, may be associated with a reduced risk of gastric cancer. Consequently, the identification of modifiable risk factors, particularly in the diet, for gastric cancer is of importance because it may lead to potential prevention opportunities.

Coffee is one of the most widely consumed beverages in the world. Because of its popularity, even small potentially unhealthy or beneficial properties could have important public health consequences. Coffee has been reported to contain more than a thousand different chemical compounds. It contains complex mixtures of biochemically active components that have been hypothesized to impact the etiology of certain diseases ranging from carcinogenesis and cancer progression to cellular apoptosis, oxidative stress and inflammatory diseases.[6-8] These constituents, such as the palmitates, kahweol and cafestol,

Corresponding Author: Dr Yuxi Su, Yuzhong District Zhongshan 2 road 136#, Chongqing, 400014, China.
Tel: +862363632064; Fax: +862363632064
Email: yuxisu@163.com
Manuscript received 18 March 2015. Initial review completed 14 April 2015. Revision accepted 26 May 2015.
doi: 10.6133/apjcn.092015.07

have been assumed to be anti-mutagenic and antioxidant, resulting in the inhibition of cancer-promoting processes.[9,10] Thus, it is important to elucidate the association between coffee consumption and cancer risk. In fact, many epidemiological studies have been performed to explore the relationship of coffee consumption and many cancer types, including gastric cancer. However, epidemiological studies have reported inconsistent findings for coffee consumption and gastric cancer risk. To derive a more precise estimation of this relationship, we performed a meta-analysis to summarize the available evidence from prospective and case-control studies.

METHORDS

Literature search

We conducted a systematic search of the literature published from 1980 to July 1st 2014 using the Cochrane, PubMed and Embase databases. The following search terms were used: "coffee", "beverages", "diet", "lifestyle" and "gastric cancer". We also performed a manual search via reference lists. Only full-length journal articles with a prospective cohort or case-control study design were considered.

Study selection

Articles were eligible for our meta-analysis if they conformed to the following criteria: (i) the study design is a cohort or case-control study; (ii) a relatively complete assessment of coffee intake was performed; (iii) the association of coffee intake with gastric cancer risk was specifically evaluated; (iv) the relative risk (RR), hazard ratio (HR), or odds ratio (OR), and corresponding 95% confidence interval (95% CI) values were available; and (v) the study adjusted for potential confounders of cancer, at least age. When duplicate reports from the same study were identified, we chose the most recent one.

Data extraction

The data from each paper fulfilling the inclusion criteria were extracted carefully by two independent reviewers. The following information from each study was recorded: (i) the first author's name, publication year and country of origin; (ii) study design (cohort study, population-based case-control study or hospital-based case-control study); (iii) study population (numbers of cases and controls); (iv) coffee consumption; (v) RR, HR or OR values from the most fully adjusted model for the highest versus the lowest coffee intake and their 95% CI; and (vi) the listed confounders adjusted for in the multivariate analysis.

Quality score assessment

The methodological quality of the included studies in the present meta-analysis was assessed by two reviewers independently according to the nine-star Newcastle-Ottawa Scale (NOS). Because no standard criteria have been established for a high-quality study, we considered a case-control study score at least 6 stars and a cohort study score at least 8 stars to be high quality.

Statistical analysis

The summary RRs and corresponding 95% CIs of the included studies were used as a measure to assess the association of coffee consumption with gastric cancer risk. As described previously,[3] the homogeneity of the effect size across studies was tested by the Q statistics (p<0.10). We also computed the I^2, which is a quantitative measure of inconsistency across studies. If substantial heterogeneity exists, the random-effects model is appropriate; otherwise, the fixed-effects model is preferred. A sensitivity analysis was conducted using both fixed- and random-effects models to evaluate the robustness of the results. The potential publication bias was examined by the funnel plot and Egger's test (p<0.10). All of the analyses were performed using STATA version 11.0 (Stata Corp, College Station, TX, USA). A p value <0.05 was considered to be statistically significant unless otherwise specified.

The ethics committee of Chongqing Medical University approved the study (CQMU-201501036).

RESULTS

Characteristics of the included studies

The systematic search of the literature identified a total of 92 studies. After excluding 54 irrelevant titles and/or abstracts, the remaining 38 full-text articles were reviewed for a more detailed evaluation. Among those articles, 16 were excluded as irrelevant or because they did not meet the inclusion criteria. Finally, 22 studies relevant to the role of coffee intake and the risk of gastric cancer were included in the present meta-analysis.[11-32]

The characteristics of these studies are presented in Table 1. The studies included in the final analysis included 7,631 cases and 1,019,693 controls. The selected studies were published between 1990 and 2014, which is a period that spans 25 years, and all of them were published in English. Among these 22 studies, 9 were prospective cohort studies, 6 were population-based case-control studies, and 7 were hospital-based case-control studies. Of the included studies, 7 were conducted in East Asian (4 in Japan, 2 in China, and 1 in Singapore), 5 were conducted in Northern Europe (3 in Sweden, 1 in Norway and 1 in Finland), 5 were conducted in other areas of Europe (1 in Italy, 1 in Spain, 2 in Turkey, and 1 in Poland), 3 were conducted in America (1 in Uruguay, 1 in USA and 1 in Venezuela), 1 was conducted in India, and 1 investigated Japanese in Hawaii. 1 study only adjusted for age, 3 studies adjusted for both age and sex, and the other 18 studies adjusted for a wide range of potential confounders of gastric cancer, such as age, body mass index, smoking, alcohol, education, residence, socio-economic status, and intake of fruit, vegetables, rice and fish.

Coffee consumption and gastric cancer risk

We calculated the summary RR values using fixed- or random-effects models depending on the heterogeneities. As shown in Figure 1A, the pooled RR of gastric cancer from the combination of included studies was 0.94 (95% CI: 0.80-1.10) for the highest category of coffee consumption compared with the lowest category. Substantial heterogeneity existed across these studies. The summary RR of gastric cancer was 0.93 (95% CI: 0.88-0.99) for coffee drinkers compared with nondrinkers (Figure 1B), and no significant heterogeneity was observed, indicating that the risk of gastric cancer decreased in coffee drinkers.

Table 1. Characteristics of the included studies

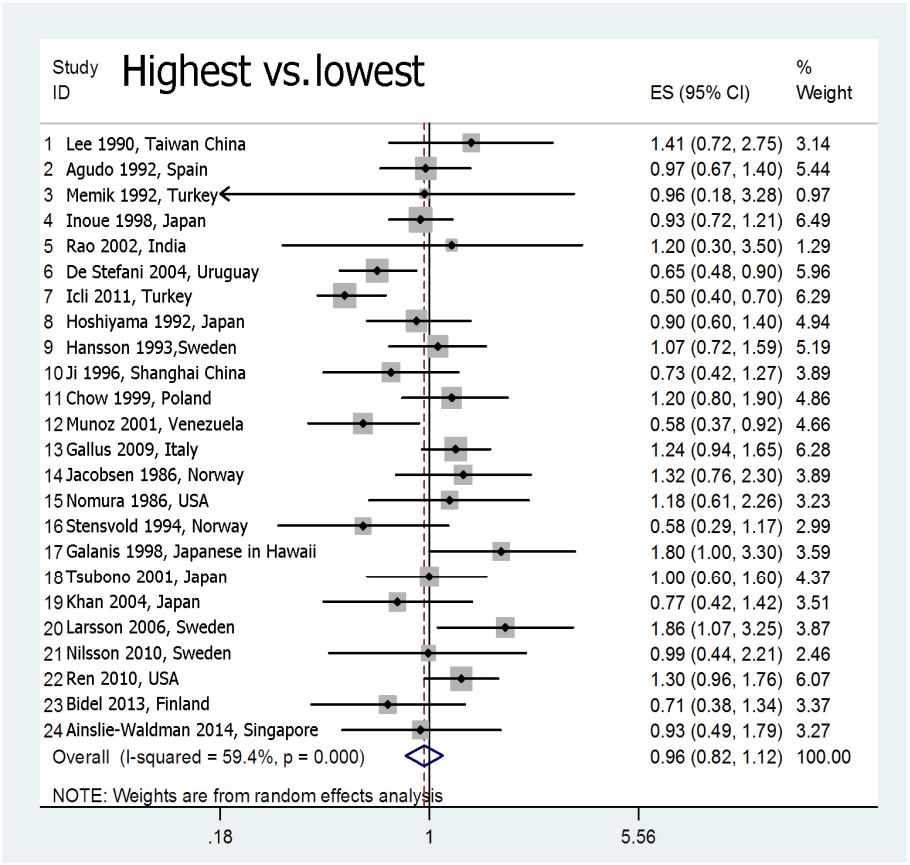
Author, year and region	Study design	Cases/ controls	Coffee consumption	OR or RR (95% CI)			Adjustments
				Overall	Men	Women	
La Vecchia 1989, Italy	Hospital-based case-control	397/1944	≥4 cups/d vs non-drinker	0.73 (0.49-1.09)	0.80 (0.49-1.32)	0.61 (0.30-1.21)	Age, sex, social class, education, marital status, smoking, alcohol intake.
Lee 1990, Taiwan	Hospital-based case-control	210/810	Drinker vs non-drinker	1.41 (0.72-2.75)			Age and sex.
Agudo 1992, Spain	Hospital-based case-control	228/227	Drinker vs non-drinker	0.97 (0.67-1.40)	0.93 (0.60-1.44)	1.06 (0.53-2.11)	Age, sex, area of residence, total calories, fruits, vegetables, preserved fish, et al.
Memik 1992, Turkey	Case-control	79/608	2～3 cups/d vs ≤1 cup/d	0.96 (0.18-3.28)			Age
Inoue 1998, Japan	Hospital-based case-control	893/21128	≥3 cups/d vs rarely	0.93 (0.72-1.21)			Age, sex, smoking, alcohol intake, tea, rice, fruit, beef.
Rao 2002, India	Hospital-based case-control	119/1577	Daily vs never/rarely	1.2 (0.3-3.5)			Age, sex.
De Stefani 2004, Uruguay	Hospital-based case-control	240/960	Tertiles	0.65 (0.48-0.90)	0.55 (0.38-0.82)	0.95 (0.54-1.67)	Age, smoking, alcohol intake, total energy intake, residence, education, BMI.
Icli 2011, Turkey	Hospital-based case-control	253/253	≥1 cups/d vs none	0.5 (0.4-0.7)			Income, bread consumption, smoking, cooking oil, fish.
Hoshiyama 1992, Japan	Population-based case-control	251/483	≥10 cups/w vs ≤1 cup/w	0.9 (0.6-1.4)			Age, smoking, dietary items including salty foods, fruits, vegetables, seaweed, boiled fish, et al.
Hansson 1993, Sweden	Population-based case-control	338/669	≥3100 ml/w vs none	1.07 (0.72-1.59)			Age, sex, socio-economic status (SES), fruits, vegetables, et al.
Ji 1996, Shanghai, China	Population-based case-control	1123/1249	Drinker vs non-drinker	0.73 (0.42-1.27)			Age, sex.
Chow 1999, Poland	Population-based case-control	476/480	≥7 cups/w vs none	1.23 (0.80-1.89)	1.4 (0.8-2.4)	1.0 (0.5-2.0)	Age, smoking, education, family history of cancer.
Munoz 2001, Venezuela	Population-based case-control	292/485	Quartiles	0.58 (0.37-0.92)			Age, sex, smoking, alcohol intake, total energy intake, SES.
Gallus 2009, Italy	Population-based case-control	769/2081	≥4 cups/d vs none	1.24 (0.94-1.65)			Age, sex, education, BMI, residence, smoking, alcohol, fruits, vegetables.
Stensvold 1994, Norway	Cohort	151(42973)	≥7 cups/d vs ≤2 cup/d	0.58 (0.29-1.17)	0.68 (0.28-1.69)	0.47 (0.16-1.39)	Age, smoking, residence.
Galanis 1998, Japanese in Hawaii	Cohort	108(11907)	≥2 cups/d vs none	1.8 (1.0-3.3)	2.2 (0.9-5.3)	1.6 (0.7-3.8)	Age, education, place of birth, smoking, alcohol.
Tsubono 2001, Japan	Cohort	419(199748)	≥3 cups/d vs none	1.0 (0.6-1.6)			Age, sex, tea, smoking, alcohol, rice, meat, vegetables, fruits, soup, et al.

BMI: body mass index; 95% CI: 95% confidence intervals; SES: socio-economic status.

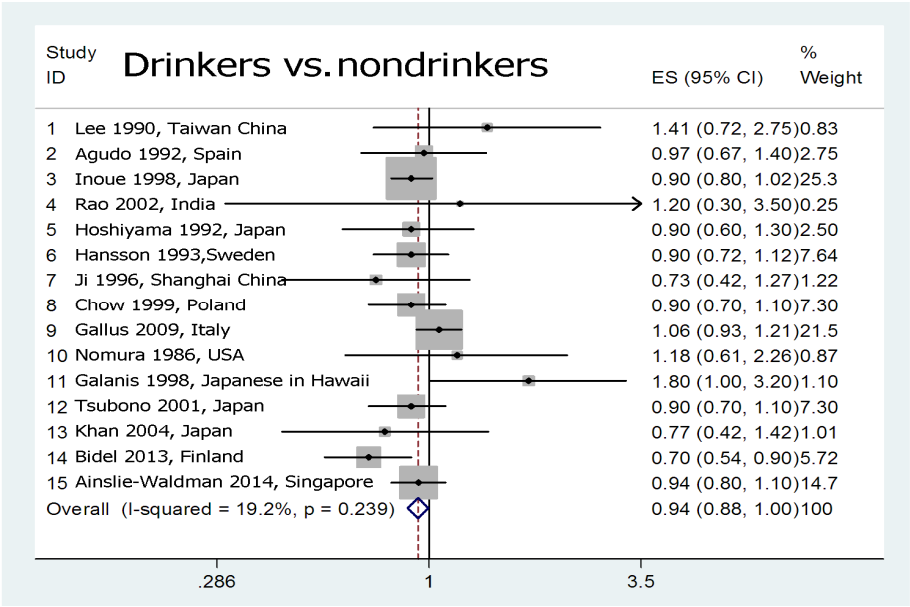
Table 1. Characteristics of the included studies (cont.)

Author, year and region	Study design	Cases/ controls	Coffee consumption	OR or RR (95% CI)			Adjustments
				Overall	Men	Women	
Khan 2004, Japan	Cohort	51 (3158)	≥several times/w vs ≤several times/m	0.77 (0.42-1.42)	1.0 (0.5-2.0)	0.3 (0.1-1.4)	Age, health status, health education, smoking.
Larsson 2006, Sweden	Cohort	160 (61433)	≥4 cups/d vs ≤1 cups/d			1.86 (1.07-3.25)	Age, time period, education, alcohol, tea consumption.
Bidel 2013, Finland	Cohort	299 (60041)	≥10 cups/d vs none	0.75 (0.40-1.41)	0.53 (0.26-1.09)	2.07 (0.53-8.15)	Age, study year, education, smoking, alcohol, physical activity, diabetes, tea, BMI.
Ainslie-Waldman 2014, Singapore	Cohort	647 (63257)	daily vs nondaily	0.54 (0.31-0.91)	0.84 (0.43-1.65)	0.22 (0.08-0.56)	Age, sex, interview year, education, smoking, BMI, caffeine, total energy intake.

BMI: body mass index; 95% CI: 95% confidence intervals; SES: socio-economic status.



(A)

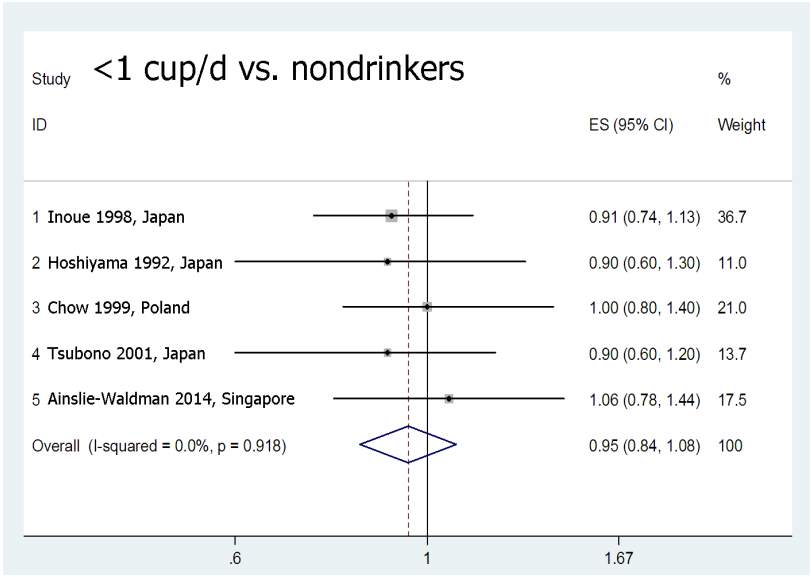


(B)

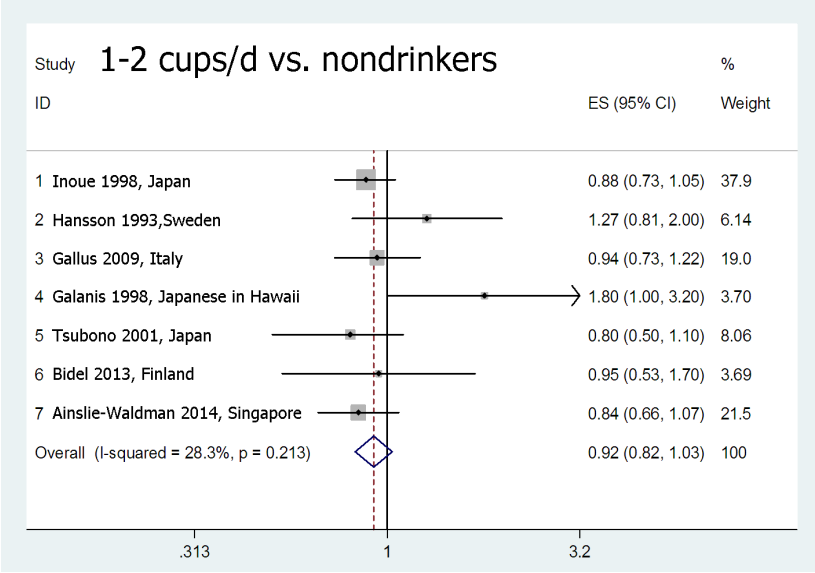
Figure 1. Meta-analysis of studies examining association between coffee consumption and the risk of gastric cancer. (A) The highest level of coffee consumption in each included study versus the lowest level of intake. (B) Coffee drinkers versus nondrinkers. Coffee consumption ≤1 cup/week was also defined as nondrinkers.

We stratified the population by coffee consumption and calculated the summary RR. As shown in Figure 2A, B, C, the pooled RR of gastric cancer for the population with <1 cup/day, 1-2 cups/day and 3-4 cups/day coffee consumption compared with nondrinkers were 0.95 (95% CI: 0.84-1.08), 0.92 (95% CI: 0.82-1.03) and 0.88 (95% CI: 0.76-1.02), respectively. No significant heterogeneities were observed in these studies. The data suggested that an increase in coffee consumption was associated with a decreased risk of gastric cancer.

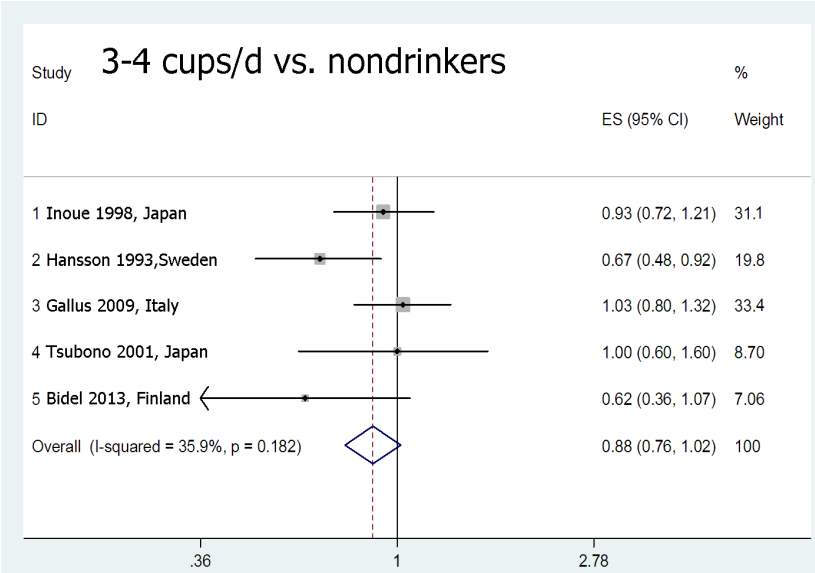
We then stratified the included studies by design, sex, population and time. As shown in Table 2, the RR of gastric cancer was 0.85 (95% CI: 0.77-0.95) for case-control studies and 1.12 (95% CI: 0.94-1.33) for cohort studies. The data of case-control studies indicated a significant protective relationship between coffee consumption and gastric cancer; however substantial heterogeneity existed across these studies. Next, the RR of gastric cancer was 0.85 (95% CI: 0.69-1.04) in men and 1.12 (95% CI: 0.94-1.33) in women, 0.93 (95% CI: 0.79-1.10) in Asian populations and 0.91 (95% CI: 0.80-1.05) in European populations. Last, when the various studies were stratified by



(A)



(B)



(C)

Figure 2. Forest plots of investigating association for various categories of coffee consumption with gastric cancer risk. (A) <1 cup/day coffee consumption versus nondrinkers. (B) 1-2 cups/day coffee consumption versus nondrinkers. (C) 3-4 cups/day coffee consumption versus nondrinkers.

time, a borderline significant association between coffee intake and decreased gastric cancer risk was shown among the studies published over the last ten years (RR=0.88, 95% CI: 0.77-1.00).

Publication bias

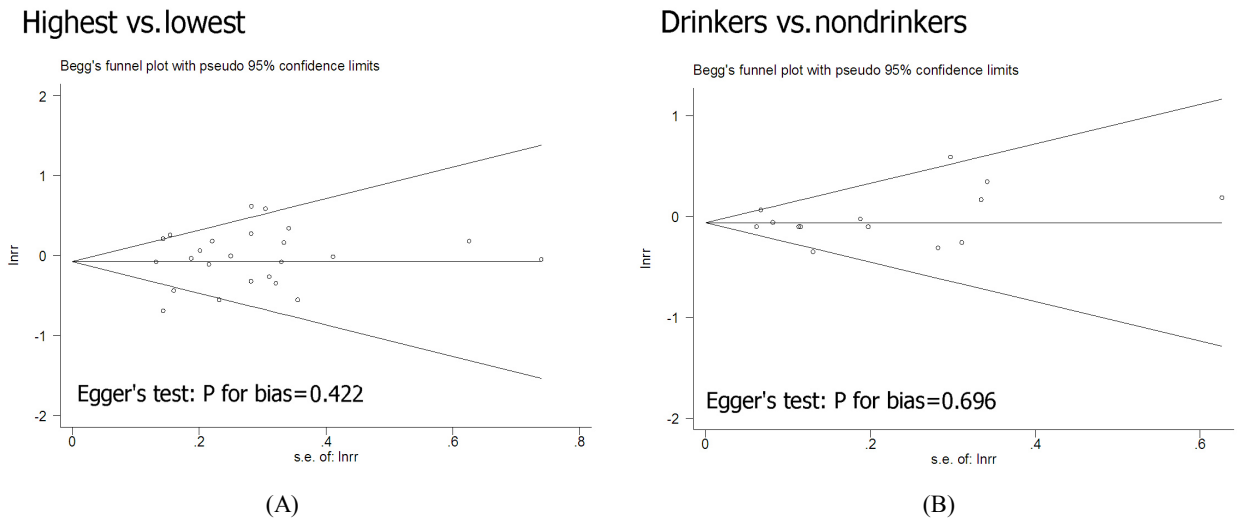
Begg's funnel plots and Egger's tests were performed to assess the publication bias in these studies. As shown in Figure 3A, B, the shape of the funnel plot did not reveal any evidence of obvious asymmetry. The Egger's test, which provides statistical evidence of the funnel plot symmetry, indicated little evidence of publication bias. No significant publication bias was found in these studies.

DISCTUSSION

Coffee is a popular beverage worldwide, and its potentially unhealthy and beneficial bioactivities have been extensively investigated in epidemiological and experimental studies. However, the role of coffee consumption in the development of various types of cancer remains unclear. A previous meta-analysis regarding coffee consumption and risk of gastric cancer, which was conducted by Botelho et al in 2006,[33] found no significant association. In the older meta-analysis, the pooled OR for the overall association between coffee intake and gastric cancer risk (highest vs lowest category of exposure) was 0.97 (95% CI: 0.86-1.09), which is similar to that found in cohort (OR=1.02; 95% CI: 0.76-1.37) and case-control studies (population-based: OR=0.90; 95% CI: 0.70-1.15; hospital-based: OR=0.97; 95% CI: 0.83-1.13). In the present meta-analysis, the pooled RR of gastric cancer was 0.94 (95% CI: 0.80-1.10) for the highest category of coffee consumption compared with the lowest category, indicating no significant association either. However, the summary RR was 0.93 (95% CI: 0.88-0.99) for coffee drinkers compared with nondrinkers, and no significant heterogeneity was observed. Moreover, when we stratified the population by coffee consumption, the pooled RR for the population with <1 cup/day, 1-2 cups/day and 3-4 cups/day coffee consumption compared with nondrinkers were 0.95 (95% CI: 0.84-1.08), 0.92 (95% CI: 0.82-1.03) and 0.88 (95% CI: 0.76-1.02), respectively. The data sug-

Table 2. Summary risk estimates for coffee consumption and gastric cancer risk.

Study	No. of studies	RR (95% CI)	Heterogeneity test	
			p value	I^2 (%)
Design				
Hospital-based case-control	8	0.75 (0.66-0.86)	0.015	59.9
Population-based case-control	6	1.00 (0.85-1.18)	0.069	51.1
Cohort	6	0.84 (0.66-1.07)	0.059	52.9
Gender				
Men	9	0.83 (0.69-1.00)	0.064	45.9
Women	10	0.86 (0.57-1.29)	0.006	61.3
Population				
Europe	9	0.86 (0.75-0.98)	0.001	70.6
Asian	8	0.88 (0.75-1.04)	0.497	0.0
Others	3	0.84 (0.47-1.51)	0.006	80.5
Time				
Before 1994	6	0.94 (0.78-1.14)	0.796	0.0
1994-2003	8	0.92 (0.79-1.09)	0.123	35.6
2004-2014	6	0.71 (0.51-0.99)	<0.001	74.4



(A) (B)

Figure 3. Funnel plot of coffee consumption and the risk of gastric cancer.

gested that an increase in coffee consumption was associated with a decreased risk of gastric cancer. Additionally, when the various studies were stratified by time, a borderline significant association between coffee intake and decreased gastric cancer risk was shown among the studies published over the last ten years (RR=0.88, 95% CI: 0.77-1.00). Our study provided an updated result on the topic of the relationship between coffee consumption and gastric cancer.

Coffee is a complex beverage composed of many bioactive compounds that have been found to exert many physiological effects. Caffeine, an important component of coffee, has potent antioxidant activities and the capabilities to inhibit oxidative DNA damage, modulate the apoptotic response and regulate the cell-cycle checkpoint function.[34-36] In addition, the coffee components cafestol and kahweol are two specific diterpenes that have been shown to have a broad range of bioactive properties resulting in a reduction in carcinogen-induced genotoxicity.[37] Coffee is also a major source of dietary chlorogenic acid, which has been carefully studied and has been shown to have chemopreventive properties against environmental carcinogenesis.[38] In fact, in several recent updated meta-analyses, coffee consumption has been reported to be associated with a reduction in the risk of various types of cancer, including prostate cancer, bladder cancer, colorectal cancer and liver cancer.[39-42] However, it is worthwhile to note that substantial heterogeneity often existed across these studies regarding coffee consumption and cancer risk. In a Swedish cohort of women, a positive association with gastric cancer risk was found for an increase of 1 cup per day (HR=1.22; 95% CI, 1.05-1.42).[28] After adjusting for smoking status, the association remained but lost statistical significance. In contrast, a recent Singapore cohort study showed that the daily versus nondaily coffee intake was associated with a statistically nonsignificant decrease in gastric cancer risk (HR=0.85; 95% CI: 0.69-1.04).[32] In women, the inverse association was strengthened and reached statistical significance (HR=0.63; 95% CI: 0.46-0.87). In the analyses restricted to individuals who had never smoked and nondrinkers of alcohol, the inverse associations were strengthened in the total cohort (HR=0.69; 95% CI: 0.52-0.91) and in women (HR=0.52; 95% CI: 0.37-0.74).

The heterogeneity among these studies may be partially attributed to misclassification of coffee intake. The coffee type, serving size, brewing method, and cup size could vary considerably across different studies depending on the population and region. The chemical components of different types of coffee can obviously vary according to different serving sizes or brewing methods. Consequently, differential misclassification of coffee intake can bias the data and the results. Furthermore, the effects of coffee content on carcinogenesis may be exerted by the combination of a variety of biological activities and could be affected by some established risk factors for cancer, such as smoking, alcohol, energy intake, fruit, and salt. Although many of the individual studies included in this meta-analysis adjusted for important confounders for gastric cancer, unmeasured variables may have biased the results. Therefore, more carefully designed studies are warranted to confirm the potential protective association of coffee consumption with gastric cancer.

Conclusion

The present meta-analysis suggests that the gastric cancer risk significantly decreases in coffee drinkers, and an increase in coffee consumption is associated with a decreased risk of gastric cancer. Certainly, these findings should be treated with caution, and more carefully designed population studies are necessary to assess the potential protective association of coffee consumption with gastric cancer.

ACKNOWLEDGEMENT

This work was supported by the research grant from National Natural Science Foundation of China (81001197, Su YX, http://isisn.nsfc.gov.cn/egrantindex/funcindex/prjsearch-list) and National Key Specialty Construction of Clinical Project (#2013-544). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

AUTHOR DISCLOSURES

The authors declare that they have no conflict of interest.

REFERENCES

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61:69-90. doi: 10.3322/caac.20107.
2. Raman M, Ambalam P, Kondepudi KK, Pithva S, Kothari C, Patel AT, Purama RK, Dave JM, Vyas BR. Potential of probiotics, prebiotics and synbiotics for management of colorectal cancer. Gut Microbes. 2013;4:181-92. doi: 10.4161/gmic.23919.
3. Hui C, Qi X, Qianyong Z, Xiaoli P, Jundong Z, Mantian M. Flavonoids, flavonoid subclasses and breast cancer risk: a meta-analysis of epidemiologic studies. PLoS One. 2013;8:e54318. doi: 10.1371/journal.pone.0054318.
4. Aziz F, Chen X, Yang X, Yan Q. Prevalence and correlation with clinical diseases of Helicobacter pylori cagA and vacA genotype among gastric patients from Northeast China. Biomed Res Int. 2014;2014:142980. doi: 10.1155/2014/142980.
5. Xu HY, Xu WL, Wang LQ, Chen MB, Shen HL. Relationship between p53 status and response to chemotherapy in patients with gastric cancer: a meta-analysis. PLoS One. 2014;9:e95371. doi: 10.1371/journal.pone.0095371.
6. Sapozhnikova Y. Development of liquid chromatography-tandem mass spectrometry method for analysis of polyphenolic compounds in liquid samples of grape juice, green tea and coffee. Food Chem. 2014;150:87-93. doi: 10.1016/j.foodchem.2013.10.131.
7. Bakuradze T, Lang R, Hofmann T, Stiebitz H, Bytof G, Lantz I, Baum M, Eisenbrand G, Janzowski C. Antioxidant effectiveness of coffee extracts and selected constituents in cell-free systems and human colon cell lines. Mol Nutr Food Res. 2010;54:1734-43. doi: 10.1002/mnfr.201000147.
8. Glei M, Kirmse A, Habermann N, Persin C, Pool-Zobel BL. Bread enriched with green coffee extract has chemoprotective and antigenotoxic activities in human cells. Nutr Cancer. 2006;56:182-92. doi: 10.1207/s15327914nc5602_9.
9. Ludwig IA, Clifford MN, Lean ME, Ashihara H, Crozier A. Coffee: biochemistry and potential impact on health. Food Funct. 2014;5:1695-717. doi: 10.1039/C4FO00042K.
10. Dias RC, Campanha FG, Vieira LG, Ferreira LP, Pot D, Marraccini P, De Toledo Benassi M. Evaluation of kahweol

and cafestol in coffee tissues and roasted coffee by a new high-performance liquid chromatography methodology. J Agric Food Chem. 2010;58:88-93. doi: 10.1021/jf9027427.
11. Lee HH, Wu HY, Chuang YC, Chang AS, Chao HH, Chen KY, Chen HK, Lai GM, Huang HH, Chen CJ. Epidemiologic characteristics and multiple risk factors of stomach cancer in Taiwan. Anticancer Res. 1990;10:875-81
12. Agudo A, González CA, Marcos G, Sanz M, Saigi E, Verge J, Boleda M, Ortego J. Consumption of alcohol, coffee, and tobacco, and gastric cancer in Spain. Cancer Causes Control. 1992;3:137-43. doi: 10.1007/BF00051653.
13. Memik F, Nak SG, Gulten M, Ozturk M. Gastric carcinoma in northwestern Turkey: epidemiologic characteristics. J Environ Pathol Toxicol Oncol. 1992;11:335-8.
14. Inoue M, Tajima K, Hirose K, Hamajima N, Takezaki T, Kuroishi T, Tominaga S. Tea and coffee consumption and the risk of digestive tract cancers: data from a comparative case-referent study in Japan. Cancer Causes Control. 1998;9: 209-16.
15. Rao DN, Ganesh B, Dinshaw KA, Mohandas KM. A case-control study of stomach cancer in Mumbai, India. Int J Cancer. 2002;99:727-31. doi: 10.1002/ijc.10339.
16. De Stefani 2004 Uruguay De Stefani E, Correa P, Boffetta P, Deneo-Pellegrini H, Ronco AL, Mendilaharsu M. Dietary patterns and risk of gastric cancer: a case-control study in Uruguay. Gastric Cancer. 2004;7:211-20. doi: 10.1007/s10 120-004-0295-2.
17. Icli F, Akbulut H, Yalcin B, Ozdemir F, Isıkdogan A, Hayran M, Unsal D, Coskun S, Buyukcelik A, Yamac D. Education, economic status and other risk factors in gastric cancer: "a case-control study of Turkish Oncology Group". Med Oncol. 2011;28:112-20. doi: 10.1007/s12032-009-9406-6.
18. Hoshiyama Y, Sasaba T. A case-control study of single and multiple stomach cancers in Saitama prefecture, Japan. Jpn J Cancer Res. 1992;83:937-43. doi: 10.1111/j.1349-7006.1992. tb02004.x.
19. Hansson LE, Nyrén O, Bergström R, Wolk A, Lindgren A, Baron J, Adami HO. Diet and risk of gastric cancer. A population-based case-control study in Sweden. Int J Cancer. 1993;55:181-9.
20. Ji B, Chow W, Yang G, McLaughlin J, Gao R, Zheng W, Shu XO, Jin F, Fraumeni JF Jr, Gao YT. The influence of cigarette smoking, alcohol, and green tea consumption on the risk of carcinoma of the cardia and distal stomach in Shanghai, China. Cancer. 1996;77:2449-56. doi: 10.1002/(SICI)1097-0142(19960615)77:12<2449::AID-CNCR6>3.3.CO;2-X.
21. Chow WH, Swanson CA, Lissowska J, Groves FD, Sobin LH, Nasierowska-Guttmejer A et al. Risk of stomach cancer in relation to consumption of cigarettes, alcohol, tea and coffee in Warsaw, Poland. Int J Cancer. 1999;81:871-6. doi: 10.1002/(SICI)1097-0215(19990611)81:6<871::AID-IJC6>3.3.CO;2-R.
22. Munoz N, Plummer M, Vivas J, Moreno V, De Sanjose S, Lopez G, Oliver W. A case-control study of gastric cancer in Venezuela. Int J Cancer. 2001;93:417-23. doi: 10.1002/ijc.1333.
23. Gallus S, Tramacere I, Tavani A, Bosetti C, Bertuccio P, Negri E, La Vecchia C. Coffee, black tea and risk of gastric cancer. Cancer Causes Control. 2009;20:1303-8. doi: 10.1007/s10552-009-9350-y.
24. Stensvold I, Jacobsen BK. Coffee and cancer: a prospective study of 43,000 Norwegian men and women. Cancer Causes Control. 1994;5:401-8. doi: 10.1007/BF01694753.
25. Galanis DJ, Kolonel LN, Lee J, Nomura A. Intakes of selected foods and beverages and the incidence of gastric cancer among the Japanese residents of Hawaii: a prospective study. Int J Epidemiol. 1998;27:173-80. doi: 10.1093/ije/27.2.173.
26. Tsubono Y, Nishino Y, Komatsu S, Hsieh C, Kanemura S, Tsuji I, Nakatsuka H, Fukao A, Satoh H, Hisamichi S. Green tea and the risk of gastric cancer in Japan. N Engl J Med. 2001;344:632-6. doi: 10.1056/NEJM200103013440903.
27. Khan MMH, Goto R, Kobayashi K, Suzumura S, Nagata Y, Sonoda T, Sakauchi F, Washio M, Mori M. Dietary habits and cancer mortality among middle aged and older Japanese living in Hokkaido, Japan by cancer site and sex. Asian Pacific J Cancer Prev. 2004;5:58-65.
28. Larsson SC, Giovannucci E, Wolk A. Coffee consumption and stomach cancer risk in a cohort of Swedish women. Int J Cancer. 2006;119:2186-9. doi: 10.1002/ijc.22105.
29. Nilsson LM, Johansson I, Lenner P, Lindahl B, Van Guelpen B. Consumption of filtered and boiled coffee and the risk of incident cancer: a prospective cohort study. Cancer Causes Control. 2010;21:1533-44. doi: 10.1007/s10552-010-9582-x.
30. Ren JS, Freedman ND, Kamangar F, Dawsey SM, Hollenbeck AR, Schatzkin A, Abnet CC. Tea, coffee, carbonated soft drinks and upper gastrointestinal tract cancer risk in a large United States prospective cohort study. Eur J Cancer. 2010;46:1873-81. doi: 10.1016/j.ejca.2010.03.025.
31. Bidel S, Hu G, Jousilahti P, Pukkala E, Hakulinen T, Tuomilehto J. Coffee consumption and risk of gastric and pancreatic cancer--a prospective cohort study. Int J Cancer. 2013;132:1651-9. doi: 10.1002/ijc.27773.
32. Ainslie-Waldman CE, Koh WP, Jin A, Yeoh KG, Zhu F, Wang R, Yuan JM, Butler LM. Coffee intake and gastric cancer risk: the Singapore Chinese health study. Cancer Epidemiol Biomarkers Prev. 2014;23:638-47. doi: 10.1158/1055-9965.EPI-13-0886.
33. Botelho F, Lunet N, Barros H. Coffee and gastric cancer: systematic review and meta-analysis. Cad Saude Publica. 2006;22:889-900. doi: 10.1590/S0102-311X2006000500002.
34. Banerjee S, Chaudhuri S, Maity AK, Saha P, Pal SK. Role of caffeine in DNA recognition of a potential food-carcinogen benzo[a]pyrene and UVA induced DNA damage. J Mol Recognit. 2014;27: 510-20. doi: 10.1002/jmr.2379.
35. Ferk F, Huber WW, Grasl-Kraupp B, Speer K, Buchmann S, Bohacek R, Mišík M, Edelbauer L, Knasmüller S. Protective effects of coffee against induction of DNA damage and preneoplastic foci by aflatoxin B. Mol Nutr Food Res. 2014;58: 229-38. doi: 10.1002/mnfr.201300154.
36. Li X, Zhuo R, Tiong S, Di Cara F, King-Jones K, Hughes SC, Campbell SD, Wevrick R. The Smc5/Smc6/MAGE complex confers resistance to caffeine and genotoxic stress in Drosophila melanogaster. PLoS One. 2013;8:e59866. doi: 10.1371/journal.pone.0059866.
37. Cavin C, Holzhaeuser D, Scharf G, Constable A, Huber WW, Schilter B. Cafestol and kahweol, two coffee specific diterpenes with anticarcinogenic activity. Food Chem Toxicol. 2002;40:1155-63. doi: 10.1016/S0278-6915(02)00029-7.
38. Stalmach A, Williamson G, Crozier A. Impact of dose on the bioavailability of coffee chlorogenic acids in humans. Food Funct. 2014;23:1727-37. doi: 10.1039/C4FO00316K.
39. Sang LX, Chang B, Li XH, Jiang M. Consumption of coffee associated with reduced risk of liver cancer: a meta-analysis. BMC Gastroenterol. 2013;25;13:34. doi: 10.1186/1471-230X-13-34.
40. Tian C, Wang W, Hong Z, Zhang X. Coffee consumption and risk of colorectal cancer: a dose-response analysis of observational studies. Cancer Causes Control. 2013;24:1265-8. doi: 10.1007/s10552-013-0200-6.
41. Lu Y, Zhai L, Zeng J, Peng Q, Wang J, Deng Y et al. Coffee consumption and prostate cancer risk: an updated meta-

analysis. Cancer Causes Control. 2014;25:591-604. doi: 10.1007/s10552-014-0364-8.
42. Cao S, Liu L, Yin X, Wang Y, Liu J, Lu Z. Coffee consumption and risk of prostate cancer: a meta-analysis of prospective cohort studies. Carcinogenesis. 2014;35:256-61. doi: 10.1093/carcin/bgt482.

Original Article

Coffee consumption and risk of gastric cancer: an updated meta-analysis

Yan Xie MD[1], Shifeng Huang PhD,MD[1], Tongchuan He PhD,MD[2], Yuxi Su PhD,MD[2]

[1]Department of Laboratory Medicine, Chongqing Key Laboratory of Pediatrics, Ministry of Education Key Laboratory of Child Development and Disorders, the Children's Hospital of Chongqing Medical University, Lab medicine of Yubei Maternity and Children Care Hospital, China International Science and Technology Cooperation base of Child development and Critical Disorders, Chongqing, China
[2]Department II of Orthopaedics, Stem Cell Biology and Therapy Laboratory, Chongqing Key Laboratory of Pediatrics, Ministry of Education Key Laboratory of Child Development and Disorders, China International Science and Technology Cooperation base of Child development and Critical Disorders, the Children's Hospital of Chongqing Medical University, Chongqing, China

咖啡饮用量与胃癌发生风险：一个更新的荟萃分析

背景与目的：咖啡是世界上最为广泛的饮料之一，很多研究发现咖啡的饮用量与胃癌之间存在一定的关系。本研究系统地分析了相关人群的风险以期得到一个较为肯定的结论。**实验方法：**搜索 2014 年 7 月之前数据库 Cochrane library, PubMed and Embase 中符合设定选入标准的相关研究。所有关于咖啡饮用量和胃癌之间关系的流行病学研究均纳入研究，计算其相对危险度的 95%可信区间。**结果：**22 例研究（9 个队列研究，13 个病例对照研究）中，总共有 7,631 位病例，1,019,693 位健康对照。大量与少量咖啡饮用者的胃癌相对危险度是 0.94（95%可信区间为 0.80-1.10），饮用者与非饮用者的胃癌相对危险度是 0.93（95%可信区间为 0.88-0.99）。本研究按咖啡饮用的量分组。每天小于一杯咖啡，1-2 杯咖啡和 3-4 杯咖啡饮用量的人群与不饮咖啡的人群胃癌发生的相对危险度分别是 0.95（95%可信区间为 0.84-1.08），0.92（95%可信区间为 0.82-1.03），0.88（95%可信区间为 0.76-1.02）。这表明随着咖啡饮用量的增加，胃癌的发生率降低。进而，将所有研究按照实验设计、性别、人群、时间分组，在最近 10 年的病例对照研究（相对危险度 0.85，95%可信区间为 0.77-0.95）中，咖啡的饮用量与胃癌的发生呈负相关（相对危险度 0.88，95%可信区间为 0.77-1.00）。**结论：**本 meta 分析的结果提示咖啡的饮用量与胃癌的发生率呈负相关。

关键词：咖啡、胃癌、meta 分析、流行病学研究、危险因素