The relationship between coffee consumption and the risk of gastric cancer; a systematic review and meta-analysis

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Abstract

Introduction: Stomach cancer is among five common malignancies whose prevalence and incidence are considerably associated with our dietary regime. Thus, the present study aims to conduct a systematic review and meta-analysis to evaluate the relationship between coffee drinking, and the risk of stomach cancer.

Materials and Methods: A comprehensive literature search of the databases, including Barakat Knowledge Network System, Cochrane, IranDoc, Web of Science, PubMed, SID, Magiran, Scopus, and Google Scholar web browser was conducted using standard keywords. Data analysis of this meta-analysis was conducted using STATA 14 software and P<0.05 was considered as a significant level for tests.

Results: A total of 24 studies with a sample size of 990605 were reviewed which showed drinking coffee prevents stomach cancer [OR=0.89, (95% CI: 0.82, 0.98)]. However, subgroup analysis by gender found no significant statistical relationship between coffee consumption and stomach cancer risk regarding male or female gender.

Conclusion: Coffee consumption prevents and reduces the risk of developing stomach cancer.

Key point

A total of 24 studies with a sample size of 990605 were reviewed which showed drinking coffee prevents gastric cancer [OR=0.89, (95% CI: 0.82, 0.98)]. However, subgroup analysis by gender found no significant statistical relationship between coffee drinking and gastric cancer risk regarding male or female gender. However, the statistically significant relationship between coffee drinking and gastric cancer risk was assessed in several countries, including Korea, Turkey, Uruguay, Venezuela, and Singapore, with the largest effect being reported in Turkey.
Materials and Methods

Study design
This meta-analysis study examines the association between coffee consumption and gastric cancer risk. The review is carried out based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for systematic review and meta-analysis studies. The protocol of this meta-analysis was registered on the site of PROSPERO (#CRD42022316450).

Studies outcomes
The primary outcome: The association between coffee consumption and gastric cancer.

Search strategy
In this meta-analysis, the Iranian databases, including Barakat Knowledge Network System, SID, Magiran, and IranDoc, along with international databases including Cochrane, Web of Science, PubMed, Scopus, and Google Scholar web browser, were searched without time or language restrictions. For papers published in languages other than Persian or English, the full article was translated to extract its data. The search strategy step was performed by standard keywords and, including “Coffee,” “Cancer,” “Neoplasm,” and “Stomach,” as well as their Persian equivalents (updated until Jan 2, 2022). Keyword combinations using Boolean operators “AND” and “OR” were also included in the database search. Additionally, the list of references of all primary studies that remained at the end of the PRISMA flowchart and entered the meta-analysis were screened by manual search.

The inclusion and exclusion criteria
PICO components
The studied population: Coffee consumers, Intervention: Coffee consumption, Comparison: Those who do not drink coffee, the studied outcomes: The risk of developing gastric cancer.

The inclusion criteria
This meta-analysis included cross-sectional, cohort, and case-control studies that explored the effect of coffee consumption on stomach cancer risk. The intervention group was coffee consumers, and the comparison or control group was the non-intervention status. The eligible studies must have evaluated the relationship between coffee consumption and stomach cancer.

The exclusion criteria
Studies that only qualitatively described the coffee effect on gastric cancer; Low-quality studies evaluated using a quality assessment checklist based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement; case-report or case series studies; lack of reporting of the required information for data analysis; studies that examined the effect of coffee consumption on other cancers such as the esophagus or oral cancers; unavailability of the full-text of articles; and studies that have evaluated the impact of other beverages like green and black tea on gastric cancer.

Qualitative assessment of studies
The two researchers independently assessed quality from different perspectives using the STROBE checklist (11). The STROBE checklist has 22 sections that cover different sections of a report. In this checklist, the sum of the scores is decisive, therefore a score of 1-15 indicates low quality, 16-30 indicates average quality and 31-44 indicates excellent quality. The cut-off point in this study was 15 points.

Data extraction
Two researchers extracted data from studies independently to minimize the biased reporting and error in data collecting. They entered the extracted data into a checklist containing the study title, researcher name, year of publication, sample size, coffee consumption dose and duration, study type, the sizes of case and control groups, the location of study, odds ratio (OR) between coffee consumption and stomach cancer risk and its upper and lower limits. A third researcher evaluated the data extracted by the two previous researchers to correct any existing discrepancies.

Statistical analysis
To examine the relationship between coffee consumption and gastric cancer risk was applied OR. The logarithm of OR was taken in each study to combine the studies’ results. The heterogeneity of the studies was assessed using the I² index and Q-Cochrane test. The random-effects model was used in this work to combine the reviewed studies (I²=53.9%). Data analysis was executed using STATA 14 software. The significance level was considered P<0.05 for all tests. Meta-regression was employed to evaluate the relationship between “coffee consumption and gastric cancer risk” and “sample size” and “year of publication.”

Results
Study selection process
Initially, 415 articles were found in the search in the mentioned databases. After checking the studies’ titles, 195 duplicate studies were excluded. The abstracts of 220 articles were explored, and 51 articles whose full texts were not available were excluded. The full texts of the 169 remaining papers were screened, and another 145 articles that met the other exclusion criteria were discarded. Eventually, 24 high-quality articles entered the meta-analysis process (Figure 1).

The specifications of the reviewed articles are given in Table 1.
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A summary of background information for the reviewed studies
We reviewed a total of 24 articles, including 14 case-control studies, 19 cohorts, and one cross-sectional study published from 1990 to 2021 with a number of samples of 990 605 people (15 865 case and 97 4740 control). The dose and duration of coffee consumption differed in the reviewed studies. However, we could not homogenize them due to the different measurement units used among these studies (Table 1).

Evaluation of the primary outcome
Generally, drinking coffee prevents stomach cancer [0.89 (95% CI : 0.82-0.98)] (Figure 2).

Evaluation of the secondary outcomes
In the subgroup analysis by study type, we observed no statistically significant association between drinking coffee and gastric cancer risk in case-control and cohort studies. However, in the cross-sectional study, drinking coffee significantly reduced the risk of stomach cancer.

In an analysis by gender, no statistically significant relationship was noted between drinking coffee and gastric cancer risk regarding male or female gender. Thus, our study does not support gender as a risk factor for stomach cancer incidence (Table 2).

In the analysis by country, statistically significant associations between drinking coffee and gastric cancer risk were reported in Korea, Turkey, Uruguay, Venezuela, and Singapore. Among them, the highest effect was found in a Turkish study which revealed that drinking coffee remarkably reduces the risk of gastric cancer in Turkey [OR = 0.51 (95% CI: 0.39-0.67)] (Table 2).

Additional analysis
As shown in Figure 3, meta-regression identified no statistically significant relationship between “the effect of coffee consumption on gastric cancer risk” and “publication year of the studies” (P = 0.689).

In Figure 4, meta-regression found no statistically significant association between “the effect of coffee consumption on gastric cancer risk” and “sample size” (P = 0.312). This finding indicates that even in studies with larger samples, drinking coffee was not considered more effective in preventing gastric cancer.

Discussion
This study states that drinking coffee prevents and reduces the risk of developing stomach cancer. A meta-analysis by Xie et al in 2016, including 7631 cases and 1019693 controls, showed that hazard ratio for stomach cancer was 0.94 (95% CI: 0.88-0.99) for the highest level of coffee consumption compared to the lowest level. Similarly, the hazard ratio was 0.93 (95% CI: 0.88-0.99) for coffee consumers versus abstainers. The pooled risk ratio (RR) for the populations with coffee consumption of less than 1 cup per day 0.95, 1-2 cups per day 0.92, and 3-4 cups per day 0.88 were, compared to those who did not drink coffee. There was a significant relationship between coffee consumption and a decrease in risk of stomach cancer in the case-control studies (RR = 0.85, 95% CI: 0.77-0.95) (36). The results of this meta-analysis corroborate the result of our present meta-analysis. Given that the former meta-analysis was published in 2016 and has not covered the studies published afterward (from 2016 to 2022), thus the current study provides a more comprehensive meta-analysis by including larger sample size and providing
Table 1: Specifications of articles, which entered into the meta-analysis process

| First author, Year of publication | Country          | Type of study      | No. of cases | No. of controls | Coffee consumption | OR       | Low OR | Up OR | Adjustments                                                                 |
|----------------------------------|------------------|--------------------|--------------|-----------------|--------------------|----------|--------|-------|-----------------------------------------------------------------------------|
| Lee HH, 1990 (12)                | Taiwan           | Hospital-based case-control | 210          | 810             | Drinker vs non-drinker | 1.41     | 0.72   | 2.75  | Age and sex                                                                  |
| Agudo A, 1992 (13)               | Spain            | Hospital-based case-control | 228          | 227             | Drinker vs non-drinker | 0.97     | 0.67   | 1.4   | Age, sex, area of residence, total calories, fruits, vegetables, preserved fish, etc |
| Memik F, 1992 (14)               | Turkey           | Case-control        | 79           | 608             | 2~3 Cups/d vs £1 Cup/d | 0.96     | 0.18   | 3.28  | Age                                                                         |
| Hoshiyama Y, 1992 (15)           | Japan            | Population-based case-control | 251          | 483             | ≥10 Cups/wk vs £1 Cup/w | 0.9      | 0.6    | 1.4   | Age, smoking, dietary items including salty foods, fruits, vegetables, seaweed, boiled fish, etc |
| Hansson LE, 1993 (16)            | Sweden           | Population-based case-control | 338          | 669             | ≥1100 mL/wk vs none | 1.07     | 0.72   | 1.59  | Age, sex, socio-economic status (SES), fruits, vegetables, etc               |
| Stensvold J, 1994 (17)           | Norway           | Cohort              | 151          | 42973           | ≥7 Cups/d vs £2 cup/d | 0.58     | 0.29   | 1.17  | Age, smoking, residence                                                      |
| Ji BT, 1996 (35)                 | Shanghai, China  | Population-based case-control | 1123         | 1249            | Drinker vs non-drinker | 0.73     | 0.42   | 1.27  | Age, sex                                                                     |
| Inoue M, 1998 (18)               | Japan            | Hospital-based case-control | 891          | 21128           | ≥3 Cups/d vs rarely | 0.93     | 0.72   | 1.21  | Age, sex, smoking, alcohol intake, tea, rice, fruit, beef                    |
| Galanis DJ, 1998 (19)            | Japanese in Hawaii | Cohort             | 108          | 11907           | ≥2 Cups/d vs none   | 1.8      | 1      | 3.3   | Age, education, place of birth, smoking, alcohol.                            |
| Chow WH, 1999 (20)               | Poland           | Population-based case-control | 476          | 480             | ≥7 Cups/wk vs none | 1.23     | 0.8    | 1.89  | Age, smoking, education, family history of cancer                           |
| Munoz N, 2001 (21)               | Venezuela        | Population-based case-control | 292          | 485             | Quartiles           | 0.58     | 0.37   | 0.92  | Age, sex, smoking, alcohol intake, total energy intake, SES                  |
| Tsabuno Y, 2001 (22)             | Japan            | Cohort              | 419          | 199748          | ≥3 Cups/d vs none   | 1        | 0.6    | 1.6   | Age, sex, tea, smoking, alcohol, rice, meat, vegetables, fruits, soup, etc   |
| Rao DN, 2002 (23)                | India            | Hospital-based case-control | 119          | 1577            | Daily vs never/rarely | 1.2      | 0.3    | 3.5   | Age, sex                                                                     |
| De Stefani E, 2004 (24)          | Uruguay          | Hospital-based case-control | 240          | 960             | Tertiles            | 0.65     | 0.48   | 0.9   | Age, smoking, alcohol intake, total energy intake, residence, education, BMI. |
| Khan MM, 2004 (25)               | Japan            | Cohort              | 51           | 3158            | ≥Several times/ wk vs ≥ several times/m | 0.77     | 0.42   | 1.42  | Age, health status, health education, smoking                                |
| Larsson SC, 2006 (26)            | Sweden           | Cohort              | 160          | 61433           | ≥4 Cups/d vs £1 cups/d | 0.77     | 0.42   | 1.42  | Age, time period, education, alcohol, tea consumption                        |
| Gallus S, 2009 (27)              | 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.   |
| Icli F, 2011 (28)                | 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                        |
| Bidel S, 2013 (29)               | Finland          | Cohort              | 299          | 60041           | ≥10 Cups/d vs none | 0.75     | 0.4    | 1.41  | Age, study year, education, smoking, alcohol, physical activity, diabetes, tea, BMI |
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| First author, Year of publication | Country | Type of study | No. of cases | No. of controls | Coffee consumption | OR      | Low OR | Up OR | Adjustments                                                                 |
|----------------------------------|---------|---------------|--------------|----------------|-------------------|---------|--------|-------|----------------------------------------------------------------------------|
| Ainslie-Waldman CE, 2014 (30)    | Singapore | Cohort       | 647          | 63257          | Daily vs non-daily | 0.54    | 0.31   | 0.91 | Age, sex, interview year, education, smoking, BMI, caffeine, total energy intake. |
| Sanikini H, 2015 (31)            | France, Germany, Greece, Italy, Norway, Spain, Denmark, Sweden, The Netherlands and United Kingdom | Cohort       | 189          | 443195         | 557-4700 mL/day vs non-drinker | 1.09    | 0.84   | 1.43 | BMI, alcohol consumption, energy intake from fat and non-fat, vegetable intake, fruit intake, etc |
| Tran KT, 2019 (32)               | UK      | Cohort       | 99           | 184            | >1-2 Cups/day vs non-drinker | 0.88    | 0.59   | 1.3  | Age, sex, deprivation, education, BMI, alcohol, smoking, fruit and vegetable intake, tea intake, physical activity, etc |
| Tran KT, 2019 (32)               | UK      | Cohort       | 55           | 184            | 3-4 Cups/day vs non-drinker | 1.14    | 0.73   | 1.79 | Age, sex, deprivation, education, BMI, alcohol, smoking, fruit and vegetable intake, tea intake, physical activity, etc |
| Tran KT, 2019 (32)               | UK      | Cohort       | 30           | 184            | ≥5 Cups/day vs non-drinker | 1.18    | 0.7    | 1.98 | Age, sex, deprivation, education, BMI, alcohol, smoking, fruit and vegetable intake, tea intake, physical activity, etc |
| Martimianaki G, 2021 (33)        | Italy   | Case-control | 8198         | 21419          | 1-2 Cups/day vs never or rare drinkers | 0.91    | 0.81   | 1.03 | Sex, age and the main recognized risk factors for gastric cancer               |
| Martimianaki G, 2021 (33)        | Italy   | Case-control | 8198         | 21419          | 3-4 Cups/day vs never or rare drinkers | 0.95    | 0.82   | 1.1  | Sex, age and the main recognized risk factors for gastric cancer               |
| Martimianaki G, 2021 (33)        | Italy   | Case-control | 8198         | 21419          | ≥5 Cups/day vs never or rare drinkers | 0.95    | 0.79   | 1.15 | Sex, age and the main recognized risk factors for gastric cancer               |
| Martimianaki G, 2021 (33)        | Italy   | Case-control | 8198         | 21419          | ≥7 Cups/day vs never or rare drinkers | 1.2     | 0.91   | 1.58 | Sex, age and the main recognized risk factors for gastric cancer               |
| Kim SY, 2021 (34)                | Korea   | Population-based Cross-Sectional | 188     | 36047          | 1–30 cups/month vs non-drinker | 0.71    | 0.58   | 0.86 | Age, sex, income group, BMI, smoking, alcohol, hypertension, diabetes, hyperlipidemia, stroke, etc |
| Kim SY, 2021 (34)                | Korea   | Population-based Cross-Sectional | 360     | 62446          | 30-60 cups/month vs non-drinker | 0.82    | 0.69   | 0.98 | Age, sex, income group, BMI, smoking, alcohol, hypertension, diabetes, hyperlipidemia, stroke, etc |
| Kim SY, 2021 (34)                | Korea   | Population-based Cross-Sectional | 191     | 35857          | ≥60 cups/month vs non-drinker | 0.8     | 0.65   | 0.98 | Age, sex, income group, BMI, smoking, alcohol, hypertension, diabetes, hyperlipidemia, stroke, etc |

Table 1. Continued
Figure 2. The plot of the relationship between drinking coffee and the risk of gastric cancer by country and publication year of the study.

Table 2. Exploring the effect of drinking coffee on gastric cancer risk in studied subgroups

| Subgroups            | OR   | Low-OR | UP-OR | P value | P(%) |
|----------------------|------|--------|-------|---------|------|
| Type of study        |      |        |       |         |      |
| Case-control         | 0.91 | 0.81   | 1.02  | 0.001   | 59.9 |
| Cohort               | 0.95 | 0.78   | 1.15  | 0.123   | 35.6 |
| Cross sectional      | 0.78 | 0.70   | 0.87  | 0.537   | 0    |
| Gender               |      |        |       |         |      |
| Men                  | 0.90 | 0.74   | 1.10  | 0.039   | 47.7 |
| Women                | 0.78 | 0.59   | 1.03  | 0.001   | 66.6 |
| Country              |      |        |       |         |      |
| Italy                | 0.99 | 0.89   | 1.10  | 0.170   | 37.7 |
| Korea                | 0.78 | 0.70   | 0.87  | 0.537   | 0    |
| UK                   | 1.03 | 0.80   | 1.33  | 0.586   | 0    |
| Taiwan               | 1.41 | 0.72   | 2.76  | ---     | ---  |
| Spain                | 0.97 | 0.67   | 1.40  | ---     | ---  |
| Turkey               | 0.51 | 0.39   | 0.67  | 0.387   | 0    |
| Japan                | 0.99 | 0.80   | 1.22  | 0.297   | 18.4 |
| India                | 1.20 | 0.35   | 4.10  | ---     | ---  |
| Uruguay              | 0.65 | 0.47   | 0.89  | ---     | ---  |
| Sweden               | 1.07 | 0.72   | 1.59  | ---     | ---  |
| China                | 0.73 | 0.42   | 1.27  | ---     | ---  |
| Poland               | 1.23 | 0.80   | 1.89  | ---     | ---  |
| Venezuela            | 0.58 | 0.37   | 0.91  | ---     | ---  |
| Norway               | 0.58 | 0.29   | 1.16  | ---     | ---  |
| Finland              | 0.75 | 0.40   | 1.41  | ---     | ---  |
| Singapore            | 0.54 | 0.32   | 0.93  | ---     | ---  |

more recent and up-to-date information. Therefore, this allows us to comment more confidently on the stomach cancer-protective effect of coffee.

A 2016 study by Deng et al, including 13 prospective studies, showed that excessive coffee consumption might increase the risk of developing stomach cancer. Furthermore, a notably elevated risk of cardia stomach cancer associated with coffee consumption was observed.
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(RR: 1.50, 95% CI: 1.09-2.07) (37). Previous meta-analysis considered coffee drinking a risk factor for stomach cancer and concluded that the risk of developing stomach cancer increased in coffee drinkers, which contradicts the results of the present meta-analysis. This discrepancy in results may be explained because these studies concentrated solely on a particular type of study (cohort), whereas our meta-analysis has covered all case-control, cohort, and cross-sectional studies concurrently.

While the following meta-analysis showed that there is no statistically significant relationship between coffee consumption and stomach cancer, Li et al conducted a meta-analysis on 13 prospective cohort studies in 2015, with 20 independent reports, including 3368 patients with stomach cancer and 1,372,811 participants during a 4.3-8 year follow-up period. The results suggested that the pooled relative risk was 1.13 (95% CI: 0.94-1.35) in comparison to the lowest level of coffee consumption. The dose-response analysis showed that the relative risk of developing gastric cancer was 1.03 (95% CI: 0.95-1.11) for drinking three cups of coffee per day. Consequently, this meta-analysis does not confirm the hypothesis that coffee consumption is related to the risk of gastric cancer (10). The variations and inconsistencies in reporting among the previous meta-analysis studies motivated us to carry out a novel comprehensive study using a systematic review and meta-analysis approach to shed light on these discrepancies.

Conclusion

In the 24 reviewed studies from the last three decades, coffee consumption has a preventive effect on developing stomach cancer and is considered to serve as a preventative and protective factor against this disease. However, in the subgroup analysis by gender, there was no statistically significant relationship between coffee drinking and stomach cancer risk regarding the male or female gender.

Limitations of the study

It did not analyze the dose of coffee consumption because of the different measurement units of coffee drinking reported in various studies (such as cups and mL). Second, given the non-uniform distribution of studies in different countries, reporting was not possible for many countries due to the lack of information available about them. Furthermore, most reviewed studies failed to address the age group of subjects. Thus, we could not carry out a subgroup analysis of the results by age. The unavailability of the full text of some studies was another limitation of this study.

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Authors’ contribution

Conceptualization: MF, MY. Methodology: MR, MM. Formal Analysis: MM. Resources: MR, HF, MY. Data Curation: MF, HF. Writing—Original Draft Preparation: All authors. Writing—Review and Editing: All authors. Project Administration: MF, HF. Funding Acquisition: MF.

Conflicts of interest

The authors declare that they have no conflict of interest regarding the contents of this article.

Ethical issues

Ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

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