INPLASY PROTOCOL

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Conflicts of interest: None.

Does Coffee, Tea and Caffeine Consumption Reduce the Risk of Incident Breast Cancer? A Systematic Review and Bayesian Network Meta-analysis

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Review question / Objective: Coffee is generally divided into regular coffee and decaffeinated coffee, and tea is mainly divided into three types, green tea, black tea and oolong tea, which are the most popular drinks worldwide. Recently, some studies have been reported a relationship between coffee and/or tea intake with tumorigenesis, such as BC, stomach cancer, colorectal cancer and glioma. The main cause of the anticancer effect is that coffee and tea contain a certain amount of caffeine, and caffeine interacts with the PI3K/AKT inhibitory kinase signaling pathway, indicating that caffeine may play important roles in tumor pathogenesis, metastasis and prognosis. However, the roles of coffee and/or tea consumption in reducing the risk of incident BC remain controversial. Although some published meta-analyses have shown that coffee and tea potentially reduce the risk of BC, other studies reached the opposite conclusion, and the recommended dosage was not conclusive. The objective of our current research was to determine the most suitable population and recommended daily dosage intake for coffee and tea that would effectively prevent BC, which could also assist in clinical therapeutic treatment. No previous systematic review has provided a comprehensive overview by performing a meta-regression and Bayesian network metaanalysis of this current topic.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 May 2020 and was last updated on 05 May 2020 (registration number INPLASY202050018).

INTRODUCTION

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decaffeinated coffee, and tea is mainly divided into three types, green tea, black tea and oolong tea, which are the most popular drinks worldwide. Recently, some

studies have been reported a relationship between coffee and/or tea intake with tumorigenesis, such as BC, stomach cancer, colorectal cancer and glioma. The main cause of the anticancer effect is that coffee and tea contain a certain amount of caffeine, and caffeine interacts with the **PI3K/AKT** inhibitory kinase signaling pathway, indicating that caffeine may play important roles in tumor pathogenesis, metastasis and prognosis. However, the roles of coffee and/or tea consumption in reducing the risk of incident BC remain controversial. Although some published meta-analyses have shown that coffee and tea potentially reduce the risk of BC, other studies reached the opposite conclusion, and the recommended dosage was not conclusive. The objective of our current research was to determine the most suitable population and recommended daily dosage intake for coffee and tea that would effectively prevent BC, which could also assist in clinical therapeutic treatment. No previous systematic review has provided a comprehensive overview by performing a meta-regression and Bayesian network meta-analysis of this current topic.

Rationale: Although the 5-year recurrence rate is not high in patients with BC, these patients require long-term medication and regular examinations, the sensitivity of chemotherapy and radiotherapy is poor when the tumor recurs, and recurrence is accompanied by a high mortality rate. Therefore, we anticipate being able to prevent the incidence of BC through therapeutic lifestyle changes, including environmental, reproductive and more easily changed dietary factors.

Condition being studied: Potential publications analyzed the association of coffee or tea consumption with the risk of incident breast cancer, compared dose-response correlations or noncoffee and tea groups and were either case-control studies or prospective cohort studies.

METHODS

Search strategy: Eligible studies evaluated coffee and/or tea consumption for the risk of incident breast cancer with their MeSH terms. Manual searches using public reference lists of each potential studies were also conducted.

Participant or population: Women.

Intervention: Coffee or tea consumption.

Comparator: Noncoffee and tea groups.

Study designs to be included: Either casecontrol studies or prospective cohort studies.

Eligibility criteria: Publications analyzed the association of coffee or tea consumption with the risk of incident breast cancer, compared dose-response correlations or noncoffee and tea groups.

Information sources: We searched PubMed, Embase, and the Cochrane Library to identify potentially eligible studies published in the last 30 years up to April 2020 with original search terms of coffee or tea and the risk of breast cancer and breast carcinoma but no language restrictions.

Main outcome(s): The incident risk of breast cancer.

Additional outcome(s): None.

Data management: Meaningful baseline characteristics were extracted using preset tables. For studies comparing doseresponse correlations, the first author, publication year, project name, country and region, research type, tested consumption, subject type, sample size, age, body mass index, alcohol intake, height, smoking, family history of BC, hormone therapy have been extracted. In addition, for studies which compared with noncoffee and tea group, first author, publication year, country and region, research type, tested consumption, subject type, sample size, age, body mass index, alcohol intake, smoking, family history of BC, previous history of benign breast diseases, and hormone therapy have been extracted.

Quality assessment / Risk of bias analysis:

To assess the risk of bias of both prospective cohort studies and casecontrolled studies, and an NOS score greater than 4 was considered acceptable quality and a score greater than 7 was considered high quality.

Strategy of data synthesis: For both hazard ratios (HRs) with their 95% confidence intervals (CIs) from effect size data and odds ratios (ORs) with their 95% CIs from dichotomous data, pairwise meta-analyses of heterogeneity were conducted when the I2 statistic was greater than 25% or the p value was less than 0.05, and regardless of the results of the heterogeneity test, random effects models were applied to assess accuracy.

Subgroup analysis: We also examined the differences in coffee/tea types, menopause status, hormone receptor status and BMI in subgroup analyses and meta-regression analyses to determine the most suitable level of coffee or tea consumption.

Sensibility analysis: No need.

Language: English.

Country(ies) involved: China.

Keywords: Coffee; tea; breast cancer; preventing; Bayesian network metaanalysis.

Dissemination plans: No need.

Contributions of each author:

Author 1 - Shu Wang - Shu Wang designed research, conducted research, analysed data and wrote paper. Author 2 - Xiang Li - Xiang li designed research, conducted research. Author 3 - Yue Yang - Yue Yang analysed data. Author 4 - Jingping Xie - Jingping Xie

Author 4 - Jingping Xie - Jingping Xie conducted research. Author 5 - Xiaochun Qin - Xiaochun Qin analysed data and conducted research.

Author 6 - Ya Zhang - Ya Zhang analysed data.

Author 7 - Yingshi Zhang - Yingshi Zhang designed research, analysed data and wrote paper.

Author 8 - Qingchun Zhao - Qingchun Zhao designed research, wrote the paper.