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Meta-analyses

Coffee and tea consumption in relation with non-alcoholic fatty liver and metabolic syndrome: A systematic review and meta-analysis of observational studies

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A R T I C L E   I N F O

S U M M A R Y

Background & aims: Diet plays a role in the onset and progression of metabolic disorders, including non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome (MetS). We aimed to systematically review and perform quantitative analyses of results from observational studies on coffee/tea consumption and NAFLD or MetS.
Methods: A Medline and Embase search was performed to retrieve articles published up to March 2015. We used a combination of the keywords "coffee", "caffeine", "tea", "non-alcoholic fatty liver disease", "non-alcoholic steatohepatitis", "metabolic syndrome". Pooled risk ratios (RRs) and 95% confidence intervals (CIs) were calculated by random-effects model.
Results: Seven studies assessed coffee consumption in NAFLD patients. Fibrosis scores were reported in four out of seven; all four studies revealed an inverse association of coffee intake with fibrosis severity, although the lack of comparable exposure and outcomes did not allow to perform pooled analysis. Seven studies met the inclusion criteria to be included in the meta-analysis on coffee consumption and MetS. Individuals consuming higher quantities of coffee were less like to have MetS (RR = 0.87, 95% CI: 0.79−0.96). However, the association of coffee and individual components of MetS was not consistent across the studies. Pooled analysis of six studies exploring the association between tea consumption and MetS resulted in decreased odds of MetS for individuals consuming more tea (RR = 0.83, 95% CI: 0.73−0.95).
Conclusions: Studies on coffee and NAFLD suggest that coffee consumption could have a protective role on fibrosis. Both coffee and tea consumption are associated with less likelihood of having MetS but further research with better designed studies is needed.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) has become the most prevalent cause of liver enzymes elevation both in industrialized and developing countries [1]. In recent years different prospective studies have showed that liver fat accumulation *per se* precedes the onset of the metabolic syndrome (MetS), a cluster of metabolic abnormalities associated with cardiovascular mortality [2]. Thus, NAFLD and MetS can be considered interrelated, as they share

common pathogenetic determinants such as insulin resistance and oxidative stress [3,4]. Although hepatic lipid accumulation is not associated with progressive liver damage in the majority of patients with NAFLD, a subset of patients display liver inflammation and fibrosis, i.e. non-alcoholic steatohepatitis (NASH), which may evolve to cirrhosis and hepatocellular carcinoma representing major indications to liver transplantation [4]. Together with genetic factors conferring susceptibility to NAFLD, lifestyle factors and especially dietary habits have been demonstrated to play a central role in the pathogenesis of both NAFLD and MetS [5–8].

Coffee and tea are the most consumed beverages worldwide after water. Coffee is prepared from the seeds of the coffee plant, genus *Coffea*, a member of the Rubiaceae family, which includes hundreds of different species (including the main Arabica and Robusta). Tea is made from leaves of the plant *Camellia sinensis*, family of Theaceae, including several varieties such as green and black tea. Although these beverages are consumed for their taste and flavor, several observational studies have lately highlighted possible beneficial effects on liver and metabolic health [9,10]. The epidemiological findings recently published have led to experimental *in vitro* and *in vivo* studies on compounds contained in coffee and tea that are providing biological plausibility for their effects. The aim of this study was to systematically review current evidence from observational studies on the effects of coffee and tea consumption on NAFLD and MetS. We also attempted to pool findings from these studies in order to provide quantitative analyses of the results.

2. Materials and methods

2.1. Study selection

A search of electronic databases Medline and Embase was performed to retrieve articles published up to March 2015. A combination of the keywords "coffee", "caffeine", "tea", "non-alcoholic fatty liver disease", "non-alcoholic steatohepatitis", "metabolic syndrome" was searched. All published studies in English language were considered, including studies meeting the following inclusion criteria: (i) had cross-sectional, case–control, or prospective design; (ii) had coffee/tea as variable of interest; (iii) evaluated NAFLD/NASH prevalence, incidence, or severity as outcome. Exclusion criterion was diagnosis of liver steatosis or fibrosis secondary to causes other than metabolic (i.e., excess of alcohol consumption, viral hepatitis). Regarding MetS, the quantitative analysis was performed whether (i) exposure to coffee/tea was clearly identified and (ii) odds ratios (ORs) or hazard ratios (HRs) with 95% confidence intervals (CIs) for the highest *versus* the lowest level of coffee/tea consumption were reported. Additional papers were retrieved by references of identified studies. This process was conducted by GG and SM independently. Disagreements were resolved through discussion.

2.2. Data extraction and study quality

Data were abstracted from identified study by using a standardized extraction form. The following information was collected: 1) first author name; 2) year of publication; 3) country; 4) study design; 5) number and gender of participants; 6) age range or mean age of the study population at baseline; 7) endpoints and cases; 8) diagnosis criteria; 9) OR/HR and 95% CIs for extreme categories of exposure; 10) covariates used in adjustments; 11) main results; 12) categories of exposure.

Study quality was evaluated according to the Newcastle–Ottawa quality assessment scale [11]. Six domains were evaluated in each included studies: representativeness of the exposed cohort,

selection of the non-exposed cohort, ascertainment of exposure, comparability of cohorts on the basis of the design or analysis (for main background characteristics and specific adjustment) and assessment of outcome. A maximum total score of 9 points was possible, with the highest score representing better quality.

2.3. Statistical analysis

In this meta-analysis, ORs and HRs were deemed equivalent to risk ratios (RRs). ORs/HRs with 95% CI for all categories of exposure were extracted for the analysis and random-effects models were used to calculate pooled ORs with 95% CIs for highest *versus* the lowest category of coffee/tea consumption. In order to quantify the exposure, sub-analyses exploring the effects of specific doses according the availability of the data were performed. To test the stability of the results, sensitivity analysis, after exclusion one study at each time, was applied. Subgroup analyses were performed to investigate the role of geographic region, gender, diagnosis criteria, sample size and amount of coffee/tea consumption. Heterogeneity was evaluated by using Higgins' I^2 statistic. I^2 values $\leq 25\%$, $\leq 50\%$, $\leq 75\%$, and $>75\%$ indicated no, small, moderate, and significant heterogeneity, respectively. A sensitivity analysis by exclusion of one study at a time was performed to assess the stability of results and potential sources of heterogeneity. Publication bias was evaluated by Begg's and Egger's test and by a visual investigation of funnel plots for potential asymmetry. Analyses were performed using Review Manager (RevMan) version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration).

3. Results

3.1. Study selection

The process of identification and study selection is summarized in Fig. 1. Among the initial 252 articles after the screening on the basis of title, 32 articles were explored by reading full-texts. Nine studies were excluded after a full-text examination for the following reasons: reported NAFLD/fibrosis following viral hepatitis or alcohol consumption ($n = 5$); reported insufficient statistics ($n = 2$); reported evaluation of individual MetS components and/or biomarkers with no reference to MetS status ($n = 2$). This inclusion strategy resulted in the final selection of 23 studies [12–34]: 7 studies [12–18] explored the association of coffee/caffeine consumption with NAFLD presence or severity; 16 studies [19–34] were conducted on MetS, 8 out of which [19–26] evaluating the association with coffee consumption, 2 [33,34] with tea, and 6 [27–32] with both coffee and tea consumption. The identification of the MetS was based mainly on original and modified version of the Adult Treatment Panel III criteria (ATPIII) [19,21–24,27,30,33,34], the International Diabetes Federation criteria (IDF) [28,29], and the Japan Society for the Study of Obesity (JASSO) criteria [20,27]. One study used the American Heart Association (AHA) criteria [26] and another study used different MetS diagnosis criteria [25]. In a study presenting two MetS criteria [27], the ATPIII was used for further analyses.

3.2. Coffee consumption and NAFLD

Seven studies [12–18] investigated the role of coffee and caffeine consumption on NAFLD (Table 1). Catalano et al. [16] first assessed bright liver score, a measure of the severity of liver steatosis diagnosed by ultrasonography, in 157 patients with NAFLD and 153 controls. Although no difference in coffee intake was observed between cases and controls, among NAFLD patients the