Coffee and Coronary Heart Disease, is there a relationship?

Swanti Deut, Rima ElChamaa, Ihab Kandil, and Samiha Rahman

University of Ottawa, Interdisciplinary School of Health Sciences

BACKGROUND

Coffee is one of the most widely consumed beverages in the world (Topik, 2009). In the past two decades, experimental studies have shown that caffeine in coffee induces various acute cardiovascular effects, including effects on circulating catecholamines, arterial stiffness, and endothelium dependent vasodilation (Smits et al., 1985; Mahmud & Feely, 2001; Papamichael et al., 2005). These effects are thought to be mediated via effects of coffee on increasing blood pressure, serum cholesterol, homocysteine levels, as well as oxidation and inflammation (Cornelis, & Sohemy, 2007).

Coffee contains several biologically active substances. Cafestrol and kahweol are diterpenoid alcohols that occur naturally in coffee beans and have been identified as hypercholesterolemic compounds (Urgert & Katan, 1997). It also contains chlorogenic acid, flavonoids, melanoidins, and various lipid soluble compounds such as furans, pyrroles, and maltol (Spiller, 1998; Yanagimoto, Ochi, Lee & Shibamoto, 2004). Many of these compounds are efficiently absorbed, have relatively high bioavailability, and have been shown to have antioxidant properties (Yanagimoto et al., 2004; Pellegrini et al., 2003).

Past studies have aimed to examine the effects of coffee consumption on the risk of developing coronary heart diseases (CHD). CHD is a collective term given to any disorder which involves the buildup of plaque in the arteries leading to the heart (Mendis, Puska, & Norrving, 2011). This include disorders such as stable angina, unstable angina, myocardial infarction (MI), and sudden coronary death (GBD 2013 Mortality and Causes of Death Collaborators, 2013). In 2013, CHD was the most common cause of death globally, resulting in 8.14 million deaths (GBD, 2013). Modulation of lifestyle factors such as exercise, stress, weight control, and diet have been shown to decrease risk of occurrence of heart disease (National Heart, Lung, and Blood Institute). Thus, identifying a link between coffee consumption and CHD development, could be imperative in reducing the risks of such disorders in the future.

Yet, findings from past epidemiological studies examining this risk have mostly been inconclusive (Cornelis, & El-Sohemy, 2007). Cohort studies have generally not supported a significant association, including a recent study which examined 44,005 men and 85,488 women with 14 and 20 years of follow up, respectively (Myers, & Basinski, 1992; Lopez-Garcia, 2006; Kawachi, Colditz, & Stone, 1994). On the other hand, case-control studies have generally shown an increased risk of CHD with increasing coffee consumption (Hammar et al., 2003; Cornelis, El-Sohemy, Kabagambe, & Campos, 2006)

Recently, however, some cohort and case-control studies have suggested a protective effect of moderate intake of coffee on CHD (Happonen, Voutilainen, & Salonen, 2004; Andersen, Jacobs, Carlsen, & Blamhoff, 2006; Kleemola et al., 2000). A new study published in Heart, which looked at more than 25,000 healthy subjects in South Korea, found that people who consume moderate amounts of coffee may be less likely to have atherosclerosis (Choi, 2015). This indicates that coffee consumption may even have beneficial effects on some biological pathways.

Research Question: Is there a significant association between coffee consumption and the subsequent development of coronary heart disease among middle-aged adults?

METHODOLOGY

A literature search of Medline and Pubmed was conducted for studies published from 2000, to identify studies that examined the association between coffee consumption and CHD, with an analytical design – either case control (retrospective), cohort (prospective), experimental, or meta-analysis. Our search strategy included articles with the titles containing the keywords 'Coffee' AND 'Coronary Heart Disease', 'Coffee' AND 'Artery', or 'Coffee' AND 'Coronary'. Our search strategy generated a total of 21 articles. Of the 21 articles, review articles, editorials, and studies conducted on clinical subpopulations were excluded. This generated a total 14 potentially relevant studies. One study was excluded, as it only focused on the pathologic mechanism of coffee based on a prior determination of a positive association. Three studies were excluded because they focused on populations with diabetes and/or cancer. Hence only 10 papers were included in the final analysis. We chose to limit our scope to only articles published between 2000-2015. The primary reason for this is that many studies published before 1990 did not provide confounder adjusted relative risks, such as smoking as well as other risk factors. This led to the overestimation in the association between coffee consumption and CHD (Wu et al., 2008). Therefore, by excluding studies published before 1990, this study was able to avoid results that were influenced by confounding factors that were previously unaccounted for.

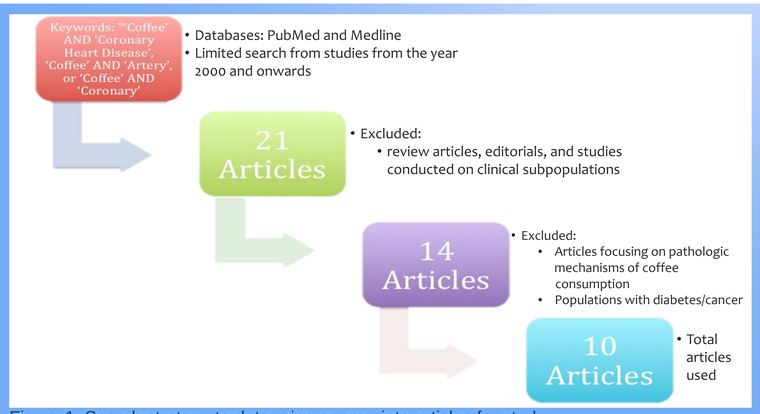

Figure 1. Search strategy to determine appropriate articles for study

ABSTRACT

Context: Coffee has been shown to increase the risk factors associated with coronary heart disease (CHD), including serum cholesterol, insulin resistance, blood pressure, and plasma homocysteine; however studies examining the association between coffee consumption and CHD have been inconclusive.

Objective: To determine if there is a relationship between coffee consumption and development of CHD among adults.

Methods: A literature review of studies published between the years 2000 to 2015, using PubMed and Medline, with the titles containing the keywords "Coffee" AND "Coronary Heart Disease", "Coffee" AND "Artery", or "Coffee" AND "Coronary" was conducted. Review articles, editorials, and studies conducted on clinical subpopulations were excluded; the ten articles which remained were examined.

Results: While the majority of case-control studies demonstrate a positive association between coffee consumption and CHD, most cohort studies have reported no such association.

Conclusions: Inconclusive results may be explained by the acute detrimental effects of coffee on coronary events, rather than a long-term adverse effect of coffee consumption.

RESULTS

Title and Type of Study	Overview of Results	Relative Risks and Odds Ratios	
Coffee Consumption and the risk of Coronary heart Disease and Death: prospective cohort	No association found between coffee drinking and the risk of nonfatal myocardial infarction (MI). Highest number of patients who died of CHD were non-coffee drinkers. Men smoked more, drank coffee more, and had higher serum cholesterol and blood pressure levels compared to women. Generally, increased coffee drinking was related to smoking status and increased serum cholesterol. All-cause mortality in women decreased by drinking more cups of coffee.	Relative Risk of CHD Mortality (95% Confidence Intervals) <1 cup/day = 1.46 (0.93 - 2.28); 1-3 cups/day = 1.00;4-7cups/day = 1.34 (1.02 - 1.77); >7 cups/day = 1.51 (1.12 2.03)	
Coffee and coronary heart disease: case-control	Increased association between drinking more than 5 cups of coffee per day and myocardial infarction or unstable angina. Those who drank equal or more than 5 cups a day were more likely to have acute coronary syndromes and were more likely to smoke.	Odds ratio: 5 cups of coffee = 2.51 (95% CI 1.43, 4.43; P 0.021)	
The J-shaped effect of coffee consumption on the risk of developing acute coronary syndromes: the CARDIO 2000 case-control study.	A J-shaped association was found between coffee consumption and acute coronary syndromes. Moderate coffee consumption was associated with lower CHD risk which was similar in men and women.	Odds Ratio (CI 95%) Moderate consumption (300mL/day): 0.67 Heavy consumption (300-600 mL/d): 1.56 Very Heavy consumption (>600ml/day): 3.10	
Coffee consumption and coronary heart disease in men and women a prospective cohort study	No significant association was found between the risk of CHD and coffee consumption. However, drinking 6 cups or more was associated with lower risk of fatal CHD.	Relative Risk for men: <1 cup/mo = 1.0; 1 cup/mo - 4 cups/wk =1.04 (95%); 5 - 7 cups/wk =1.02 (0.91 to 1.15); 2 - 3 cups/day = 0.97 (0.86 to 1.11); 4 - 5 cups/day = 1.07 (0.88 to 1.31); 6 or more cups/day = 0.72 (0.49 to 1.07) (P for trend = 0.41)	Relative Risk for women: <1 cup/mo = 1.0; 1 cup/mo - 4 cups/wk =0.97 (95% CI, 0.83 to 1.14) ; 5 - 7 cups/wk =1.02 (0.90 to 1.17); 2 - 3 cups/day = 0.84 (0.74 to 0.97); 4 - 5 cups/day = 0.99 (0.83 to 1.17); 6 or more cups/day = 0.87 (0.68 to 1.11) (P for trend = 0.82)
Coffee consumption and risk of coronary heart disease: a meta-analysis	In general, an elevated risk of CHD was positively associated with the quantity of coffee consumed per day. This was a typical finding in case-control studies, however, this was not true for prospective cohort studies. No significant association was found between coffee consumption and CHD. Although no association was found with decaffeinated coffee, more research needs to be done.	Summary of Odds Ratio of the case-control studies: Statistically significant associations between coffee consumption and CHD for the highest intake group >4 cups a day 1.83 (95% CI, 1.49 - 2.24; P<0.0001) No significant association emerged for low daily coffee intake (equal or less than 2 cups a day) 1.03 (95% CI, 0.87 - 1.21; P=0.45)	Long Term Cohort Studies No association between the consumption of coffee and CHD Relative Risk: 1.16 (95% CI, 0.95 - 1.41; P=0.14) for the highest category
The confounded relation of coffee drinking to coronary artery disease.: cohort study	This study attempted to determine whether coffee consumption or its confounder, smoking status, was related to increased risk of CHD. The findings indicated that coffee consumption was unrelated to CHD in those who never smoke, while the opposite was true in ex-smokers and current smokers. It stresses that the false association of other studies is possibly caused by 'incomplete control of smoking, by other traits of smokers, or by an adverse biological interaction of a coffee ingredient with smoking'. It concludes that smoking alone increases one's risks. There was a slightly stronger association in women who smoked and were heavier coffee drinkers.	Relative risk: Never or seldom = 1.00; <1 cup/day = 1.02 (95% CI, 0.94–1.10; P value= 0.7); 1–3cups/day = 1.03 (0.97–1.09; P value= 0.4); 4–6cups/day = 1.08; (1.00–1.07; P value= 0.05); >6 cups a day = 1.21 (1.10–1.34; P value= 0.0002)	
Coffee Consumption and Coronary Calcification The Rotterdam Coronary Calcification Study: cohort study	The findings indicated beneficial effects of coffee on coronary calcification where women typically had decreased coronary calcification when coffee consumption was moderate (3-4 cups/day) or high (>4cups/day). The benefits also existed for non-smoking men, but not for smoking men. Although the benefits of coffee consumption was observed in both men and women, the effect was stronger in women.	Odds Ratio: >3 -4 cups/day = 0.41 (95% CI, 0.25 to 0.65) >4 cups/day = 0.54 (0.33 to 0.87)	
Coffee consumption and risk of coronary heart diseases: a meta-analysis of 21 prospective cohort studies	There was no relationship found between the long-term risks of CHD and coffee consumption but moderate drinking in women was related to lower risks of CHD.	Relative risk of 95% CI: 1-3 or 3-4 cups/day = 0.96 (0.87 to 1.06) 4-5 or 5-6 cups/day = 1.04 (0.92 to 1.17) equal or <6-7 cups/day = 1.07 (0.87 to1.2)	Moderate Coffee Consumption: Relative Risk Women: 1-3 or 3-4 cups/day = 0.82 (0.73 to 0.92) Men: 1-3 or 3-4 cups/day = 0.87 (0.80 to 0.86)
Coffee consumption enhances high-density lipoprotein-mediated cholesterol efflux in macrophages: experimental study	Findings indicated that coffee consumption may have anti-atherogenic properties by upregulating gene expression of ABCG1 and SR-BI. It also increases HDL-mediated cholesterol efflux from macrophages. Ferulic acid in coffee was found to increase LDL levels in feces.	N/A	
Coffee consumption and coronary artery calcium in young and middle-aged asymptomatic adults: Cohort study	Findings supported the association between coffee consumption and lower prevalence of subclinical coronary atherosclerosis. High coffee intake was typically seen in older, men, current smokers, higher education, less frequent vigorous-intensity physical activity, obesity, hypercholesterolemia, and have lower proportion of hypertension.	Relative Ratios:(P value for quadratic trend = 0.02) <1 cups/day = 0.77 (0.49 to 1.19); 1–<3 cups/day = 0.66 (0.43 to 1.02); 3–<5 cups/day = 0.59 (0.38 to 0.93); ≥5 cups/day = 0.81 (0.46 to 1.43)	Odds Ratio: (95% CI) <1 cups/day = 0.90 (0.74 to 1.10); 1–<3 cups/day = 0.85 (0.71 to 1.03); 3–<5 cups/day = 0.80 (0.66 to 0.97); ≥5 cups/day = 0.94 (0.73 to 1.20)

DISCUSSION

Generally case-control studies show a positive association between coffee consumption and CHD, while prospective cohort studies show no such association. Several theories have been proposed to explain this.

First, case-control studies have poor control for confounding, selection, and recall bias, (Kleemola et al., 2000). This makes it increasingly difficult to pinpoint if coffee is the trigger for the development of CHD - as it may be due other causal factors. Second, case-control studies are generally limited by recall bias - for example - CHD patients are more likely to overreport coffee intake than are healthy controls, which may explain the positive association (Sofi et al., 2007).

Third, it has been suggested that throughout the observation period, some cohort studies are unable to effectively account for modification in lifestyles (such as inhibition of coffee consumption, lowering coffee intake or changing the type of coffee consumed) due to ageing of the cohort or worsening health (Panagiotakos et al., 2003). This in turn may present a negative association between coffee consumption and CHD, as there are other factors (such as changes in diet and exercise) which may prevent the development of CHD.

Fourth, prospective cohort studies collect data about the long-term intake and long-term effects of coffee consumption, while retrospective case-control studies are more robust at capturing recent intake and short-term effects (Wu et al., 2008). Since acute adverse effects on the cardiovascular system have been associated with coffee consumption, it is more likely that case-control studies show a positive associations with CHD. However, these short-term effects are usually missed by cohort studies, explaining the negative results (Sofi et al., 2007).

Limitations of the articles:

The studies chosen to conduct the literature review contain several biases and limitations that concurrently limit this study. A few of the limitations presented are the lack of specification of varying cup sizes, types of coffee (caffeinated or decaffeinated), coffee preparation methods and the strength of the coffee (mild, medium, or strong), which contributes to the existing misclassification bias in each article. Excluding Sofi et al. and Klatsky et al. articles, recall bias was found as a recurring limitation in each article pertaining to self-reported questionnaires and surveys. Non-response bias also appeared in Kleemola et al. (2000) and Klatsky et al. (2008) studies as volunteers were used to complete questionnaires and undergo health examinations, and those who were too sick or incapable were excluded. The studies were unable to completely examine the dose-response relations due to the lack of data regarding people who fit into the higher coffee drinking categories (Kleemola et al., 2000). Differential, Berkson's, lost-to-follow-up, and the healthy worker effect biases were also present in some studies.

Furthermore, most studies failed to recognize coffee additives such as sugar, milk, and/or cream which eliminates opportunities to assess their effect on coffee and therefore risk of CHD. The additional compounds can act as confounding factors by masking the relationship or creating a false association between coffee consumption and CHD. Other confounding factors included sex, age, differences in dietary and exercise habits, physical activity, and smoking which can explain the wide variety of results (Tolfer et al., 200; Panagiotakos et al., 200; Klatsky et al., 2008; Van Woodenburg et al., 2008; Wu et al., 2008). Another limitation among the studies was the absence of discussion regarding heterogeneity in relation to coffee preparation methods.

Cafestol and kahweol are cholesterol-raising compounds present in boiled coffee, but are not present in filtered coffee (Wu et al., 2008). Increasing levels of serum cholesterol is a potential risk factor of CHD and is a threat posed by unfiltered boiled coffee but not by filtered coffee, and since the type of coffee is not specified within the studies, conflicting results are prevalent. Also, the lack of knowledge regarding preparation method eliminates the chance to assess cafestol and kahweol as confounding factors in unfiltered coffee.

Smoking and the associated traits of smokers are dominant confounding factors regarding the association between coffee and CHD. (Klatsky et al., 2008). These traits include poor dietary or exercise habits, which individually can act as confounding factors. Smoking is a leading risk factor and is prominent predictor of CHD, meaning any "residual confounding by incomplete control for smoking is a likely explanatory factor" (Klatsky et al., 2008).

Limitations of our study design:

First, while studies published before the year 2000 were excluded, meta-analyses studies were considered which looked at data before that date. As discussed, older studies did not provide confounder adjusted relative risks, such as smoking as well as other risk factors. Therefore the data considered by the meta-analysis may be inaccurate.

Second, Medline and PubMed were the only databases used, this may have led to inadvertent exclusion of other relevant studies.

Third, the reviewed studies examined populations from different parts of the world, within which differences such as method of coffee preparation and cup size were not accounted for (Panagiotakos et al., 2003).

Fourth, the objective of the research was to examine the association between coffee consumption and CHD among the adult population, yet this population was very broadly defined.

CONCLUSIONS

In conclusion, our findings do not support the hypothesis that there is a significant association between coffee consumption and the subsequent development of CHD among middle-aged adults. From our analysis, moderate coffee consumption (less than 5 cups) seems to be beneficial as it appears to be associated with a lower risk of CHD. On the other hand, excessive coffee consumption (more than 5 cups) seems to be associated with the significant increase in risk factors linked to CHD. Overall the effects of coffee consumption on the development of CHD itself is inconclusive.

FUTURE DIRECTIONS

Discovering the association between coffee consumption and CHD is a significant area of research as coffee is one of the most widely consumed beverages worldwide. Future studies need to specify the biological effects of caffeine consumption from other sources of food such as tea or chocolate and possible synergistic effects. Additionally, studies focusing on the consumption of boiled coffee and the associated risks with CHD would also provide insight since it has already been acknowledged to contain cholesterol-raising compounds.

Standard serving sizes and strength of brews should be examined in future studies as they differ from country to country, and in turn may have distinctive associations with CHD (Mostofsky et al., 2012).

There is a lack of data on higher coffee drinking categories, however there were some findings showing an association between coffee intake of more than five cups/day with MI and unstable angina (Tolfer et al., 2001). Further study is necessary to create an accurate dose-response relation, especially among heavy coffee drinkers.

There were slight differences in the effects of coffee consumption among men and women. Gender-based studies should be considered more specifically in regards to the beneficial effect of coffee drinking against coronary calcification (Van Woodenburg et al., 2008).