# REVIEW ON ASSOCIATION OF CARDIOVASCULAR DISEASE WITH COFFEE CONSUMPTION. 

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#### Abstract

: Coffee is one of the most widely consumed stimulants worldwide and is generally considered to be safe or even beneficial for health. One of the stimulants that is most frequently eaten worldwide is coffee, which is typically thought to be either safe or even healthy. A functional variation at cytochnome P450 1A2 (CYP1A2) has been linked to a higher risk of-wyocardial infarction and hypertension in people who are less efficient ingetabolising caffeine. Over time, the relationship between coffeeconsumption and the risk of cardiovascular diseaséshiftedfrom a favourable to a negative direction. This long-term, multinationall ecological study used a variety of cogent data to assess whether there was any change in the relationship between coffee consumptionand mortality and incidence rates of ischemic heart disease (IHD) between 1990 and 2018. The most popular beverage eaten worldwide is coffee. Studies on its link to cardiovascular health were conducted as a result of its significance for public health. simple andocinical studies have demonstrated that polyphenols and caffeine.

Coffee's characteristic ingredients, (particularly chlorogenic acid), have been connected to cardioyascular health. The first observational research to link coffee consumption to an increased risk of coronary heart disease was published in 1,963 . Three categories of daily coffee consumption were identified: 1,3 , and 3 cups. By comparing food consumption information frith the PhenolExplorer database, polyphenol intake was determined. Several studies conducted over the past three decades have evaluafed. the link between routine coffee consumption and coronary heart disease (CHD), with varying degrees of success. This study set out to thoroughily review the information that has been published regarding the link between routine coffee drinking and the risk of coronary heart disease. The inclusion criteria were satisfied by 21 prospective studies involving 121915 fatalities and 997464 partigipants. Strong e vidence of nonlinearity was found. -K $\overline{\mathbf{E}} \overline{\mathbf{Y}}$ ORDS: coffee consumption, coffee polyphenol intake, cardiovascular risk factors, Ischemic heart disease.

\section*{INTRODUCTION:}

Evidence suggests that increased inflammation after ageing contributes to an increase in the prevalence of diseases such diabetes, metabolic syndrome, and cardiovascular disease (CVD) [1]. Perhaps $33.7 \%$ of fatalities are now attributed to CVD, making it the leading cause of death globally. By 2030, it is predicted that each year, there would be 23.6 million fatalities attriblutable to CVD [1,2]. In Iran, CVD is one of the leading causes of death [3]. Caffeine, a central nervous system stimulant and-psyehoactive substance, has been positively associated with blood pressure [8,9], systemic vascular resistance and unfavorable effects oñ endbthelial function [ 9], serum lipids concentration [10], and insulin resistance [ 11]. Other prespective studies, however, have generally not supported adverse risk effects on CVD associated with coffee consumption. According to estimates, 17.3 million fatalities worldwide occur each year as a result of cardiovascular diseases (CVD), and by 2030, that number is expected to exceed 23.6 million [1]. Along with metabolic risk factors, non-modifiable risk factors are the primary causes of CVD. That target poor diets (high in salt, saturated fat, and calories) in addition to behavioural risk factors [2]. There are still some foods, like coffee, whore function is debatable. here has been a long-standing contro- versy regarding the association of coffee consumption with the incidence of cardiovascular diseases (CVDs), hypertension (HTN), heart failure (HF), cardiac arrhythmias, and diabetes mellitus


(DM). Cardiovascular disease (CVD) is a serious health issue and a leading killer in the world. Epidemiological research has shown that diets high in pofyphenols may help reduce the risk of CVD (1-3). In addition to antioxidant capabilitieş polyphenol-enriched diets may also have additional mechanisms that include anti-inflammatory, anti-hypertensive, vasculoprotective, and lipid-lowering effects (4).

During a 24-year period of follow-up in women with CVD, this study looked at the relationship between drinking filtered caffeinated coffee and the risk of all-cause and CVD death. The extended follow-up, large cohort, and measurement of coffee consumption before and after the CVD event every 4 years were the study's key benefits; these factors allowed us to evaluate both the long-term and short-term impacts of coffee consumption. Despite several epidemiological research, the link between coffee consumption and the risk of coronary heart disease (CHD) is still debatable. The involvement of caffeine in causing ventricular arrhythmias, as well as elevations in plasma renin activity, catecholamine concentrations, and blood pressure, led to the initial suspicion that coffee consumption may be associated with CHD.'2 Although it now appears that these effects are not clinically relevant in the majority of frequent users, cross sectional observations indicating a connection between coffee consumption and blood total cholesterol

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concentrations have sparked new concerns. In the 1980 s , cross sectional studies found a positive association between coffee consumption and serum total cholesterol concentrations, which might berelated to the coffee brewing method (ie, boiled or unfiltered coffee). A later randomised research revealed that drinking boiling coffee raised serum cholesterol. Numerous case-control studies from the 1980s to the 2000s, which are subject to recollection and selection bias, revealed a favourable correlation between coffee consumption and the risk of CHD. 6-8 In contrast, although findings varied greatly between studies, meta-analyses of prospective cohort studies tended to show no connection.

Due to the massive consumption of coffee around the world, the impact of coffee on human health is thought to be of tremendous significance. However, it can be challenging to analyse the development of disease in relation to consumption of coffee, largely because it might be difficult to define a coffee beverage. In terms of brewing techniques and caffeine level, coffee, a beverage made from coffee beans, is offered in a stunning array of varieties around the world.

Even within the same nation, preparation techniques and drinking preferences vary widely. This may help to explain some of the divergent findings reported in the literature. To determine if routine coffee drinking is linked to an elevated risk of CHD, we decided to undertake a systematic review with meta-analysis of the available epidemiological studies, both case control and prospective. Due to the possibility for demggraphiq and other dietary characteristics to be conflated with coffee and tea consumption, research in this area is difficult. Clinical outcomes may be associated with the amount of coffee or tea consumed, what is added to or eaten with these beverages, or socioeconomic characteristics. Therefore, it is crucial to research a broad population with sociodemographic and "crinical features in order to evaluate the cardiovascular effecter offee and tea use. Additionally, evaluating the cardiovascular events themselves and the underlying condition (sub clinical atherosclerosis) simultaneously in a single sizable prospective cohort research maysupport a casual link. In the Multi-Ethnic Study of Atherosclerosis (MESA), we sought to investigate the association between coffee and tea intake with coronary artery calcium prevalence, progression, and cardiovascular events.

Although the most prominent bioactive component in coffee, caffeine, has been shown in randomised controlled trials to cause acute increases in blood pressure (BP) (4, 5), evidence from observational studies looking at habitual coffee consumption generally does not show any increased risk of cardiovascular disease (CVD). Some gene-coffee interaction studies have suggested that the effect of coffee on CVD risk may be modified by a functional variant (rs762551) of the cytochrome P450 1A2 gene (CYP1A2), whose encoded protein metabolises approximately $95 \%$ of caffeine in the liver and exhibits a wide inherited interindividual variability in activity. These studies are in addition to those looking into the direct associations with habitual coffee consumption


## METHOD:

1.CHOICE OF STUDIES: A computer-assisted literature search, bibliographical searches of review articles 3, and previous metaanalyses helped find epidemiological research on coffee consumption and heart disease. Fig. 1 Selection of studies to be included in a meta-analysis on the relationship between coffee consumption and cardiovascular disease from 1966 to 2013.

| 227 Records Identified Through |
| :--- |
| PubMed Database Search |
| (1966-2013) |



## 2. POPULATION STUDY:

The "Health Survey of So Paulo (ISA-Capital)," a cross-sectional population-based study conducted between 2008 and 2009 to evaluate the health and nutritional status of non-institutionalized people living in So Paulo City in Southeast Brazil.

Utilising census tracts and families that had already been selected for the National Household Sample Survey 2005 (PNAD 2005), complicated probabilistic sampling by conglomerates was utilised. Eight study domains were identified in the systematic drawing, including the following age ranges: younger than one year, one to eleven years, and three additional age ranges by sex: 12 to 19 years (adolescents), 20 to 59 years (adults), and 60 years or older (senior adults). Based on a prevalence of 0.5 , a stand ard error of 0.07 at a $5 \%$ significance level, and a design effect of 1.5 , it was calculated that a minimum sample size of 300 was required in each of the six domains.

A total of 2691 people who were 12 years of age or older were chosen to respond to questions regarding sociodemographic data, life circumstances, and diet. As a result, only 1662 of the original sample's participants decided to take part. Of those, 750 volunteers gave blood for biochemical analysis, participated in two 24 -hour dietary recalls, supplied anthropometric information, and had their arterial blood pressure measured. Only adults and older adults were included in the final sample for the present study, making a total of 557 people.

A standard questionnaire was used during participant interviews by trained professionals (cardiologists, general practitioners, nutritionists, and nurses). Only modest, insignificant discrepancies in the age and sex distributions between the research population and the target population allowed us to deem the chosen sample to be representative.
3.Information on caffeine, coffee, tea, and other foods.

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Participants in the MESA Exam $1(2000-2002)$ answered a 120 -item food frequency questionnaire that was yatidated among White, African-American, and Hispanic people and modified from the Insulin Resistance Atherosclerosis Study 14,15 jt was changed to incorporate typical chinese-descent people's cuisine.Black or green tea (included together) and coffee (caffeinated and decaffeinated were not separated) intake was reported by 13 participants as never, 1-3 times per month, once per week, twice per week, five times per week, oneelper day, twice per day, four times per day, or more than six times per day. The total amount of caffeine consumed per day fromallcaffeinated foods and beverages (not only coffee and tea) was estimated in milligrammes. The amount of-total fat, carbs, red meat, vegetables, fruits, and alcohol consumed per day was measured in grammes.

## 4. DIETARY ASSESSMENT:

Dietary assessment was based on a food-frequency questionnaire (FFQ) that was approved by the Athens Medical School's Unit of Nutrition. 42 men and 38 women, ages 25 to 67 , who completed two self-administered semiquantitative FFQs within a year and a 24-hour diet recall questionnaire done by an interviewer served as the basis for the FFQ's validation. The FFQ also included confirmation of coffee use.

Two 24 HR were used to monitor the dietary intake. The multiple pass method was used by trained interviewers to administer the first 24 hours at residences; the automated multiple pass method was used to administer the second 24 hours over the phone. The multiple pass approach is composed of five steps, whether it is automated or not: (1) a quick list, in which participants list all foods and drinks consumed continuously; a forgotten list, in which participants are asked about frequently consumed forgotten foods, such as candies, coffees, and sodas; the time and place of food and beverage intake; a detailing cycle, which is a description of the method of preparation and amounts consumed; and a last-minute check to ensure that a specific meal consumed during the day wasn't already noted. Every day of the week and every season was covered by the sample days. The Nutrition Data System for Research programme (version 2007, University of Minnesota, Minneapolis, MN, USA) was used to enter dietary information. This software is mostly based on information from the food composition table issued by the United States Department of Agriculture (USDA).


## 5. ASSESSMENT OF COFFEE CONSUMPTION:



Following a question about the type of coffee preparation (filtered, instant, espresso, or other) and whether additional ingredients were typically added to the coffee (none, milk, sugar, artificial sweetener, etc.), the participants in the 24 HR reported whether they had consumed coffee on the day before the interview. According to the study's standard cup size ( 50 mL ), daily coffee consumption was divided into three categories: less than one cup per day, one to three cups per day, and three cups per day. The reference group was the category of 1 cup/day of coffee.

The Global Dietary Database (GDD)21 provided us with data on coffee consumption (cups/day/population) ( $1 \mathrm{cup}=8 \mathrm{oz}$ ) for each nation in 1990, 1995, 2000, 2005, 2010, 2015, and 2018. The GDD is an ongoing collaborative project to generate the most accurate estimates of global dietary intake to guide global health and nutrition research and policies.

## 6.STATISTICAL ANALYSIS:

Multiple logistic regression was used to analyse the relationships between habitual coffee consumption and incident CVDs, adjusting for baseline SBP as well as a number of participant demographic, anthropometric, lifestyle, general health, and socioeconomic covariates (see the Covariates section above). We utilised a continuous coffee intake indicator (cups/day) in the interaction analyses and included the quadratic term coffee 2 in the model to account for the nonlinearity due to the nonlinear connection between coffee intake and CVD. The initial SNP-by-coffee interaction model permitted interaction with both the linear and quadratic terms of coffee.

Model 1: CVD $=$ coffee + coffee $2+\mathrm{SNP}+$ coffee $\times \mathrm{SNP}+$ coffee $2 \times \mathrm{SNP}+$ other covariates
The model was then simplified to simply allow for interaction with the linear term in the absence of interaction with the quadratic term.

Model 2 : CVD $=$ coffee + coffee $2+$ SNP + coffee $\times$ SND + other eovariates.

## 7. HABITUAL COFFEE INTAKE:

Participants were asked to-answer the question, "How many cups of coffee do you drink each day? (include decaffeinated coffee)" to provide data on coffee consumption (cups/day). A additional queryr regarding the varieties of coffee was posed to the coffee drinkers. We divided the participants into seven categories based on how muçtrcoffee they consume each day, including those who don't drink it, those who drink caffeinated coffee, and those who don't (none, one, two, threefdur, five, and more cups).

The number of cups of teatconsumed each day was also disclosed. The number of cups of tea consumed.each day was also disclosed. By combining data on coffee and tea use and making the assumption that 1 cup of each beverage containgroughly. 75 and 40 mg of caffeine, respeqtively, we estimated habitual caffeine intakes (mg/day).

## 8. OUTCOME MEASUREMENTS:

## a) BLOOD PRESSURE:

During the home visit, BP was measured using an automatic blood pressure monitor. According to national and international guidelines, participants were deemed to have high blood pressure if their systolic (SBP) and/or diastolie-(DBP) values were greater than or equivalent to 140 mmHg and 90 mmHg , respectively.
b) BLOOD SAMPLE:

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After 12-hours of overnight fasting, the blood samples were drawn through venipuncture by a nursing assistant using a standardised methodology. Enzymatic-colorimetric analysis was used to assess the serum total cholesterol (TC), EDL-c and HDL-efractions, and triglyceride (TG) levels (Roche Diagnostics GmbH, Mannheim, Germany).

Reduced HDL-c $40 \mathrm{mg} / \mathrm{dL}$ in men or $50 \mathrm{mg} / \mathrm{dL}$ in women, high TC level $200 \mathrm{mg} / \mathrm{dL}$, elevated LDL-c $>100$ $\mathrm{mg} / \mathrm{d} t$, and elevated TG $150 \mathrm{mg} / \mathrm{dL}$ were all taken into consideration. Fasting plasma glucose (FPG) was tested using the glucotquant Glucose/HK kit (GLU Roche/Hitachi 1,447,513; Roche Diagnostics GmbH, Mannheim, Germany) using an enzymatic-colorimetric glucose oxídase technique. The threshold for an increased fasting blood sugar level was $100 \mathrm{mg} / \mathrm{dL}$.


Table $11_{1}^{1}$ displays the baseline participant demographics, cardiovascular risk factors, and dietary features generally and stratified by the preseence or absence of coronary artery calcium at baseline. The gender breakdown was $52.9 \%$ worm and 62.3 years of age on average. $25.0 \%, 24.0 \%$, and $50.9 \%$ of individuals reported drinking zero, one, and one cups of doffee per day, respectively. $57.6 \%$ of the partioipants said they never drank tea, while $29.5 \%$ said they drank less than one cup per day, and $12.9 \%$ said they drank less than one cup per daýs intake of tea and coffee according to ethnicity. Coronary artery calcium prevalence was $49.9 \%$, $26.5 \%$, and $23.6 \%$ for values between $\theta$ and 100, respectively. The incidence of total cardiovascular events and hard cardioyascular events over a median follow-up of-11.1 years was 10.8 and 7.5 per 1000 person-years, respectively.

TABLE:
general research population characteristics and classified by enrollment coronary artery calcium level:

|  | Overall | No CAC | CAC $>0$ | p-value |
| :---: | :---: | :---: | :---: | :---: |
| N | 6,508 | 3,249 | 3,259 |  |
| Age, years | $62.2 \pm 10.2$ | $58.0 \pm 9.1$ | $66.4 \pm 9.5$ | <0.001 |
| Male | 3,083 (47.4) | 1,200 (36.9) | 1,883 (57.8) | $<0.001$ |
| Daily coffee consumption |  |  |  | <0.001 |
| Never | 1,554 (25.0). | 833 (27.0) | 721 (23.1) |  |
| <1 cup | 1,492 (24.0) | 7.68 (24.9) | 724 (23.2) |  |
| $\geq 1$ cup | 3,159 (50,9) | 1,483 (48.1) | 1,676 (53.7) |  |
| Tea | 3.] |  |  | 0.06 |
| Never | 3,562 (57.6) | 1,722 (56.1-) | 1,840 (59:1) |  |
| <1 cup | 1,825 (29.5) | 939 (30.6) | 886 (28.4) i |  |
| $\geq 1$ cup | 800 (12.9) | 411 (13.4) | 389 (12.5) ड |  |
| Caffeine consdmption, nig/day** | $\begin{array}{\|lll} \hline 116.6 & (32.2 & - \\ 254.1) & & \end{array}$ | $\begin{array}{lll} 110.6 & (30.2 & - \\ 244.8) \end{array}$ | $\begin{aligned} & 124.1 \\ & 278.1) \end{aligned} \quad(34.2=$ | $0.18$ |
| Race |  |  |  | <0.001 |
| White | 2,540 (39.0) | 1,096 (33.7) | 1,444 (44.3) |  |
| Chinese-American | 801 (12.3) | 399 (12.3) | 402 (12.3) |  |
| Black | 1,742 (26.8) | 981 (30.2) | 761 (23.4) |  |
| Hispanic | 1,425 (21.9) | 773 (23.8) | 652 (20.0) |  |
| Educatión ${ }_{t_{1}}$ |  |  |  | 0.20 |
|  | 1,165 (17.9) | 560 (17.3) | 605 (18.6) |  |
| High school or equivalent | 3,007 (46.3) | 1,493 (46.0) | 1,514 (46.5) |  |
| College, graduate or professional sehools | 2,328 (35.8) | 1,192 (36.7) | 1,136 (34.9) |  |
| $\therefore$ Never | 3,289 (50.6) | 1,822 (56.1) | 1,467 (45.1) |  |
| $\square$ Fermer $^{\text {rem }}$ | 2,395 (36.8) | 1,010 (31.1) | 1,385 (42.5) |  |
| Current | 817 (12.6) | 413 (12.7) | 404 (12.4) |  |
| Family history of coronary heart disease | 2,607 (42.7) | 1,144 (37.2) | 1,463 (48.2) | <0.001 |
| Antinypertensive medication | 2,421 (37.2) | 925 (28.5) | 1,496 (45.9) | $<0.001$ - |
| Lipid lowering medication | 1,067 (16.4) | 349 (10.8) | 718 (22.1) | $<0.001$ |
| Weekly alcenol (number of drinks) | $2.3 \pm 5.3$ | $2.0 \pm 4.9$ | $2.6 \pm 5.6$ | $<0.001$ |
| Body massindex, kg/m ${ }^{2}$ | $28.2 \pm 5.4$ | $28.2 \pm 5.6$ | $28.3 \pm 5.3$ | 0,46 |
| Systolic blood pressure, mm Hg | $126.5 \pm 21.4$ | $122.2 \pm 20.3$ | $130.8 \pm 21.7$ | $<0.007$ |
| Diastolic blood pressure, mm Hg | $71.9 \pm 10.2$ | $71.2 \pm 10.2$ | $72.6 \pm 10.2$ | 人0.001 |
| Total cholesterol, mg/dl | $194.1 \pm 35.7$ | $193.8 \pm 34.8$ | $194.5 \pm 36.5$ | 0.39 |
| High-density lipoprotein cholesterol, $\mathrm{mg} / \mathrm{dl}$ | $51.0 \pm 14.9$ | $52.6 \pm 15.1$ | $49.5 \pm 14.5$ | <0.001 |
| Low-density lipoprotein cholesterol, $\mathrm{mg} / \mathrm{dl}$ | $117.1 \pm 31.3$ | $116.0 \pm 30.5$ | $118.3 \pm 32.1$ | $<0.01$ |
| Triglyceride, mg/dl | $131.4 \pm 86.7$ | $126.7 \pm 81.5$ | $136.1 \pm 91.4$ | $<0.001$ |
| Fibrinogen, mg/dl | $346.1 \pm 73.6$ | $338.8 \pm 70.6$ | $353.3 \pm 75.7$ | <0.001 |
| Dietary consumption |  |  |  |  |

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|  | Overall | No CAC | CAC $>\mathbf{0}$ | p-value |
| :--- | :--- | :--- | :--- | :--- |
| Total fat, g/day | $56.5 \pm 35.9$ | $57.8 \pm 37.7$ | $55.1 \pm 33.9$ | $<0.01$ |
| Total carbohydrates, g/day | $215.2 \pm 114.2$ | $218.0 \pm 118.3$ | $212.4 \pm 110.1$ | 0.05 |

Despite being higher than for men, the coffee coefficient for women was not statistically significant. Two more cups of coffee have the same impact as five cigarettes, 112 mm Hg of systolic blood pressure, $074 \mathrm{mmol} / \mathrm{l}$ of total cholesterol, or a drop of $039 \mathrm{mmol} / \mathrm{l}$ of serum HDL cholesterol. In addition to the main effects of age and total serum cholesterol concentration, an interaction term between coffee consumption and high density lipoprotein cholesterol concentration was also not significant ( $\mathrm{p}=015$ ), as well as an interaction term between coffee consumption and systolic blood pressure ( $\mathrm{p}=044$ ).

However, it should be emphasised that the relationship between coffee and coronary heart disease death was strongest in the low risk portion of the systolic blood pressure range and the supposedly high risk part of the range of high density lipoprotein cholesterol concentrations.

## CONCLUSION:



Our research demonstrates that in this cohort, moderate coffee consumption and its polyphenols were related with a decreased risk of high SBP and DBP as well as hyperhomocysteinemia. As a result, drinking coffee, a beverage high in polyphenols, in moderation may have protective effects against some clinical cardiovascular risk factors.
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Regular tea consumption was linked to a lower prevalence and advancement of coronary artery calcium as well as a lower incidence of cardiovascular events in this large, multiethnic group. Our study confirms the American Heart Association's recommendation to include regular tea consumption as part of a heart-healthy diet. 32 Contrarily, we discovered a neutral correlation between routine coffee and caffeine consumption and incident cardiovascular events, indicating that regular use is safe. To determine whether the protective link with tea intake may be exploited or if tea drinkers typically engage in healthy behaviours that weren't assessed in this study, more research is required.

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