Coffee Consumption and Cardiovascular Risk: An Updated Overview

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Coffee is one of the most widely consumed beverages worldwide. Since coffee contains caffeine, a stimulant, coffee drinking is not generally considered to be part of a healthy lifestyle. However, coffee is a rich source of antioxidants and other bioactive compounds, and many misconceptions persist regarding the health-related effects of coffee. Because of coffee is a complex beverage containing many bioactive compounds, its biological effects may be substantial and are not limited to the actions of caffeine; consequently, the health effects of chronic coffee intake are wide ranging. Coffee consumption may reduce the risk of type 2 diabetes mellitus, hypertension, obesity and depression, but it may adversely affect lipid profiles depending on how the beverage is prepared. A growing body of evidences suggests that habitual coffee consumption is neutral to beneficial regarding the risks of a variety of adverse cardiovascular outcomes including coronary heart disease, congestive heart failure, arrhythmias, and stroke; moreover, large epidemiological studies suggest that regular coffee consumption reduces risks of both cardiovascular and all-cause mortality. A daily intake of ~2-3 cups of coffee appears to be safe and is associated with neutral to beneficial effects for most of the studied health outcomes. Nevertheless, evidences on coffee’s health effects are largely based on observational data, with very few randomized, controlled studies, and association does not prove causation. Additionally, the possible advantages of regular coffee consumption must be weighed against potential risks, mostly related to its caffeine content, such as anxiety, insomnia, tremulousness, palpitations, bone loss and fractures.

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widespread popularity, and many misconceptions persist regarding
the health-related effects of coffee[27].

Considerable attention has been focused on the possibility that
coffee may increase the risk of heart disease[22-23], particularly since
drinking coffee has been associated with increased low-density
lipoprotein cholesterol levels[7] and short-term increases in blood
pressure[20].

The relationship between coffee consumption and risk of
coronary heart disease (CHD) was first studied in the 1960s, given
that the prevalences of both drinking coffee and CHD were high
in Western countries[11]. Short-term metabolic studies found that
caffeine ingestion acutely induces cardiac arrhythmias and increases
plasma renin activity, catecholamine concentrations, and blood
pressure[12,13]. In the 1980s, cross-sectional studies found a positive
association between coffee consumption and serum total cholesterol
concentrations, which might be related to the coffee brewing method
(i.e., boiled or unfiltered coffee)[14]. A later randomized trial showed
that boiled coffee consumption increased serum cholesterol[15]. From
the 1980s to the 2000s, many case-control studies, which are prone
to recall and selection bias, showed a positive association between
coffee consumption and CHD risk[14,16]. In contrast, meta-analyses
of prospective cohort studies tended to find no association, although
results varied substantially across studies[17-19].

Since 2000, the associations between coffee consumption and
other cardiovascular disease (CVD) outcomes such as stroke, heart
failure, and total CVD mortality have also been more frequently
studied[26,21-23]. Meta-analyses have been published to summarize the
association between coffee and risk of CHD[22], stroke[23], and heart
failure[24], and these meta-analyses did not support an association
between coffee consumption and a higher CVD risk.

Additional studies have been published since the publication of
these meta-analyses[20,21,21,23,24], and another recent meta-analysis
showed that heavy coffee consumption was not associated with
risk of CVD mortality[25]. Therefore, the association between coffee
consumption and CVD risk remains unclear.

**BIOLOGICALLY ACTIVE CONSTITUENTS OF COFFEE**

Coffee is a complex beverage containing >1,000 compounds:
among the many with known biological activity are caffeine (a
potent stimulant and bronchodilator), diterpene alcohols (which can
increase serum cholesterol), and chlorogenic acid (one of many types
of antioxidant and anti-inflammatory compounds found in coffee).
Caffeine is by far the most studied compound, and this agent
largely accounts for the inherently habit-forming nature of the
beverage[25].

Coffee accounts for 71% of caffeine intake among American
adults (soft drinks are the primary source of caffeine for children and
adolescents)[29]. The caffeine content of coffee is highly variable,
even when the coffee beverage is obtained from the same outlet[30].
A standard 8-oz cup of brewed coffee can contain anywhere from
~95 to 200 mg of caffeine. However, coffee is increasingly served
in containers that are considerably larger (e.g., 12 to 16 oz), typically
delivering 180 to 300 mg of caffeine per serving[31]. Brewed
decaffeinated coffee still contains caffeine, albeit at much lower
doses that usually range from 5 to 15 mg per 8 oz.

**COFFEE AND BLOOD PRESSURE**

Coffee consumption has been associated with acute increases in
blood pressure (BP) in caffeine-naïve people but exerts negligible
effects on the long-term levels of BP in habitual coffee drinkers[32].
The acute effects of coffee are transient, and, with regular intake,
tolerance develops to the hemodynamic and humoral effects of
caffeine[33].

A recent meta-analysis showed no clinically important effects of
long-term coffee consumption on BP or risk of hypertension (HTN)
[15], and the Nurses’ Health Study also demonstrated that daily intake
of up to 6 cups of coffee was not associated with an increased risk of
HTN[34].

Furthermore, caffeine is the major acute BP-increasing compound
found in coffee but other compounds present in coffee may counteract
these acute pressor effects: in consequence, caffeine is not solely responsible for the cardiovascular effects associated with short
and long-term coffee consumption[30].

**COFFEE AND CARDIOMETABOLIC DISEASE**

Antioxidants in coffee, such as chlorogenic acid, have been recognized
to improve glucose metabolism and insulin sensitivity[37]. A recently
published randomized study found that consumption of 5 cups of
coffee per day increased adiponectin levels and decreased insulin
resistance[38]. Caffeine acutely activates 50-adenosine monophosphate–
activated protein kinase and insulin-independent glucose transport in
skeletal muscle[39]. A systematic review with meta-analysis showed
that the risk of the development of type 2 diabetes mellitus (T2DM)
was lowest in subjects who drank >6 cups daily and also was
significantly reduced for subjects who consumed 4 to 6 cups Daily[40].
Furthermore, a prospective study established a linear relationship of
coffee consumption with the reduction in T2DM, whereby even small
amounts of coffee on a daily basis conferred benefit[41]. Associations
were similar for decaffeinated and caffeinated coffee.

Coffee contains cholesterol-increasing compounds classified as
diterpenes, including cafestol and kahweol[42]. Importantly,
the concentration of these compounds depends on how coffee is
prepared. Boiled coffee has higher concentrations because diterpenes
are extracted from the coffee beans by prolonged contact with hot
water. By comparison, brewed/filtered coffee, because of the much
shorter contact with hot water and retention of diterpenes by filter
paper, has a much lower concentration of cafestol and kahweol.
In a study of 107 young adults with normal cholesterol levels
followed for 12 weeks a significant increase in total cholesterol and a
nonsignificant increase in low-density lipoprotein (LDL) cholesterol
were observed in participants consuming boiled coffee, whereas there
was no significant difference in the change in serum total or LDL
cholesterol levels between the filtered-coffee group and the group
who drank no coffee[43], and these results were replicated in a meta-
analysis and in a large cohort study[44,45].

**COFFEE AND CARDIOVASCULAR DISEASE**

Although some early studies[53], probably flawed by unmeasured
covariates[144], suggested coffee consumption might cause adverse
vascular effects, many epidemiological studies have evaluated
the potential effects of coffee on CHD generally showing neutral
effects. In particular, the meta-analysis performed by Wu et al[39]
including 21 independent prospective cohort studies from January
1966 to January 2008 suggested that moderate coffee consumption
may decrease the long-term risk of CHD compared with the light-
to-absent coffee consumption (<1 cup/day in the United States or
≤2 cups/day in Europe), moderate coffee consumption (>1 or 2 cups
daily, respectively) was associated with significantly lower rates of
CHD in the entire group of men and women.
Furthermore, several studies have suggested that it is safe for patients with established CHD to continue their habitual coffee consumption\[48,49\]: coffee ingestion was associated with an increase in parasympathetic tone\[47\] and a decrease in high-sensitivity C-reactive protein levels\[45\].

In regard to congestive heart failure (CHF), a recent large meta-analysis performed by Mostofsky et al\[53\] reported a J-shaped relationship between coffee consumption and the incidence of CHF: a statistically significant association between coffee and CHF was observed, with the strongest inverse association noted for 4 servings per day with increased CHF risks for both higher and lower levels of coffee consumption, with no evidence that the relationship varied by sex or by baseline history of myocardial infarction or diabetes.

Data linking coffee consumption to increased risk of arrhythmias are inconsistent. Recent studies have suggested that coffee appears not to increase arrhythmias; to the contrary, long-term coffee drinking might actually reduce the risk of abnormal cardiac rhythms. In a recent Kaiser Permanente study of adults living in California, an inverse relationship between habitual coffee consumption and risk of hospitalization for arrhythmia was observed during long-term follow-up, and the authors concluded that people who drank 4 cups of coffee per day tended to have fewer cardiac arrhythmias, including less atrial fibrillation (AF)\[40\]. Moreover, controlled interventional studies and placebo-controlled trials show that in normal adults even high-dose caffeine in isolation does not affect prevailing cardiac rhythm and rate and also does not cause and/or worsen clinically significant ventricular or supraventricular arrhythmia\[50-52\]. In the Women’s Health Study, In the Danish Diet, Cancer, and Health study, and in the Framingham Heart Study caffeine consumption was not associated with the risk of the development of AF or flutter\[53-56\].

The mechanisms conferring potential protection against arrhythmias are still largely unknown, but according to 1 hypothesis, caffeine inhibits adenosine in the heart, as it does in the brain. Endogenously secreted adenosine affects cardiac electrical conduction and cardiomyocyte repolarization and may cause shortening of the atrial and ventricular refractory periods, thereby predisposing to arrhythmias. Caffeinated coffee intake could theoretically confer cardioprotection by attenuating these negative effects of endogenous adenosine\[49\].

### COFFEE AND STROKE

Coffee may reduce the risk of ischemic stroke. A recent meta-analysis performed by D’Elia et al\[57\] demonstrated that 1 to 3 and 3 to 6 cups of coffee per day were associated with a decreased risk of stroke, whereas habitual consumption of ≥6 cups of coffee per day was not associated with any effect on stroke risk, and the authors concluded that coffee consumption is not associated with a higher risk of stroke and that habitual moderate consumption may exert a protective effect\[58\]. In the Swedish Mammography Cohort\[59\] the findings also suggested that coffee consumption was associated with a statistically significant lower risk of stroke, and the inverse association of coffee consumption and mortality from stroke was also observed in a diabetic population\[60\] and in the Nurses’ Health Study\[61\]. Exactly how coffee lowers the risk of stroke is unknown, but postulated mechanisms include coffee’s anti-inflammatory and insulin-sensitizing effects\[62,64\].

### COFFEE AND MORTALITY

In the National Health and Nutrition Examination Survey I\[65\], coffee intake of participants who were 65 years of age or older exhibited a dose-response protective effect whereby increasing habitual consumption of coffee was associated with lower risk of adverse cardiovascular events and heart disease mortality.

In another study performed by Lopez-Garcia et al\[66\] an inverse association between coffee consumption and all-cause mortality was seen mainly due to a moderately reduced risk of CVD mortality and was independent of caffeine intake; decaffeinated coffee was also associated with a small reduction in all-cause and CVD mortality.

Furthermore, in the recent National Institutes of Health-AARP Diet and Health Study\[67\], after adjustment for tobacco smoking and other potential confounders, men who drank ≥6 cups of coffee per day had a 10% lower risk of death and women had a 15% lower risk, irrespective of whether they drank caffeinated or decaffeinated coffee; inverse associations were observed for deaths due to heart disease, respiratory disease, stroke, injuries and accidents, diabetes, and infections, but not for deaths due to cancer.

### COFFEE AND THE “U-SHAPED” ASSOCIATION

A very recent meta-analysis performed by Ding et al\[68\] demonstrated a nonlinear association between coffee consumption and risk of CVD (CHD and stroke): moderate coffee consumption (3-5 cups per day) was associated with lower CVD risk, and heavy coffee consumption (≥6 cups per day) was neither associated with a higher nor a lower risk of CVD.

The authors suggest that this kind of relationship might be due to a combination of beneficial and detrimental effects: for moderate coffee consumption, beneficial effects may be greater than adverse effects, whereas for heavy consumption detrimental effects may counterbalance beneficial effects.

Furthermore, no significant association between decaffeinated coffee consumption and CVD risk was observed: nevertheless, the consumption of decaffeinated coffee was much lower than caffeinated coffee and individuals with hypertension or other CVD-related conditions might switch from regular coffee to decaffeinated coffee.

### COFFEE AND OTHER HEALTH EFFECTS

Coffee may reduce the risk of depression, a known risk factor for the development of CVD, as well as an independent predictor of poor prognosis\[69\]: the effect may be due largely to the caffeine content because women consuming decaffeinated coffee did not show a reduced risk\[70\].

Coffee consumption may also benefit efforts at weight control, increasing the thermic effect of food and fat oxidation in normal-weight subjects\[71\].

Other beneficial health effects may include reduced risks of Alzheimer’s dementia\[70,71\] and other diseases of the central nervous system including Parkinson’s disease\[71-73\]. Additionally, coffee may improve asthma symptoms\[74\], enhance performance in sustained high-intensity exercise\[75\], prevent symptomatic gallstones\[76\] and be associated with protection against some infectious and malignant diseases, particularly of the liver\[77-79\].

In contrast, many individuals experience palpitations, anxiety, tremulousness, and trouble sleeping after drinking coffee, particularly when it contains higher doses of caffeine\[80\]. Moreover, caffeinated coffee increases the risk of bone loss and fractures, even if it has been estimated that the amount of calcium lost from consuming 1 cup of coffee can be offset by mixing in just 2 tablespoons of milk and also that a daily glass of milk might offset the calcium loss and reductions in bone mineral density due to coffee consumption\[81-83\].
Furthermore, people who consume coffee typically do so on a daily basis, often due to caffeine dependence. Caffeine is a central nervous system stimulant, and its regular use typically causes mild physical dependence as evidenced by the development of tolerance, withdrawal symptoms (headaches, irritability, fatigue, depressed mood, anxiety, and difficulty concentrating), and cravings with abstinence.[4][5]

CONCLUSION

According to the existing literature, the currently available evidence on cardiovascular effects related to habitual coffee consumption is largely reassuring. Coffee can be included as part of a healthy diet for the general public and also for those with increased cardiovascular risk or CVD. Those with dyslipidemia may consider brewed and filtered coffee as opposed to preparations made from boiling beans without filtering. A daily intake of ~2-3 cups of coffee appears to be safe and is associated with neutral to beneficial effects for most of the studied health outcomes.

While many of coffee’s benefits probably derive from its caffeine content, decaffeinated coffee seems to offer some health benefits too and may be a reasonable option for those who experience uncomfortable effects from caffeine stimulation. Drinkers of decaffeinated coffee in particular might be advised to ensure adequate calcium consumption from dietary sources to guard against potential adverse outcomes related to bone health. On the other hand, Decaffeinated coffee may be a good option, particularly because many of coffee’s potential benefits likely derive from sources other than its caffeine.

Finally, it is possible that individuals who consume coffee differ in other important dietary and sociological aspects from the nonconsumers. Therefore, the possibility that coffee consumption may be acting as a surrogate marker of some other dietary or lifestyle risk factor cannot be fully excluded.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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