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Archivio istituzionale della ricerca

Cardiovascular health and coffee: Insights from a recent cohort study

This is the final peer-reviewed author's accepted manuscript (postprint) of the following publication:

Published Version:

Mattioli, A.V. (2025). Cardiovascular health and coffee: Insights from a recent cohort study. NMCD. NUTRITION METABOLISM AND CARDIOVASCULAR DISEASES, 35(10), 1-3 [10.1016/j.numecd.2025.104115].

Availability:

This version is available at: <https://hdl.handle.net/11585/1018725> since: 2026-06-15

Published:

DOI: <http://doi.org/10.1016/j.numecd.2025.104115>

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Reassessing Coffee's Role in Cardiovascular Health: Insights from a Recent Cohort Study

Abstract

Coffee consumption has long been a subject of debate in cardiovascular health, with concerns over its potential pro-arrhythmic effects and transient increases in blood pressure. The recent study by Zhou et al. provides compelling evidence that moderate coffee intake (1–3 cups per day) is associated with reduced all-cause and cardiovascular mortality, particularly among individuals with pre-existing cardiovascular and cerebrovascular diseases. This commentary expands on the study's findings, highlighting potential mechanisms of protection, including anti-inflammatory and antioxidant effects, as well as its impact on endothelial function and metabolism. Additionally, it underscores key knowledge gaps, such as the influence of brewing methods, genetic variability in caffeine metabolism, and sex differences in cardiovascular responses to coffee consumption. While habitual coffee intake appears safe and potentially beneficial for most individuals, further research is needed to refine personalized recommendations based on genetic, hormonal, and metabolic differences. Given coffee's widespread consumption, incorporating these insights into clinical guidelines and public health recommendations could have significant implications for disease prevention and management.

Keywords

Coffee, cardiovascular disease, mortality, caffeine metabolism, sex differences, endothelial function, arrhythmias, inflammation, antioxidants, public health.

The study by Zhou et al. makes a valuable contribution to the ongoing discussion about the health effects of coffee consumption, particularly in individuals with cardiovascular and cerebrovascular diseases (CVD). [1] While several studies have explored the relationship between coffee intake and overall mortality, this research stands out by focusing on a population with pre-existing cardiovascular conditions. [2,3] Using data from the NHANES database, the authors provide compelling evidence that moderate coffee consumption—specifically, 1 to 3 cups per day—is associated with a significant reduction in all-cause and cardiovascular-related mortality. This study strengthens the growing body of literature suggesting that coffee may play a protective role in cardiovascular health. [1] By applying multivariate Cox regression and competitive risk models, the authors have ensured that their findings are statistically robust, accounting for key confounders such as smoking, hyperlipidemia, and diabetes. A particularly interesting aspect of their results is the dose-response relationship they observed: while moderate coffee consumption was associated with a 25% lower risk of all-cause mortality and a 35% reduction in CVD-related deaths, consuming more than 4 cups per day did not provide additional benefits. This finding reinforces the notion that moderation is key, even when it comes to potentially beneficial dietary habits. [4,5]

From a clinical perspective, these results have important implications. [4,5] Historically, coffee consumption has been approached with caution, particularly for subjects at high risk for cardiovascular diseases, due to some concerns; i.e. about its potential pro-arrhythmic effects, transient increases in blood pressure, and its influence on autonomic cardiac regulation. [6,7] The Brisighella Heart Study analyzed the epidemiological association between coffee consumption and both peripheral and central blood pressure, as well as arterial stiffness parameters. The findings suggest that moderate coffee intake is associated with lower systolic blood pressure (SBP), pulse pressure (PP), aortic BP, and aortic PP compared to non-coffee drinkers. Interestingly, individuals consuming 2 or more

cups per day showed more favorable blood pressure profiles, indicating that concerns about coffee-induced hypertension may be overestimated, particularly with moderate consumption. [8]

Caffeine, the primary bioactive compound in coffee, is known to stimulate the sympathetic nervous system, which can lead to increased heart rate, elevated blood pressure, and heightened myocardial excitability. [7] In some individuals, particularly those with underlying cardiac conditions such as atrial fibrillation (AF), ventricular arrhythmias, or heart failure, excessive caffeine intake has been suspected to trigger or exacerbate arrhythmic events by promoting adrenergic stimulation and altering intracellular calcium handling in cardiomyocytes. [7,8]

Despite these concerns, accumulating evidence suggests that habitual coffee consumption does not appear to significantly increase arrhythmic risk in the general population, and in some cases, it may even be neutral or mildly protective. [8] Studies have indicated that moderate coffee intake may be associated with a lower incidence of AF and a reduced risk of sudden cardiac death, possibly due to its antioxidant properties, anti-inflammatory effects, and favorable impact on endothelial function. [8,9] The potential mechanisms behind these benefits may involve coffee's role in enhancing nitric oxide (NO) bioavailability, reducing oxidative stress, and stimulating glucagon-like peptide-1 (GLP-1) secretion, all of which contribute to better vascular health. [10,11] Another noteworthy finding is that the protective effect of coffee appeared to be more pronounced among smokers, raising intriguing questions about potential interactions between caffeine metabolism and oxidative stress in high-risk populations. [12] Given that smoking is a major contributor to endothelial dysfunction and increased cardiovascular risk, it is possible that certain compounds in coffee, such as polyphenols, may counteract some of the oxidative damage associated with tobacco use. While this does not suggest that coffee can offset the harms of smoking, it highlights the need for further research into how

coffee's bioactive components influence different metabolic pathways in high-risk individuals. However, individual responses to caffeine can vary significantly based on genetic predisposition, underlying cardiovascular status, and caffeine metabolism rates. [13]

Despite these promising findings, several critical questions remain unanswered, warranting further investigation to fully understand the relationship between coffee consumption and cardiovascular health. One of the most pressing uncertainties concerns the specific bioactive compounds responsible for the observed protective effects. Coffee is a complex beverage containing caffeine, polyphenols, diterpenes, melanoidins, and other bioactive molecules, each of which may exert distinct physiological effects. [12,13,14] While caffeine is often considered the primary active ingredient, recent studies suggest that polyphenols—such as chlorogenic acid—may play a more significant role in reducing inflammation, improving endothelial function, and enhancing insulin sensitivity. [12-15] The independent and synergistic effects of these compounds remain poorly understood, making it essential to disentangle their specific contributions to cardiovascular health. Another crucial aspect that this study does not address is the impact of different brewing methods and coffee types on cardiovascular outcomes. The preparation of coffee—whether filtered, unfiltered, espresso, French press, or instant—can influence its chemical composition and, consequently, its health effects. [7,10,13,14] For example, unfiltered coffee, such as French press or Turkish coffee, contains higher levels of diterpenes like cafestol and kahweol, which have been shown to increase LDL cholesterol levels and could potentially counteract some of coffee's cardiovascular benefits. Conversely, filtered coffee significantly reduces diterpene content, which may result in a more favorable lipid profile. [7,10,13,14] Understanding how different brewing techniques alter coffee's cardiovascular

impact is crucial for refining dietary recommendations, particularly for individuals at high risk of dyslipidemia or atherosclerosis.[15,16]

Similarly, the distinction between caffeinated and decaffeinated coffee warrants further exploration. Caffeine is well-known for its stimulatory effects on the central nervous system and metabolism, On the other hand, decaffeinated coffee retains many of the beneficial polyphenols without the stimulant effects, making it a potentially safer option for caffeine-sensitive individuals. Some studies suggest that decaffeinated coffee may still offer cardiovascular protection, but whether it confers the same degree of benefit as regular coffee remains unclear. [2,15]

Furthermore, it is important to note that many epidemiological studies, including the manuscript by Zhou H and coworkers [1], use a single self-reported dietary assessment to estimate long-term exposure. This assumes that individuals maintain the same consumption levels over decades, which may not be methodologically precise. Such an approach, while common, could introduce potential biases due to changes in dietary habits over time. To improve accuracy, it would be appropriate to integrate repeated dietary assessments into long-term studies

Beyond the physiological effects of coffee's individual components, genetic variability in caffeine metabolism also plays a crucial role in determining its health impact. Variations in the CYP1A2 gene, which encodes the primary liver enzyme responsible for caffeine metabolism, influence how quickly individuals process and eliminate caffeine from their bodies. Slow metabolizers may experience prolonged caffeine exposure, which could heighten the risk of hypertension, arrhythmias, and other cardiovascular effects, while fast metabolizers may tolerate higher caffeine intake without significant cardiovascular consequences. [17,18] A growing body of evidence suggests that sex differences may play a role in coffee metabolism and its cardiovascular effects, yet this aspect remains largely

unexplored in the current study. Women, particularly premenopausal women, may metabolize caffeine differently than men due to the influence of estrogen on CYP1A2 enzyme activity, which is responsible for caffeine breakdown. [19,20] Additionally, hormonal fluctuations across the menstrual cycle and the impact of oral contraceptive use or hormone replacement therapy may alter caffeine clearance rates and modify cardiovascular responses to coffee consumption. [21] These differences could potentially contribute to variations in blood pressure regulation, endothelial function, and arrhythmic risk between men and women. [19]

Future research should incorporate sex-stratified analyses to determine whether coffee's cardioprotective effects differ between men and women and whether specific subgroups, such as postmenopausal women, may derive greater or lesser benefits from coffee consumption.

Finally, long-term prospective studies are needed to assess the lifelong impact of habitual coffee consumption on cardiovascular health, particularly in high-risk populations such as elderly individuals, patients with advanced heart disease, and those with metabolic disorders. While current findings suggest a protective role for moderate coffee intake, additional data are needed to clarify the ideal dosage, frequency, and form of coffee that maximizes benefits while minimizing potential risks. Overall, this study provides strong evidence that moderate coffee consumption is not only safe but may also be beneficial for individuals with cardiovascular disease. While additional research is needed to refine clinical recommendations, these findings suggest that coffee could be considered as part of a heart-healthy diet rather than being unnecessarily restricted. Given the widespread consumption of coffee worldwide, incorporating these insights into public health messaging and dietary counseling could have significant implications for disease prevention and management.

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