American Journal of Hypertension, 2026, **39(7)**, 840–843
https://doi.org/10.1093/ajh/hpag028
Published: April 19, 2026
Debate

OXFORD

Debating coffee and hypertension: coffee does not increase the risk of chronic hypertension

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Key words: **coffee; blood pressure; cardiovascular risk; sympathetic nervous system.**

Background

There is no documented evidence regarding when and how coffee beverages first began to be consumed by humans. *Coffea arabica* and *Coffea canephora*, the two main plant species from which coffee beans are obtained, were known and documented in Ethiopia since the early 14th century. Since then, coffee beverages, with their legends and history, have become among the most popular drinks consumed globally.

Over the years, the effects of coffee on different organs of the human body have been studied extensively. Evidence from these studies, including the information highlighted in a recent review published in *The New England Journal of Medicine*,[1] demonstrates the widespread impact of caffeine intake on multiple organ systems. The cardiovascular and cardiometabolic effects of caffeinated beverages include antioxidant, anti-inflammatory, lipid-modulating, insulin-sensitizing, and thermogenic actions.[2] These mechanisms are believed to contribute to the observed reduction in all-cause mortality following coffee consumption, with the largest risk reduction occurring at moderate levels of consumption.

Despite the large amounts of evidence on the cardiovascular effects of coffee consumption, some aspects remain controversial. This is the case, for example, for the debated issue concerning the effects of caffeinated coffee on cardiac arrhythmias. Indeed, a recent paper did not show any pro-arrhythmogenic effects of coffee.[3] Another debated issue concerns the impact of regular coffee intake on blood pressure (BP). Professor Paolo Palatini and I have been invited by the Editor of the Journal to present a brief debate outlining the pros and cons related to the pressor effects of habitual coffee consumption on chronic hypertension and, more broadly, its influence on cardiovascular risk in the population with high BP values. My arguments supporting the cons are presented below.

Acute effects of coffee on blood pressure

The acute consumption of caffeinated coffee triggers a rise in BP, which appears to be mediated by sympathetic activation, as demonstrated by the increases in venous plasma norepinephrine levels and efferent postganglionic muscle sympathetic nerve activity reported in different studies.[4,5] However, this pressor response has not consistently been observed across studies, as some reports have found no significant BP elevation following acute coffee intake.[6,7] One interesting hypothesis proposed to explain this heterogeneity suggests that this hemodynamic alteration is detectable primarily in non-habitual coffee drinkers, but not in habitual coffee drinkers. Additionally, it is interesting to note that decaffeinated coffee has also been shown to increase BP and sympathetic drive in non-habitual drinkers. Taken together, these findings suggest that: (1) differences in habitual coffee consumption may lead to variations in acute BP responses, and (2) caffeine *per se* may not be responsible for the pressor effect, with the other components of coffee potentially playing a role in its acute impact on BP (if any).

Chronic effects of coffee on blood pressure

The vast majority of published studies examining the chronic effects of coffee consumption on BP have been based on cross-sectional designs and have relied primarily on office BP measurements. The results of these studies, which have also been included in several meta-analyses, have been heterogeneous, showing that habitual coffee consumption may be associated with augmented, unchanged, or even reduced BP values.[8–15] Our group had the opportunity to reassess the relationship between BP and coffee consumption by analyzing data collected from the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study.[16] This investigation, started in 1990, was carried out in a large sample of subjects representative

Received: February 2, 2026. **Revised:** February 23, 2026. **Accepted:** March 23, 2026

of the general population of Monza (town near Milan, Italy) with respect to gender and age distribution. A total of 3200 subjects were recruited, and 2054 (64% of the original sample) agreed to participate. The study design can be summarized as follows. For each participant, several variables were collected, including clinic, home, and ambulatory BP. Medical history, with special focus on the family and personal history of cardiovascular risk factors and events, drug therapy, and psychosocial variables, was also collected. Two follow-up surveys were planned to obtain longitudinal data. The first follow-up was conducted approximately 10 years after the original survey, that is, between 2001 and 2003, and included 2051 participants, representing about 70% of the original sample. The final follow-up was carried out between 2017 and 2018 in 562 participants, who underwent the same measurements as in the first two surveys. Data on fatal and non-fatal cardiovascular events, including stroke, myocardial infarction, and heart failure, were also collected.

This study design allowed the assessment of the relationships between coffee consumption, long-term BP levels across decades, the development of hypertension, and the risk of cardiovascular events. All analyses were adjusted for confounders such as alcohol intake, cigarette smoking, and physical activity levels. The main findings were as follows. First, sphygmomanometric clinic BP values were not increased in habitual coffee consumers. Instead, these values were slightly but significantly lower (particularly for the systolic component) in individuals consuming three or more cups of coffee per day when compared with non-consumers. The lack of a coffee-induced pressor effect and the superimposability of BP in coffee consumers and non-consumers were confirmed by home BP measurements and 24-hour ambulatory BP monitoring.[17] The analysis of the 24-hour BP profile also demonstrated similar daytime and nighttime absolute BP values in individuals consuming more than three cups of coffee per day as compared with non-consumers (Figure 1). A similar pattern was observed for 24-hour systolic and diastolic BP variability, a

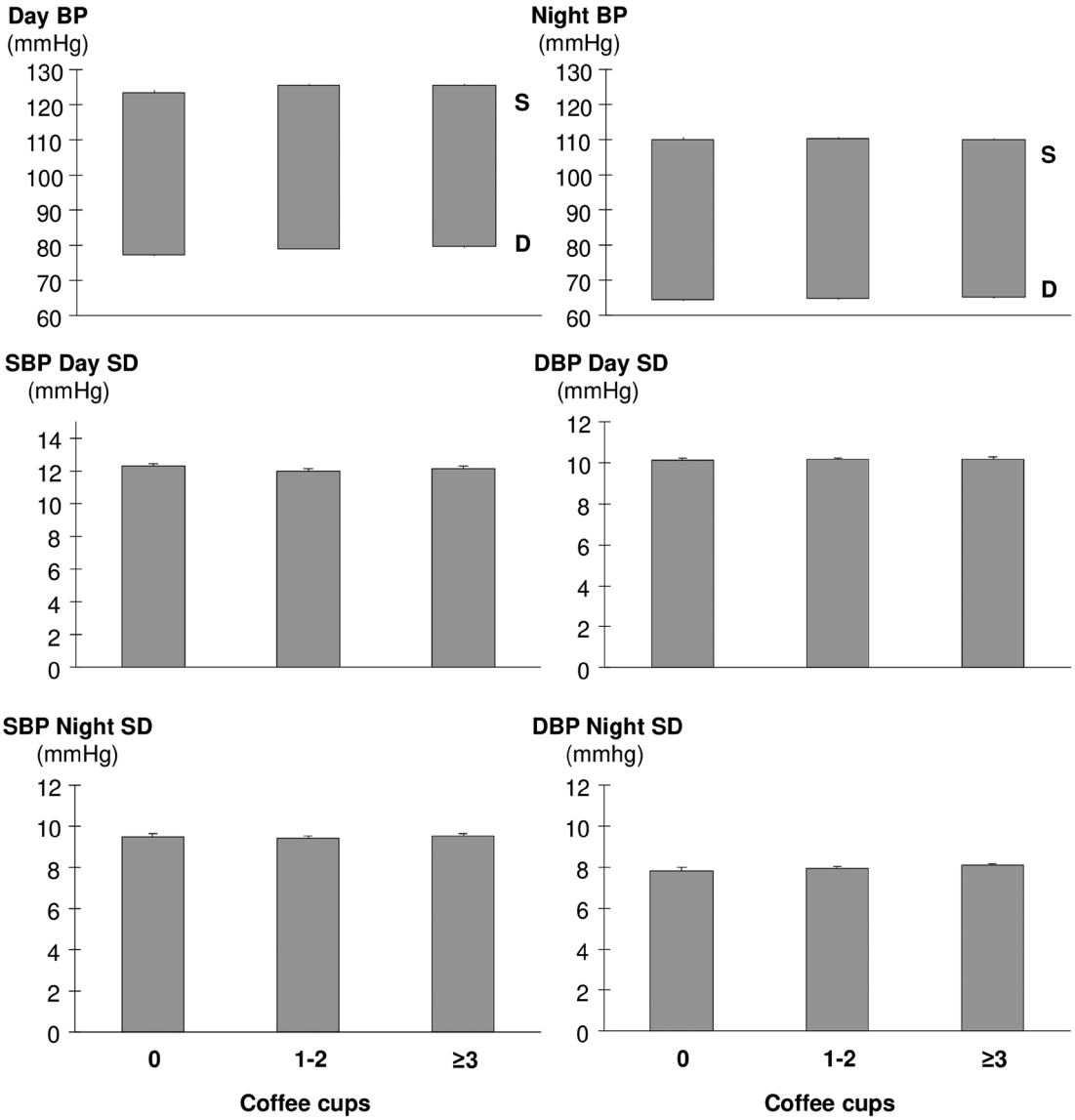

Figure 1 *Upper panels*: Daytime and nighttime systolic (S) and diastolic (D) blood pressure (BP) levels in the PAMELA study population subdivided into three groups based on the number of cups of coffee consumed per day. *Middle panels*: Daytime systolic and diastolic blood pressure (SBP and DBP) (standard deviation) in the PAMELA study population subdivided into three groups based on the number of cups of coffee consumed per day. *Lower panels*: Nighttime SBP and DBP (standard deviation) in the PAMELA study population subdivided into three groups based on the number of cups of coffee consumed per day. Note the lack of significant differences among groups (original figure prepared using data from Quarti-Trevano et al.[17]).

parameter that is closely associated with subclinical organ damage and cardiovascular events, independent of absolute BP load (Figure 1).

As mentioned above, the PAMELA study also allowed us to determine the long-term effects of coffee consumption on BP through a 10-year prospective analysis.[18] The longitudinal data showed comparable BP changes during the 10-year follow-up with heavy, moderate, and no coffee consumption. Similarly, no significant differences in the incidence of new-onset hypertension were observed during the follow-up, as demonstrated by the assessment of both office and out-of-office BP values.

Coffee consumption and cardiovascular events

The design of the PAMELA study also allowed us to assess the effects of coffee consumption on cardiovascular and all-cause mortality in individuals with hypertension over a prolonged follow-up period of 25 years.[19] Analyses adjusted for the afore mentioned confounding factors revealed no significant differences in the hazard ratios for cardiovascular and total fatal events between coffee consumers and non-consumers during follow-up. These findings remained unchanged even when 24-hour ambulatory BP measurements, rather than office sphygmomanometric BP values, were used to define the development of new-onset hypertension.

Coffee consumption, blood pressure, and sympathetic activity

Over the years, several hypotheses have been proposed to physiologically or pathophysiologically explain the heterogeneity of BP responses to coffee consumption observed across different study populations. One such hypothesis suggests that the presence of sympathetic overactivity may predispose individuals to the pressor effects of coffee. Our group is currently testing this hypothesis by analyzing PAMELA data and using resting heart rate values as a surrogate marker of sympathetic activity.[20] More specifically, we are stratifying the PAMELA population of coffee consumers according to resting heart rate values below or above 80 beats per minute. This threshold was selected based on findings from our previous study,[21] which demonstrated that hypertensive patients with resting heart rate values above 80 beats/minute exhibit significantly increased muscle sympathetic nerve activity, as measured by microneurography, compared with individuals with lower resting heart rates (below 80 beats/minute).

Conclusions

The findings discussed in this paper provide documented evidence supporting the neutral effects of chronic coffee consumption on BP. It is likely that the effects of coffee depend on the balance between its oxidative vasodilatory properties and its sympathetically mediated vasoconstrictive actions. Due to this balance, BP values remain unaffected by chronic coffee consumption.

Acknowledgments

None declared.

Funding

None declared.

Conflicts of interest

None declared.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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https://doi.org/10.1093/ajh/hpag028
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