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COMMENTARY

Coffee and health: explaining conflicting results in hypertension

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It is well established that dietary intake and other lifestyle factors play an important role in hypertension.[1] Available evidence suggests hypertensive patients should follow a weight-reducing diet, restrict alcohol and salt intake, reduce smoking and incorporate regular physical activity into their lifestyle. Another area of much interest relates to the impact of coffee consumption on blood pressure (BP), which was first debated nearly 30 years ago.[2] Coffee is one of the most widely consumed non-alcoholic beverages in Western society, although research pertaining to its effects on health, and particularly hypertension, remains equivocal.

Previously reviewed evidence from a variety of cross-sectional and longitudinal epidemiologic studies of the effects of coffee consumption on BP appear to be inconsistent, demonstrating no effects, positive relations and inverse relations.[3] There are only two prospective cohort studies to date that have examined the influence of coffee intake on the risk of hypertension development, which present conflicting findings. Winkelmayer *et al.*[4] demonstrated no relationship between coffee intake and incident hypertension in 155 594 US women followed up over 12 years. However, in a cohort of 1017 men followed up over 33 years, coffee drinkers had a greater incidence of hypertension in unadjusted analyses and consumption of one cup of coffee significantly raised systolic and diastolic BP by 0.19 and 0.27 mm Hg, respectively, in adjusted models.[5] The nonsignificant association with incident hypertension after multivariate adjustment may therefore suggest that coffee drinking plays only a minor role. However, a confounding problem with such prospective studies is that individuals with heightened BP may be advised to moderate their coffee intake, thus impacting upon the findings.

Recent meta-analyses that have examined the influence of coffee and caffeine intake on BP from randomized controlled trials (RCTs) also present conflicting findings. In an analysis of 11 trials, the BP effects of coffee were estimated as 2.4 and 1.2 mm Hg for systolic and diastolic BP, respectively, compared with the non-coffee groups,[6] which contrasts with smaller effects of 1.22 and 0.49 mm Hg in a larger meta-analysis of 16 studies.[7] The mean treatment duration was similar in both analyses, although mean caffeine dosage was higher in the earlier study[6] (see Table 1), which may explain the discrepancy in effect size. Hypertensive status, genetic vulnerability to hypertension and interactions with smoking and mental stress may also be important. A small amount of evidence suggests that pressor responses to coffee are exaggerated in hypertensives and additive in combination with smoking or mental stress,[3] although in stratified analyses, baseline BP was not associated with effects of coffee on BP in RCTs.[7] Also a recent finding demonstrated that acute administration of coffee resulted in blunted BP responses to mental stress among habitual coffee consumers but was enhanced among non-drinkers.[8] These effects were independent of caffeine and also demonstrate the potential importance of habituation.

Of note, the effects of coffee on vascular function have been examined as a mechanism of hypertension risk. Recent interest has focused on the association between coffee consumption and inflammatory molecules such as C-reactive protein and interleukin-6, which are indicators of vascular inflammation and therefore have relevance to hypertension.[9] Tsioufis *et al.*[10] demonstrated an association between heavy coffee consumption (>4 cups/day) and inflammatory processes in a small sample of Greek hypertensive smokers, which was supported by cross-sectional findings from a larger study of over 3000 healthy Greek men and women.[11] In contrast, other recent reports suggest that coffee has anti-oxidant properties[12] and ingredients such as flavonoids, potassium, magnesium and chlorogenic acid that could exert anti-inflammatory effects and lower the risk of type II diabetes[13] and other inflammatory diseases.[14] Other studies have used direct measures of vascular function. In a cross-sectional study of 228 healthy Greek men and women, chronic coffee consumption was associated

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Table 1 Key studies in the association of coffee and hypertension

Study	*Subjects and design*	*Findings*	*Comments*
Winkelmayer *et al.*[4]	Prospective cohort: 155 594 US ♀ followed up for 12 years for incident hypertension. Coffee intake assessed from FFQ	Coffee consumption not associated with incident hypertension.[a,b] Inverse U-shaped association between caffeine and hypertension	Association for caffeinated tea intake and cola with hypertension
Klag *et al.*[5]	Prospective cohort: 1017 US ♂ followed up annually for 33 years for incident hypertension and BP. Coffee intake from FFQ	Coffee drinkers had greater incidence of hypertension compared to non-drinkers (28.3 vs 18.8%; $P=0.03$). Not significant after multivariate adjustments[a]	No interactive effects with smoking
Andersen *et al.*[14]	Prospective cohort: 41 836 US ♀ followed up for 15 years for death attributed to inflammatory and cardiovascular diseases. Coffee intake from 127-item FFQ	Linear inverse relation for death from inflammatory disease and coffee intake (28–33% lower among coffee drinkers compared with non-drinkers). U-shaped association for CVD death and coffee[a,b,c]	No interactive effects with smoking
Jee *et al.*[6]	Meta-analysis of 11 RCTs ($n=522$) to assess effect of coffee on BP in treatments lasting >24 h	Systolic and diastolic BP increased by 2.4 and 1.2 mm Hg. Mean treatment duration = 56 days and dose = 5 cups/day (650 mg caffeine/day)	BP effects greater in younger subjects
Noordzij *et al.*[7]	Meta-analysis of 16 RCTs ($n=1010$) to assess the effect of coffee and caffeine on BP and HR in treatments lasting >7 days	Systolic and diastolic BP increased by 4.16 and 2.14 mm Hg for caffeine tablets and 1.22 and 0.49 mm Hg for coffee. Negligible effects on HR. Mean treatment duration = 42 days and dose = 725 ml/day, (488 mg caffeine/day) for coffee trials	BP effects larger in trials with >50% ♀ and boiled coffee. Hypertension status, age or habitual coffee intake not related

Abbreviations: ♂ men; ♀ women; FFQ, food frequency questionnaire; BP, blood pressure; HR, heart rate; RCT, randomized controlled trial; CVD, cardiovascular disease.
[a]Multivariate models adjusted for body mass index, age, alcohol use, physical activity, smoking status and family history of hypertension.
[b]Additional adjustment for oral contraceptive use.
[c]Additional adjustment for education, multivitamin use, energy intake, whole and refined grains, red meat, fish, fruit and vegetables.

with a detrimental effect on aortic stiffness.[15] However, manipulating certain components of coffee has provided interesting findings. The removal of hydroxyhydroquinone, a potentially pro-oxidative component of coffee, has been shown to provide antihypertensive benefits by regulating vascular tone and improving the bioavailability of nitric oxide in spontaneously hypertensive rats (SHR).[16] Further studies by this group have shown improvements in endothelial function and attenuation of vascular hypertrophy and hypertension in SHR following 8 weeks administration of a purified form of chlorogenic acid.[17] Whether or not this can be replicated in humans remains to be seen.

There may be a number of reasons why the relationship between coffee and health remains equivocal. Firstly, it is more likely that the combination of nutrients and chemicals from the whole diet has greater health implications than individual components alone. It is also possible that pharmacologically active components of coffee may act to inhibit harmful effects of other dietary components. For example, coffee may inhibit alcohol-related hypertensive effects by a mechanism associated with lowering serum γ-glutamyl transpeptidase. Filtered coffee (3 cups/day) given to 42 mildly hypertensive men while maintaining habitual alcohol intake over 4 weeks reduced systolic and diastolic BP by 7–10 and 3–7 mm Hg, respectively, which was reversed on cessation of coffee intake.[18] Secondly, the relationship between coffee drinking and health is often confounded by large cultural and psychosocial factors. For example, in a British cohort, coffee consumption was associated with a cosmopolitan lifestyle compared with tea drinking, which is the more traditional beverage and associated with lower socioeconomic status.[19] It is well established that psychological stress impacts upon eating behaviours and it is feasible that exposure to daily stressors partly underlies coffee drinking habits. In addition, there is a wide variety of preparation methods, sources and types of coffee, which makes it difficult to make comparisons between studies from different regions. Indeed, an increasing use of the filter method over time may have led to less exposure to atherogenic coffee

lipids,[20] which could explain the shift in balance towards a healthier coffee. Whether milk, cream or other additives are used and the freshness of the coffee beans may also critically impact upon the findings. Thirdly, cross-sectional observations may be confounded by inaccurate self-report measures of coffee intake, but RCTs that attempt to blind participants to the experimental condition are challenging, because it is difficult to mask the taste, aroma and other physical and mental cues of the beverage.

A final issue relates to delineating between the effects of various active components in coffee. It has been estimated that coffee consists of over 2000 compounds. A well-known ingredient, caffeine, has potent physiological effects such as adenosine-receptor antagonism, stimulating free fatty acid release from peripheral tissues, promoting endothelial dysfunction and is thought to decrease insulin sensitivity by activation of the sympathetic nervous system, although tolerance may develop from habitual intake. Caffeine given as tablets resulted in BP elevations four times greater than for caffeinated coffee in a recent meta-analysis of RCTs.[7] Associations between caffeinated cola and risk of hypertension but not with caffeinated coffee were demonstrated,[4] thus suggesting a protective effect of specific components found in coffee or the possibility of residual confounding from higher total calorie intake and poorer lifestyle in consumers of sugary fizzy drinks. Lopez-Garcia *et al.*[21] found a positive association with caffeine intake and coronary heart disease in age-adjusted analyses, which was attenuated after controlling for smoking, although no such relationships were observed for coffee. Additional evidence suggests that caffeine intake may only be a risk factor in individuals who are genetically slow caffeine metabolizers.[22]

In summary, there is no clear evidence for a causal relationship between caffeinated coffee and hypertension. Coffee intake appears to have small effects on BP in short-term intervention trials, which may reduce with habitual intake (see Table 1), although the magnitude of these effects could have relevance given that a downward shift of 2–3 mm Hg in the population distribution of BP results in substantial reductions in cardiovascular mortality. There is a trend from recent studies to suggest some health benefits of coffee intake, although further experimental work is needed to understand fully the various pharmacologically active components of coffee and their interactions with factors such as genetic risk, other dietary components and confounding lifestyle habits such as smoking and psychosocial mediators. The coffee–health equation therefore remains an important research question that has implications for public health and the global coffee business. More studies are clearly needed before modulation of coffee consumption features in guidelines of hypertension or cardiovascular risk management.[23,24]

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