

# Caffeine Consumption and Cardiovascular Risks: Little Cause for Concern

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Caffeine consumption is virtually ubiquitous in our society. It is naturally found in coffee, tea, chocolate, and cola drinks. Furthermore, caffeine is often added to beverages, foods, pain relievers, and other products. In the United States, coffee accounts for  $\approx 70\%$  of the caffeine consumed.<sup>1</sup> A report in this issue of *JAHA* by Dixit and colleagues describes the relations between the reported intake of caffeinated products and the occurrence of arrhythmias assessed by 24-hour Holter monitoring in the Cardiovascular Health Study. The investigation included  $>1300$  adults and all participants were  $>65$  years of age at baseline.<sup>2</sup> The authors report no association for atrial or ventricular arrhythmia prevalence and reported intake of caffeinated products. The Dixit article provides an opportunity to briefly review the pharmacology of caffeine related to the cardiovascular system and to share recent information and insights from clinical studies and population reports concerning caffeine intake and cardiovascular risk factors, cardiovascular disease (CVD) outcomes, and arrhythmias.

## Cardiovascular Risk Factors: Blood Pressure and Lipids

In a mechanistic study published in the late 1970s, it was reported that 250 mg of caffeine, administered orally in a clinical research unit to adults not regularly ingesting caffeine products, raised plasma renin 57%, plasma norepinephrine 75%, plasma normetanephrine 207%, and blood pressure 14/

10 mm Hg.<sup>3</sup> A single dose of caffeine was given, the amount typically present in 12 ounces of filtered coffee. Maximal plasma caffeine levels were observed 1 hour after consumption, and habituation was not investigated.<sup>4</sup> Other pharmacologic research has corroborated these findings, shown that caffeine has diuretic effects, and demonstrated that the highest blood caffeine concentrations are typically observed in the afternoon.<sup>5</sup>

Clinical studies have reported the chronic effects of caffeine products on blood pressure and results have generally been null. It is believed that genetics, smoking, and other aspects of the diet may modify effects.<sup>6</sup> A meta-analysis by Zhang in 2011 that included  $>170\ 000$  adults and  $>32\ 000$  new cases of hypertension reported no association between caffeine intake and the development of hypertension.<sup>7</sup> An ambulatory blood pressure study that investigated 24-hour urinary caffeine and caffeine metabolites levels in  $>800$  adults reported that each doubling of caffeine excretion was associated with  $\approx 0.6$  mm Hg *lower* blood pressure. The caffeine effects were significant even after statistical adjustment for blood pressure medication use.<sup>8</sup>

Research has suggested that both plasma total cholesterol and low-density lipoprotein cholesterol may increase if the coffee is boiled during the brewing process.<sup>5,9</sup> A meta-analysis based on 12 randomized controlled trials of coffee consumed daily for 45 days showed that caffeine intake led to statistically significant increases for total serum cholesterol (mean increase 8.1 mg/dL), low-density lipoprotein cholesterol (mean increase 5.4 mg/dL), and triglycerides (mean increase 12.6 mg/dL). The greater increases in lipid levels were observed for boiled coffee compared to filtered coffee, and decaffeinated coffee had little effect on blood lipid levels.<sup>10</sup>

## Atherosclerotic CVD Outcomes

A meta-analysis that included data from 36 studies,  $>1\ 000\ 000$  participants, and  $>36\ 000$  CVD cases demonstrated a nonlinear relationship between chronic coffee consumption and CVD risk. Compared with the lowest category of coffee intake (median, 0 cups per day), the relative risk of CVD was 0.89 for a median of 1.5 cups per

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day, 0.85 for a median of 3.5 cups per day, and 0.95 for a median intake of 5 cups per day. The authors concluded that coffee consumption was associated with both coronary heart disease and stroke; the lowest CVD risk occurred at 3–5 cups per day, and heavy coffee consumption was not associated with increased CVD risk.<sup>11</sup> A companion study by the same authors investigated mortality in 3 large prospective cohorts. They reported that both caffeinated and decaffeinated coffee intakes were positively associated with lower risk for all-cause mortality and cardiovascular mortality.<sup>11</sup>

## Arrhythmias

With the background of the caffeine effects on CVD risk factors and atherosclerotic CVD events in perspective, how should we interpret the Dixit article? The authors report the frequency of atrial and ventricular arrhythmias assessed by 24-hour Holter monitor recordings in older Americans who were participating in an observational cohort study in 1992. The mean age of the participants was 72 years, ≈20% of the participants had clinical coronary artery disease, individuals with persistent atrial fibrillation (≈2%) on the Holter monitoring were excluded from the data analyses, and <4% reported taking anti-arrhythmic agents. Using linear regression models, the authors showed that the frequency of premature atrial contractions, premature ventricular contractions, supraventricular tachycardia, and runs of ventricular tachycardia were not associated with the number of caffeine servings (tea, coffee, or chocolate) consumed on a regular basis. Subgroup analyses according to tea, coffee, or chocolate serving intake also did not show any associations between caffeine serving intake with the prevalence of arrhythmias.

The Dixit findings are relevant to healthy older adults who are relatively asymptomatic and who report modest amounts of caffeine intake. There is a plethora of literature in the modern era that further supports their findings in more broadly based patient populations. For example, a meta-analysis published in 2013 reviewed >115 000 patients from 7 studies (1 case-control and 6 cohorts), and found no data to support an increased risk of atrial fibrillation with caffeine. Rather, there was a suggestion of an inverse association between caffeine exposure and risk of atrial fibrillation.<sup>12</sup> Other meta-analyses have confirmed these findings.<sup>13</sup>

Data examining risk of ventricular arrhythmias are similarly robust, and indicate no increase in arrhythmia risk when caffeine is consumed. For example, in a prospective study of patients with known supraventricular tachycardia, the subjects were randomized to caffeine versus placebo prior to electrophysiology study and the investigators found no difference in the inducibility of arrhythmias.<sup>14</sup> Additionally, patients with a new myocardial infarction and who consumed

caffeine in doses up to 500 mg daily (equivalent to 5–6 cups of coffee) did not experience an increase in the frequency or severity of ventricular arrhythmias.<sup>14</sup> Another study examined the experience of 50 patients known to have ventricular arrhythmias. The participants received 200 mg of caffeine or placebo in a crossover trial prior to exercise testing within 30 minutes and there was no greater risk of ventricular arrhythmias after the caffeine exposure.<sup>14</sup>

Many studies examining caffeine intake have focused on the number of “cups of coffee” regularly consumed. The epidemiology of coffee consumption itself has changed significantly over the last 2 decades, with the advent of coffee shop franchise expansion over the entire United States in the 1990s and worldwide in the 2000s. In 2015, of the 100 million coffee drinkers in the United States, 30 million had a preference for “specialty beverages”—lattes, cappuccinos, and mochas.<sup>15</sup> In addition, energy drinks sprang into being. For example, Red Bull was first produced in 1987 and sold more than 5.6 billion cans in 2014.<sup>16</sup> Caffeine consumption in isolation appears to be benign, but there is a growing body of evidence that substances such as taurine and guarana in some caffeinated beverages may be unhealthy. There are multiple case reports in the literature regarding arrhythmias and/or death following excessive energy drink consumption prior to exercise. According to the Substance Abuse and Mental Health Services Administration, there were >20 000 emergency room visits related to energy drinks in 2011.<sup>17</sup> Many specialized caffeinated beverages have a large number of calories and that may be a health hazard for the development of hyperglycemia and diabetes mellitus. A restaurant double espresso (2 ounces, 150 mg caffeine, 0 calories) habit may not be problematic, but how healthy is a Venti Peppermint Mocha (20 ounces, 415 mg caffeine, 440 calories) or a Monster Energy (16 ounces, 160 mg caffeine, 300 calories)?<sup>3</sup>

Modern technology provides the opportunity to design studies to collect immense amounts of observational data related to arrhythmias. We no longer rely on a 24 to 48-hour snapshot of a person’s life using traditional Holter monitors. We have the capacity to easily implant loop recorders that are smaller than a penlight battery. The procedure is performed with very little risk to the patient, and the device captures and broadcasts wireless data for 3 years or more, 24 hours a day, and 7 days a week. Smart phone apps are also available that allow individuals to provide other information instantaneously to a study site or coordinator. Individuals who are at high risk to develop a cardiac arrhythmia could have a loop recorder implanted, the participant could transmit beverage consumption information in real time, and the two data sources could be linked and analyzed. These types of research possibilities are opening new opportunities to investigate the occurrence of arrhythmias.

In summary, recently published studies, including prospective cohorts, clinical investigations, and meta-analyses, generally show coffee consumption is safe for the heart. Concerning CVD risk factors, there is little evidence that chronic coffee intake consumption raises blood pressure. Boiled coffee brewing may raise atherogenic lipid levels, and other brewing methods do not appear to have this effect. Finally, there is little risk for atrial or ventricular arrhythmias at most of the levels of caffeine consumption in our society. Future research in this area is especially of interest concerning newer caffeinated beverages with greater amounts of caffeine per serving and with a large number of calories. Implantable and wearable devices have become available to identify cardiac arrhythmias, and this type of technology will provide new opportunities for research, diagnosis, and cardiovascular care.

## Disclosures

Dr Wilson has no conflicts of interest related to this article. Dr Bloom has no conflicts of interest related to this article.

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