Caffeine and arrhythmia1–3

Martijn B Katan and Evert Schouten

Many dietary supplements promise to improve physical and mental functioning, but caffeine, an age-old food component, is one of the few that delivers. Caffeine makes its consumers awake and alert, and it improves performance (1). Therefore, coffee could be called a functional food. But is it safe? If coffee were discovered today, it would probably be regarded, in the European Union’s terminology, as a “novel food” (2) and be subjected to severe scrutiny by regulatory agencies. Would coffee and other caffeine-containing beverages such as tea, colas, and guarana—a soft drink made from the caffeine-rich seeds of a South American fruit—pass such scrutiny? Many ills have been ascribed to caffeine, but few have been substantiated. In this issue of the Journal, Frost and Vestergaard (3) address the effect of caffeine on a disease that laypersons often associate with caffeine—namely, disruption of cardiac rhythm.

The electrical signal for contraction of the heart originates in the sinoatrial node, from which it traverses the atria until it reaches the atrioventricular node. Activation then spreads over the ventricles to complete one cycle of contraction. In arrhythmia, the coordination of contraction is lost. The underlying cause of arrhythmia is usually a reentry phenomenon in which the electric stimulus circulates around a core of unexcitable tissue. Cardiac tachyarrhythmias are divided into arrhythmias of the ventricles—the chambers that pump blood into the aorta and the lungs—and arrhythmias of the atria and the atrioventricular node. Arrhythmias are often due to structural heart disease caused by atherosclerosis, hypertension, valvular disease, or cardiomyopathy, and they rarely occur in persons with structurally normal hearts. Sustained ventricular arrhythmias are a frequent and life-threatening complication of myocardial infarction, because the lack of oxygen resulting from coronary stenosis may damage muscle tissue and impede the smooth diffusion of electrical currents. This may lead to fatal ventricular arrhythmia, in which the heart no longer contracts properly, the tissues no longer receive blood, and the patient dies.

Such ventricular tachyarrhythmia is the most frequent proximate cause of sudden death, and any dietary component suspected of promoting it should be scrutinized seriously. However, there is a consensus that caffeine does not promote ventricular arrhythmia, except in extraordinary circumstances and at a very high dose. One example of such an extraordinary circumstance is the case of a 25-y-old woman with preexisting prolapse of the mitral valve who drank 50 mL of a “natural energy” guarana health drink that contained the same amount of caffeine as 8 cups of strong coffee. She developed intractable ventricular fibrillation and died (4). But such events are rare; most cardiac patients tolerate normal amounts of caffeine without difficulty (5).

Supraventricular tachyarrhythmias are less dangerous than ventricular tachyarrhythmias, but they can still give rise to palpitations, hemodynamic failure, and even syncope (6). Atrial fibrillation is a common form of supraventricular tachyarrhythmia, occurring in 5–10% of persons aged >65 y. In its paroxysmal form, it may also occur in younger persons. In sustained atrial fibrillation, there is continuous rapid activation (300–600 times/min) of the atria by multiple meandering reentry wavelets. Although the atria respond electrically, there is no coordinated mechanical action—ie, no blood is pumped into the ventricles. Some of the electrical pulses are conducted to the ventricles, where they usually give rise to a fast and irregular rhythm. Elevated atrial pressure, increased muscle mass, fibrosis, and inflammation may also cause atrial fibrillation. Hyperfunctioning of the thyroid gland and alcohol abuse are also known risk factors for arrhythmias. Atrial flutter is a milder form of atrial arrhythmia than is atrial fibrillation; the atrial rate is slower but still ~300 activations/min. Often, every second beat is conducted to the ventricles, yielding a heart rate of ~150 beats/min. Atrial flutter can progress to atrial fibrillation, and its causes are similar.

Frost and Vestergaard describe the association of caffeine intake with the subsequent incidence of atrial fibrillation or flutter in almost 48 000 participants in the Danish Diet, Cancer, and Health Study. Or rather, they describe the lack of such an association, because the incidence of atrial fibrillation was unrelated to caffeine intake. Could the relation between caffeine intake and atrial fibrillation have been obscured in their study by random or systematic error? This is always a concern, but it seems less likely here, because the same study did yield a significant positive association of high alcohol intake with atrial fibrillation in men (7), and the relative risk was similar to that observed in the Framingham Study (8). This consistent finding increases confidence that an effect of coffee on atrial fibrillation would have

1 From the Wageningen Centre for Food Sciences and the Wageningen University Division of Human Nutrition, Wageningen, Netherlands.
2 Supported by the Wageningen Centre for Food Sciences, an alliance of major Dutch food industries, TNO Nutrition and Food Research, Wageningen University and Research Centre, Maastricht University, and the Dutch government.
3 Reprints not available. Address correspondence to MB Katan, Wageningen Centre for Food Sciences, Bomenweg 2, 6703 HD Wageningen, Netherlands. E-mail: wcfs1@wur.nl.
been detected if it existed, because people tend to report their coffee intake more accurately than their intake of alcohol. Thus, the positive finding with respect to alcohol increases confidence in the negative conclusion with respect to caffeine. Coffee intake in this study was high, as is usual in Scandinavia. The participants in the lowest quintile consumed an average of 248 mg caffeine/d, which is equivalent to 2–3 cups of coffee, and the intake of 997 mg caffeine/d reported by the top quintile is equivalent to \( \approx 10 \) cups. Thus, this study provides no information about zero intakes of coffee, and it remains possible that total abstinence from caffeine does reduce the incidence of atrial fibrillation. However, the lack of an association over the wide range of reported intakes makes that possibility less plausible.

If coffee does not affect the risk of arrhythmia, then what should be the advice to cardiac patients? Such a judgment requires a look at the effect of caffeine on cardiac risk factors. High intakes of coffee and caffeine raise homocysteine concentrations, but whether a high homocysteine concentration directly affects cardiac health remains to be seen. Unfiltered coffee raises serum cholesterol concentrations, but that effect is not due to caffeine but to a lipid that is absent from filtered coffee. The caffeine in coffee does cause an increase of 2.4 mm Hg in systolic blood pressure when 5 cups are consumed daily (9) (10). That effect is enough to justify counseling high-risk patients to moderate their caffeine intake, but other interventions—eg, smoking cessation, weight loss, exercise, and a healthy diet low in saturated and trans fats—yield larger benefits and should come first.

MBK previously received grants from the Institute for Scientific Information on Coffee and from Nestlé to study health effects of coffee.

REFERENCES