

## Beverages Of Daily Life: Impact Of Caffeine On Atrial Fibrillation

Anna Vittoria Mattioli MD PhD FACC FESC

*Department of Life Science, Sect of Cardiology; University of Modena and Reggio Emilia, Modena (Italy).*

### Summary

In recent years, clinical and observational studies reported that caffeine consumption was associated with cardiac arrhythmias, affected heart rate variability, and subsequently increased cardiovascular risk. The analysis of these paper shows that data are controversial and strongly depends on methodology. Moderate intake of caffeine seems to have protective effects on arrhythmias, on contrary high intake of caffeine seems to be associated with increased risk of atrial fibrillation. There is a deep difference when we analysed intake of caffeine from coffee compared to other sources. In very recent time an increase in caffeinated beverages, namely energy drinks, has been reported in young people and several arrhythmic complications has been observed. A review of literature is presented.

### Introduction

Lifestyle factors, particularly dietary intake, have been recognized as important, modifiable risk factors for cardiovascular disease. The majority of studies analyzed the relationship between lifestyle and atherosclerosis, whereas little is know about influence of lifestyle on arrhythmias.

The aim of the present review is to evaluate the effects of caffeine as component of beverages of daily life on development of AF. We focused on coffee consumption and on the new developed energy drinks that became very popular among young people.<sup>1</sup>

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice. It is estimated to currently affect over 6 million patients in Europe and approximately 3.0 million in the United States, and this number is projected to at least double in the next 25 years because of the increasing proportion of the ageing population.<sup>2</sup>

### Coffee, Caffeine And Atrial Fibrillation

Caffeine is the most widely consumed behaviorally active substance in the world and almost all caffeine comes from dietary sources, most of it from coffee.<sup>3,4</sup> Associations between coffee, caffeine and AF have had conflicting results.<sup>5,6,7</sup> Coffee contains several hundred different substances including lipids, carbohydrates, minerals, vitamins, alkaloids and phenolic compounds. Nevertheless effects of coffee on cardiovascular system have been mainly related to caffeine.

Caffeine is an alkaloid present in coffee beans, in humans come

from a number of dietary sources i.e. tea, coffee, cocoa beverages, chocolate bars and soft drinks and recently energy drinks. (ED). The content of caffeine of these items ranges from 4 to 180 mg/150 ml for coffee, 15 to 29 mg/180 ml for cola, 24 to 50 mg/150 ml for tea, 2 to 7 mg/150 ml for cocoa and 1 to 36 mg/28 mg for chocolate, 100 to 286 mg for common ED, however some brands of ED contain 550 mg caffeine per can or bottle.<sup>8,9,10</sup>

The clinical effect of intakes of caffeine from coffee, tea, caffeinated soda and energy drinks on AF remain inconclusive. The patho-physiology of the arrhythmias have been described in detail, however the mechanism underlying electrical changes and the possible triggering factors remain largely unknown. Several studies evaluated the acute effects of caffeine on heart rate and found controversial results.

Studies on human atrial myocytes from patients with AF suggests that an adenosine mediated signaling pathways could lead to increased spontaneous sarcoplasmic reticulum calcium release and could contribute to the initiation of AF.<sup>11</sup>

Caffeine may mediate AF by resulting in neurohormonal stimulation and sympathetic activation and the effects could be enhanced in nonhabitual coffee drinkers.<sup>12</sup>

Caffeine toxicity produces supraventricular tachycardia, atrial fibrillation and ventricular fibrillation.<sup>13,14</sup>

The risk of cardiac arrhythmias associated with daily consumption of caffeine does not seem to be increased at ventricular level, but more information is needed about supraventricular level.

Clinical studies found a significant decrease of heart rate after acute ingestion of 100 or 200 mg of caffeine in non-habitual coffee consumers, whether in habitual coffee consumers the lack of effects on heart rate depends on rapid tachyphylaxis of caffeine.<sup>15,16</sup> A different response in habitual and non habitual consumers was previously observed in hypertensive patients.

The Framingham Heart study and a Danish study showed no association between daily caffeine intake and incident AF.<sup>17,18</sup> Similarly in the Women Health study, caffeine consumption was not associat-

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None.

### Corresponding Author:

Anna Vittoria Mattioli, MD PhD, FACC, FESC  
Department of Biomedical Science- Sect of Cardiology University of Modena and R.E.  
Via del pozzo, 71  
41100 Modena (Italy).

ed with an increased risk of incident AF in a selected population of initially healthy middle-aged women.<sup>19</sup> In the Multifactor Primary Prevention Study, the consumption of 1 to 4 cups of coffee/day was associated with an increase risk of atrial fibrillation, whereas drinking more than 4 cups a day was not associated with a risk of atrial fibrillation. This analysis was carried on in Goteborg on a large number of patients and evaluated hospitalization for atrial fibrillation. The main limitation was the lost of asymptomatic episodes of arrhythmias not leading to hospitalization.<sup>20</sup>

These discrepant findings on the association between coffee and caffeine consumption and atrial fibrillation are related to differences among coffee and caffeine intake.<sup>21</sup> Coffee is a complex beverage that include hundred of substances i.e. several antioxidants. High antioxidant levels in coffee were reported but this high contribution to the total dietary intake of antioxidant was not noted<sup>22,23</sup> Green and black coffee beans contains different quantity of antioxidant, 15,9 and 22.6 mmol tot antioxidant/100 g, respectively. This difference depends on the roasting process that damages some antioxidants.<sup>24</sup>

An important issue is whether the antioxidants derived from coffee are bioactive and bioavailable. Several studies demonstrated bioactivity of coffee that suggests coffee contribution to antioxidant process, coffee consumption is associated with a reduction of plasmatic gamma-glutamyl transpeptidase, a marker of early oxidative stress.<sup>25</sup>

In healthy volunteers the acute ingestion of caffeinated instant coffee did not result in supraventricular arrhythmias.<sup>26</sup> However, many patients with paroxysmal atrial fibrillation indicate coffee intake as a triggering factor for arrhythmia, and there is a fairly widespread belief that caffeine intake is related to the development of AF<sup>27</sup> Acute stress was also associated with an increase in coffee consumption in almost all subjects, habitual and nonhabitual drinkers.<sup>28</sup>

We found that increasing level of coffee consumption was associated with a significantly greater risk of acute atrial fibrillation in patients without cardiac disease.<sup>29</sup> High espresso coffee consumption (>3 cups a day) was associated with an increase risk of AF but patients habitual drinkers had a low probability of spontaneous conversion of the arrhythmia.

Other studies identified moderate coffee consumption (1–4 cups coffee/d) as a contributor to AF risk,<sup>20</sup> whereas another study showed that caffeine was associated with less successful cardioversion in hypertensive patients.<sup>7</sup> It is plausible that the effects of caffeine varies in habitual versus non-habitual consumers and also depends on the dose, on the modality of preparation and on the modality of intake, i.e. coffee after meals. Further studies are necessary to clarify the relation of caffeine exposure to risk of incident and recurrent AF in healthy individuals and patients with a predisposition for AF.

### Energy Drinks And Atrial Fibrillation

In 2012 the Food and Drug Administration investigated the energy drinks (ED) that contained caffeine, due to alert on safety. Several types of these caffeinated drinks were linked to unexpected death in young and healthy subjects<sup>30</sup> Energy drinks are a group of beverages, available to general public, used to provide boost in energy, maintain wakefulness, provide alertness, and promote cognitive and mood enhancement.

Energy drinks are the most popular dietary supplement in the American adolescent and young adult. About 6% of young men in United States report to consume ED daily.<sup>30</sup>

The International Society of Sports Nutrition (ISSN) published a

position paper on Energy drinks that analyzed effects of ED on exercise performance, and explore the safety of these beverages.<sup>31</sup>

Energy drinks contain caffeine and often other substances such as guarana (containing guaranine, similar to caffeine), ginkgo biloba, taurine (an amino acid) and carbohydrates. Interestingly ED that contain natural ingredients such as ginkgo (classified as “dietary supplements”) so that manufacturers of these products are not required to include the caffeine content of these herbal supplements in the nutritional information.<sup>31</sup>

The guarana plant and berry has one of the highest naturally occurring levels of caffeine, and there are also traces of theophylline and theobromine. Instead of referring to caffeine, many companies and websites market their products using the term ‘guaranine’ when describing the active ingredient.

Safety concern comes from isolated case report that has not established a direct link.

The caffeine content of common ED has been reported to range from about 100 to 286 mg.<sup>9</sup> However some brands of ED contain 550 mg caffeine per can or bottle.<sup>10</sup>

Since ED often contains other stimulants (i.e. herbs) that can have a synergistic effect with caffeine, more research is needed to determine the long-term effects of habitual intake of ED.<sup>32</sup> There are currently only a few studies (acute or long term) that have investigated the side effects of ED.<sup>33,34</sup>

Clauson et al reported four documented case reports of caffeine-associated deaths, as well as four separate cases of seizures associated with the consumption of energy drinks. However, the authors were quick to point out that the amounts of ginseng, taurine, and guarana found in these beverages are less than the amounts thought to beget any harmful reaction or curative benefit. It is possible that a combination of different substances and caffeine facilitate arrhythmias.<sup>33</sup>

Usman and coworkers reported a case of a young boy presented with palpitations and high blood pressure after consumption of an ED containing caffeine, taurine (124 mg), inositol (17 mg), Panax ginseng (6.98 mg). The tachycardia and hypertension returned to normal after discontinuation of ED consumption.<sup>35</sup>

Bichler and coworkers investigated a combination of caffeine and taurine (two common ingredients in ED) in a double-blind study of college students. Subjects consumed either caffeine and taurine pills or a placebo and then completed a memory assessment while heart rate and blood pressure were monitored. The combination of two caused a significant decline in heart rate and an increase in mean arterial blood pressure.<sup>36</sup>

A cardiac arrest has been reported in a healthy 28-year-old man after consuming seven to eight cans of a caffeinated ‘energy drink’. The patient developed ventricular fibrillation and was successfully defibrillated. Subsequent testing did not show evidence of any coronary artery disease.<sup>37</sup>

We reported 2 cases of atrial fibrillation in young patients after ingestion of ED, in one case it was mixed with alcohol. Both patients underwent cardioversion of arrhythmias. [data presented at the National Meeting of the Italian Society of Cardiology 2013, paper under submission].

It is well known that alcohol mixed to energy drinks has become very popular among young. This mix can facilitate cardiac arrhythmias in young apparently healthy subjects. Combination of alcohol and energy drinks is associated with decreased awareness of physical and cognitive impairment caused by alcohol intake. Additionally, due

to the stimulant properties of the added caffeine and the dilution of the alcohol, individuals may remain alert longer, allowing for extended time in which to consume alcohol, which may lead to binge drinking. There is some evidence that at lower levels, caffeine may attenuate some of the intoxicating effects of alcohol, but this effect is not evident at higher caffeine levels.<sup>38,39</sup>

It is concerning that products with an unclear record of safety in adolescents and young, and reported adverse effects, have become so easily accessible. Currently, no central data collection exists for side effects induced by ED. As the number of users of energy drinks has been growing rapidly, it is crucial to keep up with understanding the potential toxic effects of these beverages and food to prevent arrhythmias and other disease.

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