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Characterizing the Impact of Caffeine on Heart Arrhythmias

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Abstract

Caffeine is one of the most commonly consumed stimulants and is found in many items like coffee and energy drinks. Heart arrhythmias are irregular heart rhythms, which can occur when the electrical signals that control the heart's rhythm are not functioning properly. Due to the stimulant properties of caffeine, it is theorized that caffeine consumption may cause tachycardias-like ventricular arrhythmias. This review article describes the relationship between caffeine intake and heart arrhythmias using a comprehensive PubMed search. A comprehensive search was conducted using the search terms "caffeine arrhythmia" which was conducted and a total of 26 search results were obtained. The majority of clinical studies suggest that there are no strong associations between caffeine consumption and arrhythmias. There is little evidence suggesting a direct relationship between caffeine and ventricular arrhythmias (relative Risk 1.00, 95% CI 0.94 - 1.06; 13.5%, $p = 0.32$). Conversely, caffeine consumption has an inverse relationship with the risk of atrial fibrillation (p for overall trend = 0.015; p for nonlinearity = 0.27). Caffeine related deaths are uncommon, but certain groups such as infants, psychiatric patients, and athletes may have an increased risk of arrhythmias following caffeine consumption. Overall, caffeine consumption is not strongly linked to heart arrhythmias and limited studies suggest it may reduce the risk of arrhythmias. Although there is not a strong relationship between caffeine intake and heart arrhythmias, it does cause other cardiovascular problems including high blood pressure and hence should be consumed responsibly (40 - 180 mg/day).

Keywords

Caffeine, Arrhythmias, Atrial Fibrillation

1. Introduction

Caffeine is a central nervous system stimulant and is the most widely consumed psychoactive drug with approximately 80% of adults consuming it in the United States [1]. Caffeine acts as a cognitive enhancer through increasing intracellular concentrations of cyclic adenosine monophosphate (cAMP), and can be found in many forms including coffee, energy drinks, oral pills, and injectables [2].

Heart arrhythmias are irregular heartbeats that can cause cardiovascular events including heart failure, strokes, and myocardial infarctions. About 48 out of 100,000 adults have ventricular arrhythmias, abnormal heart beats in the lower chambers of the heart [3]. Heart arrhythmias occur when the electrical signals that control the heart's beating are not functioning properly. They can be tachycardias (fast heartbeats), bradycardias (slow heartbeats), or irregular beats (atrial fibrillation (AF)) [4]. Caffeine is linked to tachycardia, which is a risk factor for supraventricular tachycardias, AF, and ventricular arrhythmias due to very rapid heartbeats [5]. Caffeine can also cause other cardiovascular problems such as hypertension [6].

It is hypothesized that there is a dose-dependent relationship between caffeine and heart arrhythmias, but the exact relationship between the two has not been established. In addition to heart rhythm issues, caffeine can also spike blood pressure and cause cerebrovascular accidents and myocardial infarctions [6]. One in four people consumes caffeine sources three or more times a day. Given its vast and high consumption, there is a need to better understand the relationship between caffeine and arrhythmia [7]. The purpose of this study was to characterize the relationship between caffeine intake and heart arrhythmias.

2. Methods

A comprehensive medical literature search was conducted utilizing the search terms "caffeine arrhythmia" on PubMed. The search was limited to publications of randomized clinical trials, meta-analysis, and systematic reviews recently published in English since 2010. Studies must have discussed caffeine and its impact on heart arrhythmias. Studies not published in English, literature review type manuscripts, and studies that did not discuss both caffeine and heart arrhythmias were excluded from this medical literature review.

Parameters of interest include the author/study name, study type, intervention, primary endpoints of included study, results, and key study conclusions. The impact of caffeine consumption on a cardiovascular related outcome and any safety considerations were also recorded (**Figure 1** and **Table 1**).

3. Results

After initial screening, 26 studies that met the search terms were identified, of which 13 met the inclusion criteria. A total of 13 studies were eligible and relevant for this medical review, of which 7 were randomized controlled clinical trials, 3 were meta analyses, and 3 were systematic reviews.

Table 1. Summary of selected clinical studies assessing the impact of caffeine on heart rhythms.

Author	Study type	Intervention	Primary endpoint	Results	Study conclusions
Priccila Zuchinali, *et al.* 2016	Systematic Review and Meta-Analysis	Caffeine administration	Impact of caffeine on VA	Risk of ventricular premature beats in humans within 24 hour of caffeine consumption: was 1.00 (95% CI 0.94 - 1.06; I(2) 13.5%, $p = 0.32$)	There is no significant relationship between caffeine consumption and VPB's
Ramy Abdelfattah, et al. 2018	Meta-Analysis	Caffeine consumption (focused on coffee) 40 - 180 mg of caffeine and higher dosages (436 mg)	Caffeine consumption and risk of AF	No difference in AF rate in those who drank less than 2 cups of coffee compared to more than 2 cups 1.068 (0.937 - 1.216) Subjects who drank less coffee were at higher risk of AF Subjects who drank more than 436 mg of caffeine had a lower rate of AF	Caffeine consumption (coffee) does not increase the occurrence of AF. The risk of AF was reduced with caffeine consumption exceeding 436 mg/d.
Min Cheng, et al. 2014	Meta-Analysis	Habitual caffeine intake	Impact of habitual caffeine intake and AF	Caffeine consumption was weakly associated with reduced risk of AF (RR: 0.90, 95% CI: 0.81 - 1.01, $p = 0.07$). Low and high doses of caffeine were both associated with a decreased AF risk (RR: 0.89, 95% CI: 0.80 - 0.99, $p = 0.032$; RR: 0.84, 95% CI: 0.75 - 0.94, $p = 0.002$, respectively). The dose-response analysis revealed a 6% decrease in AF risk per 300 mg/d increase in habitual caffeine intake (RR: 0.94, 95% CI: 0.90 - 0.99).	The findings suggest caffeine consumption might reduce AF risk
Gregory M. Marcus, et al. 2023	Randomized Controlled Trial	Consumption of caffeinated coffee	Relationship between caffeine consumption and daily premature atrial contractions	Caffeinated coffee consumption did not significantly increase daily premature atrial contractions (PACs) compared to caffeine avoidance (rate ratio: 1.09; 95% CI: 0.98 to 1.20; $p = 0.10$). Caffeine was associated with a higher number of premature ventricular contractions (PVCs) (rate ratio: 1.51; 95% CI: 1.18 to 1.94)	Caffeine consumption did not result in more daily premature atrial contractions compared to avoidance of caffeine.
Daniel Caldeira, et al. 2013	Systematic Review and Meta-Analysis	Caffeine Consumption	Impact of caffeine consumption and risk of AF	Caffeine consumption was not associated with an increased risk of AF (OR 0.92, 95% CI 0.82 to 1.04, I(2) = 72%) High-quality studies showed a 13% reduced odds of AF with lower heterogeneity (OR 0.87; 95% CI 0.80 to 0.94; I(2) = 39%) Low-dose caffeine exposure had a protective effect (OR 0.85, 95% CI 0.78 to 0.92, I(2) = 0%)	Caffeine intake is not associated with increased risk of AF. Low caffeine consumption could have a protective effect.

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Priccila Zuchinali, *et al.* 2016	Randomized Clinical Trial	Administration of high-dose caffeine to patients with HFrEF	Effect of high-dose (500 mg) caffeine on frequency of supraventricular and ventricular arrhythmias	500 mg caffeine administration to HFrEF patients did not lead to an increase in ventricular or supraventricular premature beats during continuous electrocardiographic monitoring or a symptom-limited exercise test. No differences were observed between caffeine and placebo groups for arrhythmia frequencies or exercise test-derived variables ($p > 0.05$)	Acute intake of high caffeine doses did not induce arrhythmias in patients with systolic heart failure and patients at high risks of ventricular arrhythmias.
Robert Lemery, *et al.* 2015	Randomized Controlled Trial	Administration of caffeine or placebo to patients with symptomatic supraventricular tachycardia who were undergoing an electrophysiologic study prior to catheter ablation.	To investigate the electrophysiological effects of caffeine on atrial and ventricular tissues	Caffeine caused significant increases in resting systolic and diastolic blood pressures compared to placebo. Resting HR remained similar between the groups. Caffeine didn't affect atrial or ventricular refractory periods or AV node conduction. Nearly all patients developed SVT, with no significant difference in SVT inducibility or induced tachycardia cycle length between caffeine and placebo groups.	Caffeine intake had no significant effect or evidence on cardiac conduction and refractoriness. Caffeine did not have an effect on SVT induction or rapid rate of induced tachycardias.
David Lagier, *et al.* 2018	Randomized Controlled Trial	Administration of peri-operative oral caffeine (400 mg every 8 hours for 2 days) to patients undergoing heart valve surgery with cardiopulmonary bypass	The rate of AF during the postoperative hospital stay.	There was no significant difference in the incidence of AF during hospital stay between the caffeine group and the placebo group (33% vs. 29%, $p = 0.67$), as well as during the first 3 postoperative days (18% vs. 15%, $p = 0.60$). Adenosine plasma levels were associated with the primary outcome, but caffeine administration led to a higher incidence of postoperative nausea and vomiting (27% vs. 7%, $p = 0.005$).	Oral caffeine administration did not prevent postoperative AF after heart valve surgery with cardiopulmonary bypass, however it was associated with an increased rate of postoperative nausea and vomiting.
Remo H M Furtado *et al.* 2021	Meta-Analysis	Administration of Caffeine in two Spanish Cohorts Participants classified into 3 groups based on caffeine (coffee) consumption (Less than or equal to 3 cups per month, 1 to 7 cups per week and more than 1 cup per day)	To investigate the association between caffeine consumption (coffee) and the risk of developing AF.	1 - 7 cups of coffee per week was linked to reduced risk of AF (HR = 0.53, 95% CI 0.36 - 0.79), higher consumption of caffeine (more than 1 cup of coffee per day) did not show significant association (HR = 0.79, 95% CI 0.49 - 1.28). Both cohorts depicted an inverse relationship between moderate coffee intake and reduced risk of AF (HR = 0.60, 95% CI 0.44 - 0.82).	Moderate caffeine consumption (1 - 7 cup of coffee per week) was associated with a reduced risk of AF in both cohorts.

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Gregory M Marcus *et al.* 2022	Randomized Controlled Trial	Participants were given instructions to consume or avoid self-selected triggers in randomized 1 week blocks for 6 weeks	Self selected triggers. AFEQT score at 10 weeks. AFEQT score is used to assess the impact of AF on the quality of life of individuals facing AF.	446 total participants. Self-selected triggers encompassed caffeine (n = 53), alcohol (n = 43), reduced sleep (n = 31), exercise (n = 30), lying on left side (n = 17), dehydration (n = 10), large meals (n = 7), cold food or drink (n = 5), specific diets (n = 6), and other personalized triggers (n = 4). AFEQT scores demonstrated no notable difference, during the subsequent 4-week post-intervention phase. A notable decrease in daily AF episodes emerged following trigger testing, in contrast to controls (adjusted relative risk, 0.60; 95% CI, 0.43 - 0.83; $p < 0.001$). A meta-analysis of individualized trials showed solely alcohol exposure correlated with significantly escalated AF event risks.	Testing of AF triggers did not affect AFEQT but was associated with a lower rate of AF. Exposure to alcohol only increased AF risk, exposure to caffeine did not increase AF risk.
Belinda Gray *et al.* 2019	Randomized Controlled Trial	Caffeinated energy drink consumption in patients with LQTS aged 16 - 50.	To determine whether caffeine consumption (energy drinks) in patients with LQTS would result in an increase in QTc by more than 20 milliseconds. Change in blood pressure was also assessed.	24 LQTS patients (mean age 29 ± 9 years, 54% female, 33% probands) consumed ED and acted as their own controls with a one-week washout. Primary outcome: No significant QTc change with ED compared to control (12 ± 28 ms vs. 16 ± 27 ms, $p = 0.71$). Systolic and diastolic blood pressure increased significantly with ED (7 ± 16 mmHg vs. 1 ± 16 mmHg, $p = 0.046$ and 8 ± 10 mmHg vs. 2 ± 9 mmHg, $p = 0.01$), correlated with serum caffeine (14.6 ± 11.3 vs. 0.5 ± 0.1 μmol/L, $p < 0.001$) and serum taurine (737 ± 199 vs. −59 ± 22 μmol/L, $p < 0.001$). Three patients experienced dangerous QTc prolongation (≥50 ms) after energy drink consumption.	Caffeinated ED's causie an increase in blood pressure. Dangerous QTc prolongation was observed in some LQTS patients therefore young patients with LQTS are recommended to consume ED with caution.
Guido Mandilaras *et al.* 2022	Randomized Controlled Trial	Administration of ED and placebo to healthy children and adolescents.	To investigate the acute cardiovascular effects of ED in healthy children and adolescents.	ED consumption by healthy children and adolescents resulted in a significant increase in SVES compared to the placebo. No dangerous arrhythmias were observed, ED consumption lowered mean heart rate but did not affect QTc intervals.	ED consumption was associated with an increased number of SVES in healthy children and adolescents. Significant decrease in HR was observed which was possibly caused by rise in systolic and diastolic blood pressure. No significant QTc changes were seen after ED consumption and were similar to placebo. Minors with heart rhythm conditions may develop malignant arrhythmias after ED consumption.

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Isabel Lasheras *et al.* 2021	Systematic review	Acute consumption of ED.	To investigate the effects of acute ED consumption on HR and ECG parameters.	After evaluating 43 clinical studies, ED consumption led to a rise in resting HR in 71.1% of studies (pooled $p < 0.001$, significant in 38%), exercise-related HR elevation in 55.5%, and post-exercise HR elevation in 71.4% (pooled p-value < 0.001). Evidence on PR interval was contradictory, while corrected QTc increased compared to baseline in all but one study, surpassing the pathological limit in two instances. T wave changes were noted in two studies, with one reporting a 5:1 ratio of ectopic beats	Acute consumption of ED can change ECG in certain risk populations, at risk underaged individuals should consume with caution.

Table Legend: VA = Ventricular arrhythmias; AF = Atrial Fibrillation; HFrEF = Heart failure with reduced ejection fraction; CI = confidence interval; RR = relative risk; VPM = Ventricular premature beats; SUN = Seguimiento Universidad de Navarra; PREDIMED = Prevencion con Dieta Maditerranea; HFrEF = heart failure and left ventricular systolic dysfunction; HR = heart rate; Atrial Fibrillation Effect on Quality of Life = AFEQT; LQTS = long qt syndrome; QTc = corrected QT interval; ED = energy drinks; SVES = supraventricular extrasystoles; ECG = electrocardiographic.

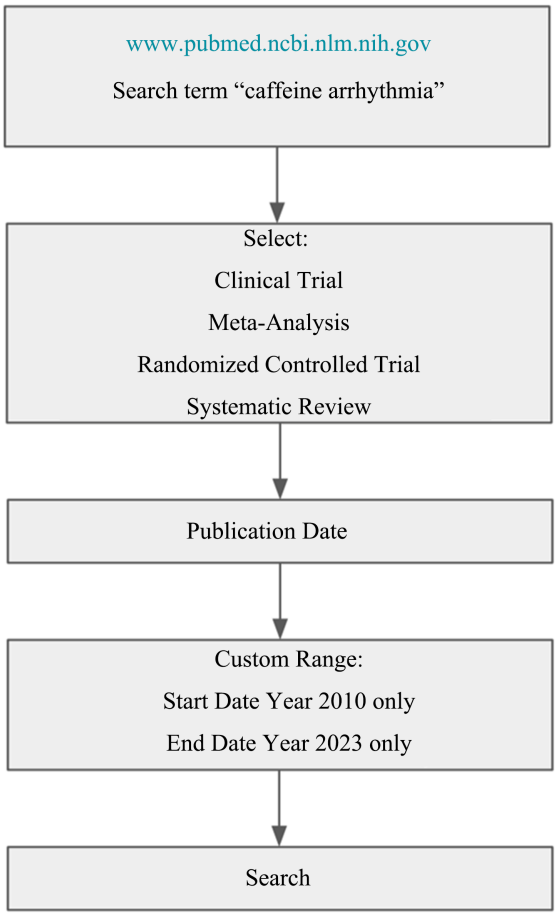

Figure 1. Method flowchart.

3.1. Caffeine Consumption and Atrial Fibrillation

Several studies evaluated the impact of caffeine consumption and risk of AF. A meta-analysis suggested that 40 - 180 mg of caffeine consumption through coffee sources did not increase risk of AF [8]. Additionally, 436 mg of caffeine daily reduced risk of AF [8]. One study had similar findings that caffeine consumption reduced risk of AF [9]. The dose response analysis suggested that there is a 6% decrease in AF risk per 300 mg/d increase in caffeine consumption (no upper limit evaluated) [9]. Another study also depicted a reduced risk of AF with low caffeine consumption (Odds Ratio 0.85, 95% CI 0.78 to 0.92, I(2) = 0%) [10]. The cohort study suggested that caffeine consumption did not result in higher chance of AF. Both cohorts depicted an inverse effect of moderate caffeine consumption and risk of AF [11].

Oral caffeine administration did not increase the risk of AF in patients who underwent heart valve surgery with cardiopulmonary bypass. However, caffeine was linked to a higher risk of postoperative nausea and vomiting [12]. One randomized controlled trial depicted that AF triggers did not affect Atrial Fibrillation Effect on Quality of Life (AFEQT) and did not result in AF [13].

3.2. Caffeine Consumption and Ventricular and Supraventricular Arrhythmias

Other studies have evaluated the relationship of caffeine consumption on supraventricular arrhythmias and tachycardias. In one study, 500 mg of caffeine was administered to patients with heart failure with reduced ejection fraction (HFrEF), however, it did not cause an increase in ventricular or supraventricular premature beats [14]. Furthermore, caffeine intake had no effect on heart rhythm, supraventricular tachycardia (SVT), or tachycardias [15]. However, it did lead to an increase in systolic and diastolic blood pressure [15]. Conversely, energy drink (ED) consumption increased the number of supraventricular extrasystoles in children and adolescents [16]. ED consumption lowered HR but did not affect QTc intervals and no dangerous arrhythmias were observed [16]. ED consumption can also alter ECG in some populations (underaged) [17].

Additional studies evaluated various ventricular arrhythmias including premature ventricular contractions and atrial arrhythmias. One study suggested that caffeine consumption did not result in more premature atrial contractions, however, there was an increase in the number of premature ventricular contractions [18]. However, a study evaluating the impact of caffeine on ventricular arrhythmias found an insignificant relationship between caffeine intake and frequency of ventricular premature beats [19]. Energy drink consumption, including caffeine, did cause QTc prolongation in some patients, and also increased blood pressure [20].

4. Discussion

A majority of the included studies suggest that caffeine does not increase the in-

cidence of heart arrhythmias or other heart rhythm conditions. Studies evaluating the consumption of caffeine and risk of AF stated that caffeine did not increase the risk. Some studies even found that caffeine had an inverse effect on incidence of AF and had a protective effect. However, the level of caffeine consumption needed to elicit these effects is unclear as all studies used different dosages. One study stated that this protective effect happens with low caffeine consumption, whereas another study stated that AF risk was reduced with high caffeine consumption hence it is difficult to tell the ideal amount of caffeine to reduce AF risk [8]. A meta-analysis depicted that moderate caffeine intake reduced AF risk in both of the study cohorts [13]. Hence, the specific dosage of caffeine to reduce AF is not clearly defined. Furthermore, caffeine did not increase AF risk in the postoperative period in patients who underwent heart valve surgery with cardiopulmonary bypass. This is also applicable to HFrEF patients [14]. Studies investigating the impact of caffeinated energy drinks showcased a different trend of results with ED consumption leading to some long QT syndrome patients experiencing dangerous QTc changes upon intake, these results could also be because of other substances found in energy drinks such as taurine [20]. Among children, ED also changed electrocardiogram (ECG) in certain populations such as underaged individuals. Some minors may also develop malignant dysrhythmias after ED consumption. It is important to take into account as ED brand and exact quantity was not mentioned [16].

One study showed caffeine did not increase the incidence of heart arrhythmias, which is similar to other review articles and papers [21].However, caffeine does cause an increase in systolic and diastolic blood pressure, which can lead to hypertension. One study suggested that people with hypertension have a 50% increased chance of developing AF [22]. Future studies should evaluate the exact pathophysiology of caffeine and its impact on heart rhythms.

Although the majority of the evaluated studies suggest there is no significant impact of caffeine consumption on heart arrhythmias, there are certain populations at risk of heart arrhythmia issues. Minors are an "at risk" population when caffeine consumption from EDs can lead to malignant dysrhythmias and altered ECG [17]. Caffeine should also be avoided by patients diagnosed with LQTS because it causes an increase in QTc [20]. Caffeine can also lead to other cardiovascular issues such as increases in systolic and diastolic blood pressure, which can cause myocardial infarctions. Caffeine consumption was also seen to cause nausea and vomiting in the postoperative period in some patients [12]. These patient populations should proceed with caution when deciding to drink caffeine and how much. Additionally, other adverse effects of caffeine consumption including GI disturbances, tachycardia, and heart palpitations should be considered before use.

Limitations to this study include the small number (13) of studies that were eligible for this medical literature review. Only a handful of medical arrhythmia conditions were evaluated, with the majority of the studies looking at AF. However, this may be a reflection of the most common heart arrhythmia as opposed

to study homogeneity. Additionally, a few studies evaluated EDs' impact on heart rhythm, however the effects of ED consumption cannot be directly attributable solely to caffeine. Many EDs contain other ingredients for example carnitine, taurine, etc., which may also impact heart arrhythmias. Additionally, the dosages evaluated in each of these studies varied, limiting generalizability of this review. Future studies should evaluate various caffeine doses and incidence of heart arrhythmias in large, randomized controlled clinical trials. The method of caffeine administration and exact dosage used should be controlled. Additional studies should evaluate the heart arrhythmia risk in patients with predisposing cardiac conditions and/or other special populations. Studies should also have a large sample size to see caffeine impact on heart arrhythmias on a more diverse range of patients.

5. Conclusion

This medical literature review evaluated the relationship between caffeine and heart arrhythmias. Most studies evaluated have not found a significant association between caffeine and arrhythmia, while certain populations such as children and patients diagnosed with LQTS may be at risk. Moreover, some studies suggested that caffeine may be cardioprotective, but the exact dosage of consumption to elicit this effect is not clear. Future research is needed to fully elucidate the potential benefits of caffeine. Future studies could focus on FDA doses of caffeine (low, moderate, high) in order to generalize caffeine intake, caffeine's short term and long-term impact on heart arrhythmias in individuals of different demographics should be conducted to identify at-risk individuals.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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