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Caffeine Reduces Myocardial Blood Flow During Exercise

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ABSTRACT

Caffeine consumption has been receiving increased interest from both the medical and lay press, especially given the increased amounts now available in energy products. Acute ingestion of caffeine usually increases cardiac work; however, caffeine impairs the expected proportional increase in myocardial blood flow to match this increased work of the heart, most notably during exercise. This appears to be mainly due to caffeine's effect on blocking adenosine-induced vasodilatation in the coronary arteries in normal healthy subjects. This review summarizes the available medical literature specifically relating to pure caffeine tablet ingestion and reduced exercise coronary blood flow, and suggests possible mechanisms. Further studies are needed to evaluate this effect for other common caffeine-delivery systems, including coffee, energy beverages, and energy gels, which are often used for exercise performance enhancement, especially in teenagers and young athletes.

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KEYWORDS: Athletes; Caffeine; Cardiovascular effects; Endothelial function; Myocardial blood flow

Caffeine (1,3,7-trimethylxanthine) is one of the most widely used pharmacologically active drugs in the world and is found in products such as colas, coffee, tea, energy beverages, dietary supplements, over-the-counter medications, and chocolate. It has been estimated that worldwide caffeine consumption is approximately 76 mg/d per person; in the United States and other developed countries, the average consumption rate exceeds 230 mg/d.[1]

As the popularity and consumption of energy beverages has increased, sudden cardiac death has been reported in teenagers and young athletes who have consumed these products.[2] Most energy beverages also contain guarana, a rainforest vine with seeds that contain high levels of caffeine.[3] High levels of caffeine, especially in individuals who do not consume caffeine on a regular basis, may play a role in caffeine toxicity and possible cardiac death.[3] The use of energy beverages is often advertised in conjunction with amateur and professional sports, and cardiac arrest in the setting of caffeine use and exertion has been described.[4]

On October 17, 2012, a California Superior Court lawsuit was filed against Monster Energy (Monster Beverage Corporation, Corona, Calif) by the parents of Anais Fournier, a 14-year-old Maryland teenager who died after drinking two 24-ounce Monster Energy Drinks in 24 hours. After autopsy, the cause of death was noted as "cardiac arrhythmia due to caffeine toxicity."[5] Energy beverages have been shown to acutely reduce endothelial function; however, energy beverages also may contain a variety of constituents, and the contribution of caffeine alone is unclear.[6]

Given the increase in caffeine availability and reports of adverse events, an understanding of the cardiac effects of caffeine is urgently required. This review summarizes the available medical literature specifically relating to caffeine ingestion and reduced exercise coronary blood flow, suggesting possible mechanisms. This review specifically focuses on the effects of caffeine on the coronary arteries, especially the reduced coronary blood flow noted with exercise.[7-9]

MATERIALS AND METHODS

MEDLINE, Embase, and Google database searches were conducted in an iterative manner for the English-language scientific literature published from 1976 to December 2012.

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Search terms included "caffeine," "endothelial function," "myocardial blood flow," "coronary blood flow," "flow-mediated dilatation," "myocardial perfusion reserve," "athletes," and "cardiovascular effects." No specific keywords were required as inclusion criteria. To avoid the potential role of coingestants or contaminants in producing myocardial effects, only studies describing the administration of caffeine tablets to subjects were included. The bibliographies of articles from the search were searched for relevant articles, and links on websites containing published articles were searched for pertinent information.

CLINICAL SIGNIFICANCE

- Many people ingest caffeinated products, especially energy drinks, before or during exercise.
- Caffeine reduces myocardial blood flow during exercise, at the very time when increased flow is required.
- Clinically significant effects, including ischemia and arrhythmia, may occur when caffeine and exercise are combined.
- These mechanisms may play a role in sudden cardiac death associated with energy drink use.

Caffeine Pharmacology and Physiology

Caffeine is a methylxanthine whose use results in phosphodiesterase inhibition, adenosine receptor antagonism, and release of catecholamines.[3] When taken orally, caffeine is absorbed rapidly, with time to maximum plasma concentration of 45 minutes (range, 15-120 minutes) and an average half-life of 5 hours (range, 2-12 hours).[1] Caffeine is present in a number of commonly consumed beverages in varying amounts and concentrations (**Table 1**). Caffeine is mainly metabolized into paraxanthine (80%), theobromine, and theophylline.[10] Higher caffeine doses, repeated dosing, and habitual caffeine intake generally result in prolongation of its half-life and reduced clearance of caffeine and its metabolites, creating the potential for caffeine toxicity.[1]

Caffeine produces a number of cardiac effects that seem to occur in a more pronounced manner in caffeine-naïve subjects or those consuming higher doses of caffeine (**Table 2**). Excessive consumption of caffeine may acutely cause caffeine intoxication, resulting in tachycardia, elevated blood pressure, increased myocardial contractility, vomiting, hypokalemia (from beta-adrenergic stimulation), cardiac arrhythmias (atrial flutter, atrial fibrillation, atrioventricular-nodal reentry tachycardia, ventricular tachycardia, and ventricular fibrillation), seizures, and death.[2,3]

Reduced coronary blood flow may be a symptom of endothelial dysfunction, which affects the ability of the endothelium to regulate vascular resistance (see Coronary Vasodilatation).[11] During stress (including exposure to cold, mental arithmetic, anger, ingestion of a meal, or exercise) and with certain exposures (cigarette smoking, cocaine, alcohol), the impaired ability to dilate the coronary arteries could result in supply−demand imbalance or coronary spasm, potentially leading to myocardial ischemia or cardiac arrhythmia.[12]

The effects of caffeine may be altered by genetic polymorphisms, metabolic induction/inhibition of cytochrome

Table 1 Caffeine Content of Selected Beverages

Beverage	Serving Size (fl oz)	Caffeine Content(mg)	Caffeine Concentration (mg/fl oz)
Soft Drinks			
Coca Cola, Coca Cola ZERO (The Coca-Cola Company, Atlanta, Ga)	12 fl oz	34 mg	2.8 mg/fl oz
Diet Coke (The Coca-Cola Company)	12 fl oz	45 mg	3.8 mg/fl oz
Dr Pepper (Dr Pepper Snapple Group, Plano, Tex)	12 fl oz	55 mg	4.6 mg/fl oz
Coffee and Tea			
McDonald's (Oak Brook, Ill) cup of brewed coffee	16 fl oz	100 mg	6.3 mg/fl oz
Starbucks (Seattle, Wash) Bold Pick of the Day Coffee	16 fl oz	330 mg	20.6 mg/fl oz
Starbucks Espresso Roast Coffee	1 fl oz	75 mg	75.0 mg/fl oz
Typical cup of tea	8 fl oz	50 mg	6.3 mg/fl oz
Starbucks Tazo Awake Brewed Tea	16 fl oz	135 mg	8.4 mg/fl oz
Energy beverages			
AMP Energy (PepsiCo Inc, Purchase, NY)	16 oz	142 mg	8.9 mg/fl oz
Red Bull (Red Bull GmbH, Fuschl am See, Austria)	8 oz	77 mg	9.6 mg/fl oz
Monster Energy (Monster Beverage Corporation, Corona, Calif)	16 oz	160 mg	10.0 mg/fl oz
Rockstar (Rockstar Inc, Las Vegas, Nev)	16 oz	160 mg	10.0 mg/fl oz
NOS (Coca-Cola Company)	16 oz	260 mg	16.3 mg/fl oz
Energy shots			
5-hour Energy (Living Essentials, Wabash, Ind)	2 oz	207 mg	103.5 mg/fl oz

Sources: Product labels, company reports, and independent post-marketing analyses.

Table 2 Effects of Acute Caffeine Ingestion on the Heart

Effect	Mechanism	References
No change or increased heart rate	Increased sympathetic stimulation	39-41
Increased systolic and diastolic blood pressure by 5%-10%	Increased peripheral vascular resistance	39,40,42,43
Increased myocardial contractility	Increased sympathetic stimulation	39,40
Caffeine toxicity associated with cardiac arrhythmias, including atrial fibrillation, atrial flutter, atrioventricular-nodal reentry tachycardia, and ventricular tachycardia	Inhibits phosphodiesterase activity and decreased calcium uptake into the sarcoplasmic reticulum; direct effects on inhibiting sodium current in the sodium channel. Both lead to prolongation of signal-averaged QRS complexes, in addition to vagal stimulation.	44-48
Inhibition of intracellular enzyme phosphodiesterase	Reduced conversion of cyclic adenosine monophosphate to adenosine monophosphate causing prolonged and intensified beta-receptor activation with positive inotropic and chronotropic effects	49,50
Reduced myocardial blood flow with exercise	Reduced coronary vasodilatation secondary to blockage of adenosine receptors	7-9,36

system (medications, drugs), individual factors (age, weight, sex), the presence of hepatic diseases, environmental exposures, recent use of caffeine, chronic use of caffeine, and whether it is consumed at rest or with exercise.[13] For example, caffeine-naïve subjects are more sensitive to the physiologic effects of caffeine and have a significantly increased resting heart rate compared with subjects habituated to caffeine.[14] Further, subjects who have exercised in the past 5 hours or are consuming caffeine during exercise seem to be more sensitive to caffeine effects.[8,13] Caffeine is mainly metabolized in the cytochrome system of the liver by the enzyme cytochrome 1A2.[15] The activity of enzyme cytochrome 1A2 can be influenced by factors such as sex, age, and smoking.[15] In general, women have lower enzyme cytochrome 1A2 activity than men.[16] Further, women and nonsmokers with lower enzyme cytochrome 1A2 activity have been shown to experience more toxic effects after consuming caffeine when compared with individuals with higher enzyme cytochrome 1A2 activity.[16] There is a significant interaction between caffeine and a selective serotonin reuptake inhibitor, fluvoxamine, a strong enzyme cytochrome 1A2 inhibitor, which may result in caffeine toxicity.[17]

Coronary Vasodilatation

Vasodilatation of the coronary artery is the net result of augmentation in relaxation of the smooth muscle surrounding the blood vessels, as well as removal of the stimuli for contraction.[18] The endothelium (thin layer of cells that line the artery) is a key regulator of the vascular permeability, hemostasis, and underlying smooth muscle cell tone (resistance).[19] Thus, the endothelium is critical to normal vessel tone and variation; therefore, normal endothelial function in important for coronary artery function and health in the short and long term, and endothelial dysfunction is detrimental to artery function.[19] Of note, in cases where there is impairment in endothelium dependent vasodilatation, maximal coronary flow response to adenosine may be reduced even in the absence of stenosis.[11]

The main intracellular stimuli that can result in the vasodilatation of blood vessels include the following:[20,49,50]

- Hyperpolarization mediated: Changes in the resting membrane potential of the cell affect the level of intracellular calcium through modulation of voltage-sensitive calcium channels in the plasma membrane, mediated via adenosine.
- Cyclic adenosine monophosphate mediated: Adrenergic stimulation results in elevated levels of cyclic adenosine monophosphate and protein kinase A, which results in increasing calcium removal from the cytoplasm, mediated via prostacyclin.
- Cyclic guanosine monophosphate mediated: stimulation of protein kinase G, via nitric oxide.

To gauge normal coronary artery vasodilatation and contraction in vivo, we require surrogate measures of function. Myocardial blood flow can be measured indirectly using a number of methods, including the following:

- Positron emission tomography (PET) measuring myocardial perfusion reserve.[21] The major limitations of PET include higher costs, availability of imaging agents, less apparent and more difficult to evaluate artifacts, and high radiation doses.[21]
- Flow-mediated dilatation of the brachial artery induced by reactive hyperemia is an accurate method for measuring brachial artery endothelial function in humans and is an accepted noninvasive surrogate for coronary artery endothelial function.[22] Limitations of flow-mediated dilation include that it is not easily reproducible, it is not established to be directly related to cardiovascular events (ie, not established as a prognostic risk factor), and many extrinsic factors influence its results (recent exercise, food, drink, smoking, and medications).[22]

Table 3 Caffeine Effects on Myocardial Blood Flow at Rest and Exercise.

No. of Healthy Subjects Studied (Male)	Mean Age (y)	Caffeine Ingestion (Testing Performed)	Measuring Tool	Criteria	Results	Reference
15 (5)	58 ± 13	200 mg (testing 50 min later)	Myocardial perfusion reserve using PET	Ratio of myocardial blood flow during bicycle stress divided by myocardial blood flow at rest.	Exercise-induced myocardial blood flow response decreased 14% after caffeine ingestion ($P < .05$).	[7]
18 (11)	27 ± 6	200 mg (testing 50 min later)	Myocardial perfusion reserve using PET	Ratio of myocardial blood flow during bicycle stress divided by myocardial blood flow at rest.	Resting myocardial blood flow was not affected. Exercise-induced myocardial blood flow response decreased 22% after caffeine ingestion ($P < .01$).	[8]
40 (33)	53 ± 6	200 mg (testing 60 min later)	Flow-mediated dilatation of the brachial artery	Percent flow-mediated dilation as (maximum diameter minus baseline diameter)/baseline diameter × 100.	Resting flow-mediated dilation increased 10% after caffeine ingestion ($P < .001$).	[23]
10 (10)	26.8 ± 5.2	300 mg (testing 60 min later)	Forearm blood flow responses to acetylcholine, an endothelium-dependent vasodilator, and to sodium nitroprusside, an endothelium-independent vasodilator.	Forearm blood flow was measured by using a strain-gauge plethysmograph.	Resting forearm blood flow was not affected by oral caffeine ingestion. Resting forearm blood flow response to acetylcholine was increased 25% ($P < .05$).	[24]
10 (3)	30 ± 3	360 mg (6 mg/kg)	Forearm blood flow was made at baseline and at 20-min intervals.	Forearm blood flow was measured by using the indirect plethysmographic venous occlusion technique.	Before exercise, caffeine increased both systolic blood pressure 17% and mean arterial pressure 11% but had no effect on forearm blood flow. During dynamic exercise, caffeine attenuated the increase in forearm blood flow by 53%, $P < .05$.	[9]

PET = positron emission tomography.

Acute Caffeine Ingestion and Effects on Coronary Blood Flow During Exercise

The studies measuring the effects from acute caffeine ingestion on coronary blood flow with exercise are summarized (**Table 3**).

Myocardial Blood Flow Studies

After caffeine ingestion at rest, myocardial blood flow does not change significantly in PET studies.[8] However, in healthy subjects who consume caffeine and then exercise afterward, there are significant reductions in myocardial blood flow.

The first study involved 10 women and 5 men, with a mean age of 58 years. The authors measured myocardial blood flow by PET after ingestion of 200 mg of caffeine, followed by 50 minutes of exercise (stationary bicycle).[8] They did not show resting data. Exercise myocardial blood flow response was reduced 14% during exercise after caffeine ingestion.

The second study involved 18 healthy subjects, with a mean age of 27 years, who underwent both resting and exercise myocardial blood flow (stationary bicycle) with PET 50 minutes after taking 200 mg caffeine.[7] Although resting myocardial blood flow was unaffected by caffeine, exercise myocardial blood flow was reduced by 22% after caffeine consumption. This study also looked at the effect during altitude simulation (hypobaric hypoxia) and noted that myocardial blood flow was reduced even more by 39%.

Taken together, these studies show that PET measurement of myocardial blood flow in individuals exercising approximately 1 hour after 200 mg of caffeine consumption is reduced in the range of 14% to 22%.[7,8] This reduction is even greater if exercise is performed at hypoxia at altitude (39%).[8] In patients with coronary artery disease who consume caffeine and then exercise, the reductions are even more significant (18%-25%).[7] These studies suggest that the normal exercise-induced hyperemic flow response may at least be antagonized in part by caffeine.[8]

Flow-Mediated Vasodilatation Studies

The flow-mediated dilation studies noted no significant effect of caffeine or a minor improvement in flow-mediated dilation at rest.[23,24] Unfortunately, several studies did not conduct evaluations of flow-mediated dilation during exercise. One study showed reduced forearm blood flow with exercise after caffeine consumption.[9]

The first study involved 40 subjects (33 men), with a mean age of 53 years, who received 200 mg caffeine. The flow-mediated dilation at rest was noted to be unchanged 1 hour after receiving 200 mg caffeine.[23] These subjects had no significant change in their heart rate or systolic or diastolic blood pressure after this dose; this is interesting because caffeine ingestion usually results in an increase in heart rate and systolic and diastolic blood pressures in healthy, normotensive subjects.

Another study involved 10 young men (mean age, 27 years) and measured forearm blood flow by using a strain-gauge plethysmograph and averaging 3 measurements and expressed as milliliters per minute per 100 mL of forearm tissue volume.[24] One hour after taking 300 mg of caffeine, there was no demonstrated change in resting forearm blood flow.[24] Although heart rate did not change, the subjects' systolic and diastolic blood pressures both increased after caffeine consumption. Also, there was an improved forearm blood flow response to acetylcholine, an endothelium-dependent vasodilator suggesting that endothelial function may have been enhanced.

Another study examined the acute effects of caffeine on forearm blood flow during dynamic leg exercise in 10 trained, caffeine-naïve cyclists (7 women and 3 men) who were studied at rest and during bicycle ergometry before and after the ingestion of 6 mg/kg caffeine (~300 mg caffeine) or 6 mg/kg fructose (placebo) with 250 mL of water.[9] After consumption of caffeine or placebo, subjects rested for 100 minutes (rest protocol) or rested for 45 minutes followed by 55 minutes of cycle ergometry at 65% of maximal oxygen consumption (exercise protocol). Measurements of mean arterial pressure, forearm blood flow, heart rate, skin temperature, and rectal temperature and calculation of forearm vascular conductance were made at baseline and at 20-minute intervals. Plasma angiotensin II was measured at baseline and at 60 minutes post-ingestion in the exercise protocols. Before exercise, caffeine was noted to increase both systolic blood pressure (17%) and mean arterial pressure (11%) without affecting forearm blood flow or forearm vascular conductance. During dynamic exercise, caffeine attenuated the increase in forearm blood flow (53%) and forearm vascular conductance (50%) and accentuated exercise-induced increases in angiotensin II (44%).

Taken together, these studies suggest that caffeine in doses of 200 to 300 mg does not affect resting myocardial blood flow as measured by flow-mediated dilation or forearm blood flow. However, the one study including exercise suggested that caffeine can alter the cardiovascular response to dynamic exercise in a manner that may modify regional blood flow and conductance.[9]

Mechanisms for Caffeine Effects on Exercise Coronary Blood Flow

Possible mechanisms for caffeine's effect to reduce myocardial blood flow are listed in **Table 4** and discussed in more detail in this section. Caffeine ingestion has been shown to inhibit soluble guanylate cyclase with subsequent suppression of the conversion of guanosine triphosphate into cyclic guanosine monophosphate.[25,26] Cyclic guanosine monophosphate serves as the second messenger of the l-arginine/nitric oxide system; consequently, a decrease in cyclic guanosine monophosphate levels could account for the impairment of nitric oxide—mediated effects.[27] In blood vessels, cyclic guanosine monophosphate leads to relaxation of vascular smooth muscles, which would lead to vasodilatation

Table 4 Possible Mechanisms for Effects of Acute Caffeine Ingestion Reducing Myocardial Blood Flow with Exercise

Effect	Result	References
Inhibition of soluble guanylate cyclase	Reduced cyclic guanosine monophosphate thus reduced NO, a powerful vasodilator	25,26
Stimulating the release of calcium from the endothelial reticulum	Activation of eNOS to increase production of NO (a vasodilator)	10
Decrease insulin sensitivity	Uncoupling of eNOS with reduced production of NO (a vasodilator)	29
Inhibition of the suppressing effect of adenosine A1 receptors on renin production	Increased production of angiotensin II (a vasoconstrictor)	30
Blocking coronary adenosine A2 receptors	Blocking effects of endogenously produced adenosine thus increased coronary artery tone (vasoconstriction)	31
Stimulating release of adrenal norepinephrine	Increased coronary alpha-2 adrenergic receptor mediated coronary vasomotor tone (vasoconstriction)	34,35
Facilitation of norepinephrine release from sympathetic nerve endings	Increased coronary alpha-2 adrenergic receptor mediated coronary vasomotor tone (vasoconstriction)	9
Accentuated exercise-induced increases in angiotensin II	Increased production of angiotensin II (a vasoconstrictor)	9

eNOS = endothelial nitric oxide synthase; NO = nitric oxide.

and increased blood flow.[28] By blocking cyclic guanosine monophosphate formation, caffeine may thus prevent vasodilatation. Acute caffeine ingestion also may decrease insulin sensitivity in healthy adults, which could contribute to derangement of nitric oxide production and oxidative stress, possibly through uncoupling of the endothelial nitric oxide synthase.[28,29]

Caffeine may augment vascular oxidant stress via increased production of angiotensin II, a powerful vasoconstrictor, by inhibiting the suppressing effect of adenosine A1 receptors on the production of renin.[30] This inhibitory effect of caffeine is more potent at adenosine A2A receptors that exert direct vasodilator effects, particularly in ischemic conditions, and mediate the process of reactive hyperemia more so than A1 receptors.[31] Levels of angiotensin II were measured in one study and shown to increase in subjects exposed to caffeine and subsequent exercise.[9]

Caffeine also can lead to an overall increase in coronary artery tone and constriction. Caffeine blocks both coronary adenosine A2 receptors and the downstream effects of endogenously produced adenosine on coronary artery vasodilatation in a dose-dependent fashion, leading to overall increased coronary artery tone and net vasoconstriction.[31-33] Caffeine also has been shown to stimulate release of adrenal norepinephrine leading to stimulation of coronary alpha-2 adrenergic receptors, increasing coronary vasomotor tone with net vasoconstriction.[34,35] In the sympathetic nerve endings in the heart, caffeine also facilitates norepinephrine release, leading again to increased coronary alpha-2 adrenergic receptor—mediated coronary vasomotor tone and net vasoconstriction.[9]

DISCUSSION

A dose of caffeine between 200 and 300 mg taken orally does not appear to have any acute detrimental effect on myocardial blood flow at rest.[23] However, if the subject is exposed to exercise, it appears that the usual adenosine- and sympathetic-mediated increased coronary vasodilatation that should match the augmentation in cardiac work is significantly reduced.[7,9] In light of the propensity of individuals to consume energy products that contain high levels of caffeine and then exercise, the resultant supply—demand mismatch in the heart could lead to possible cardiovascular complications, such as myocardial ischemia, spasm, and arrhythmia, even in healthy individuals. These deleterious effects may be more pronounced with exercise at altitude (eg, climbing at high terrestrial altitude and skiing).[8]

There was some variability noted in the effects of caffeine on myocardial blood flow as measured by surrogate tools. This is likely related to variations in patient population (age, sex), time of measurement after taking caffeine, and different measurement methodologies used to indirectly measure endothelial function. In addition, each measuring tool has its limitations, including reproducibility and being affected by intrinsic factors. However, in a well-run measuring center that follows strict dietary, exercise, and medication protocols for its test subjects and has well-trained technologists who use specific landmarks to perform ultrasound measurements, the reproducibility of the measures is good.[22]

Caffeine also may have a dual role, so that it increases or decreases endogenous nitric oxide production, causing increased or decreased endothelial function under different circumstances. The balance of the vasodilator effect of caffeine as an endothelium-dependent vasodilator and the vasoconstrictor effect of caffeine as an adenosine-receptor antagonist may regulate vascular function.[24] The latter effect appears to be important in those who have consumed caffeine and then exercise approximately 1 hour later, the point at which caffeine levels in the blood are at their peak.

Although there are several possible mechanisms by which acute caffeine ingestion may affect endothelial function and myocardial blood flow during exercise, it is likely that caffeine antagonizes the coronary artery vasodilator effects mediated by its inhibition of adenosine receptors.[9,36-38]

The significance of these changes is unknown at this time. However, one possibility is that if there is reduced myocardial blood flow; this may result in a supply−demand imbalance and ischemia that could lead to arrhythmia. In addition, during a period of endothelial dysfunction, coronary artery spasm could occur, leading again to ischemia and arrhythmia. One case report noted significant coronary artery spasm in a healthy adult after consuming high levels of caffeine in the form of an energy beverage.[4] Given the possibility that endothelial dysfunction may play a role in morbidity with concomitant caffeine intake and exercise, more research is recommended to clarify the significance of these effects.

CONCLUSIONS

Acute caffeine ingestion in humans elicits various cardiovascular effects, some of which may be deleterious, especially in the setting of stress or exercise. These effects are frequently more pronounced in the caffeine-naïve individual or in those acutely ingesting higher doses such as are present in energy beverages. In addition, there are important pharmacologic differences in individual caffeine levels affected by multiple variables, including age, sex, medications, and drugs. In healthy individuals who perform aerobic exercise 1 hour after consumption of 200 to 300 mg of caffeine, a reduction in myocardial blood flow has been noted by indirect tests. Additional research is needed to understand and characterize the underlying mechanisms of caffeine. Moreover, it is critical to assess the safety of high-dose caffeine ingestion in those who are younger, caffeine naïve, or planning to exercise in the next few hours. Specific research needs to be done on the impact of energy products on coronary blood flow, because many of the caffeine-containing sports liquids and gels contain other ingredients that may interact with caffeine and alter the net effect on the coronary artery function during exercise.

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