The effect of aerobic exercise and caffeine supplementation on the cognitive performance and balance of college student-athletes recovered from COVID-19

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Article Info	Abstract
	Background: The SARS-CoV-2 virus is viewed as one of the defining crises of the current era, with various adverse ramifications for sports performance. **Aim:** The objective of the present study was to investigate the effect of aerobic exercise and caffeine supplementation on the cognitive performance and balance of college student-athletes recovered from COVID-19. **Materials and Methods:** Forty male student-athletes aged between 18 to 25 years from the Imam Khomeini International University of Qazvin were randomly assigned to four groups: 1. exercise + caffeine supplementation, 2. aerobic exercise + placebo, 3. aerobic exercise, and 4. control, in a pre-test post-test design. The Shapiro-Wilk test was used to check the normality of data distribution and covariance analysis was used for inter-group comparison. **Results**: The ANCOVA analysis showed significant differences in cognitive performance and balance among the four groups ($P<0.05$). Pairwise comparisons using the Bonferroni post-hoc test showed statistically significant differences in cognitive performance and balance between the aerobic exercise + caffeine group versus the aerobic exercise + placebo group ($P<0.05$) and the aerobic exercise versus the control group ($P<0.05$). Also, there was significant differences in mean cognitive performance and balance indices between AE+CAF versus CONT ($P<0.005$) and AE+CAF versus AE ($P<0.005$). **Conclusion:** The results of this study show that aerobic exercise with caffeine supplementation can improve cognitive performance and balance of student-athletes recovered from COVID-19.

1. Introduction

In December 2019, a novel viral disease emerged in the province of Hubei, China, which quickly became a global pandemic that was named COVID-19 caused by the SARS-CoV-2 virus [1]. The SARS-CoV-2 virus has a significant negative impact on human health, primarily affecting the respiratory system and resulting in symptoms such as fever, cough and difficulty breathing. Other symptoms including fatigue, headache and loss of taste or smell have also been reported [2]. This virus spread rapidly worldwide, prompting governments to implement public health measures like social distancing, travel restrictions, mandatory mask-wearing in public spaces and quarantines intended to curb viral transmission [3]. While necessary to reduce virus transmission, these measures have adversely affected various health aspects, including fatigue, lethargy and weakness [4]. Also, the SARS-CoV-2 virus can cause a range of symptoms varying by severity, underlying conditions and age [2, 5].

Studies have shown that some COVID-19 side effects can persist for months, characterized as post-acute sequelae of COVID-19 or 'long COVID-19' [6]. Huang et al. (2021) reported that individuals who recovered from COVID-19 experienced symptoms like fatigue, muscle weakness, sleep problems, anxiety and depression for up to six months after recovery [7].

The COVID-19 pandemic has significantly disrupted the sports world, causing many athletes to face interruptions in training and competitions due to the closure of sporting venues and restrictions on mass gatherings. Social distancing measures have also limited opportunities for athletes to participate in team sports and group training sessions, further impacting their physical and cognitive development. Prolonged inactivity and social isolation resulting from the pandemic have negatively impacted athletes' motor and cognitive performance, including their balance. Moreover, athletes who contract COVID-19 may experience neurological symptoms that can further impair their balance and cognitive performance [8, 9].

Cognitive performance refers to mental processes and abilities involved in acquiring, processing and utilizing information. These processes include attention, perception, memory, language, reasoning, problem-solving and decision making. Maintaining cognitive performance is essential for learning, problem-solving and decision-making, and can be influenced by factors such as age, genetics, environment and lifestyle. Thus, it is critical to prioritize preserving cognitive performance for overall health [10]. Balance is the capacity to maintain postural stability and control during physical activity. Balance refers to "the ability to sustain or control equilibrium while standing, walking or performing other tasks under conditions of varying postural demands and sensory environments." Maintaining balance is essential for safe and effective movement, and involves integrating sensory input from vision, vestibular and somatosensory systems. Impairments in balance can result in injuries and other health issues, particularly for older adults [11]. Therefore, cognitive performance and balance are essential components of athletic performance and student athletes' health [12, 13].

However, the adverse effects of social restrictions and contracting COVID-19 can compromise these capacities [8, 9], making it crucial to implement strategies to mitigate these complications. Proper nutrition and

physical activity can have a positive impact on the health of patients with COVID-19 [14].

The studies have indeed shown that maintaining a healthy diet and engaging in regular physical activity can help reduce the risk of severe illness and improve overall physical and mental wellbeing, including for those with COVID-19 [15, 16]. Therefore, prioritizing these strategies can benefit enhancing the overall health and athletic performance of student athletes [12]. Aerobic exercise is a type of physical activity that elevates heart rate and breathing rate. Scientific research shows that aerobic exercise provides numerous benefits for cognitive performance, such as improving attention, memory, and executive performance [17]. These effects may arise from several mechanisms, including increased blood flow to the brain, release of growth factors that promote neuron growth, and modulation of neurotransmitter systems like dopamine and serotonin [18, 19].

Additionally, aerobic exercise has been found to enhance balance and reduce the risk of falls in older adults. The mechanisms underlying these effects are believed to include improvements in muscle strength, flexibility, and coordination, as well as changes in sensory systems that aid in balancing [20]. Therefore, it is recommended as part of a healthy lifestyle to sustain cognitive and physical well-being [21, 22]. Caffeine is a commonly consumed psychoactive substance present in various foods and beverages, such as coffee, tea, chocolate, and soda. Its ability to enhance alertness and decrease fatigue has made it a popular choice for improving cognitive performance [23]. In addition, caffeine has also been investigated for its impact on balance [24]. A study found that providing caffeine supplements to fatigued young football players improved their balance and certain physical and skill fitness characteristics [25]. In addition, supplementation with caffeine has been shown to acutely enhance various aspects of exercise performance in many but not all studies [26].

As researchers continue to search for effective treatments for COVID-19, there has been increasing interest in the potential role of caffeine in modulating immune system function and improving outcomes in COVID-19 patients. Several studies have investigated the effect of caffeine supplementation on immune system function in various contexts, including exercise and disease. Horrigan et al. (2006) has been shown caffeine has both stimulatory and inhibitory effects on the immune system, depending on the dose and the context in which it is administered. At low doses, caffeine has been shown to enhance immune function by increasing the production of cytokines and other immune mediators. However, at high doses, caffeine has been shown to have a suppressive effect on the immune system by inhibiting the production of cytokines and other immune mediators [27].

Given the potential role of caffeine in modulating immune system function, there is growing interest in its potential use as a treatment for COVID-19. Caffeine and caffeine-containing pharmaceuticals have the potential to inhibit the 3-chymotrypsin-like protease (3CLpro) of SARS-CoV-2, the virus that causes COVID-19. The 3CLpro is an important enzyme in the replication cycle of the virus, and inhibiting its activity may prevent the virus from replicating and spreading [28]. Aerobic exercise has been shown to improve cognitive function by increasing blood flow

to the brain [29], stimulating the release of neurotrophic factors [30]. Caffeine has been shown to improve sports performance by affecting brain function in general [31]. These synergistic effects might be effective on cognitive performance and balance.

Given the critical importance of exploring strategies to prevent and control complications associated with COVID-19, there is currently limited research investigating the effects of aerobic exercise and caffeine supplementation on cognitive performance and balance in college student-athletes recovering from COVID-19. The few studies has examined exercise interventions in COVID-19 patients having focused primarily on recovery of improvements in immune function and respiratory muscle strength, with little specific attention to cognitive and balance outcomes [32]. Given that some COVID-19 patients report neurological symptoms that can further impair their balance and cognitive performance [8, 9], interventions to aid recovery in these domains could be valuable. Exercise has well-established benefits for cognition [33] and balance [19] under normal circumstances, and caffeine is known to provide acute cognitive enhancements and balance for some individuals [23, 25]. However, no studies have yet tailored aerobic exercise or caffeine supplementation programs specifically for COVID-19 recovered student-athletes aiming to optimize cognitive and balance recovery. More research is needed to determine effective exercise and supplementation dosages, durations and frequencies to benefit this population, as well as how these interventions may interact and provide synergistic benefits for cognition and balance. Such research could help inform recovery guidelines and return-to-play

protocols for student-athletes recovering from COVID-19. Therefore, the objective of this study was to investigate the effects of aerobic exercise and caffeine supplementation on cognitive performance and balance in college student athletes recovered from COVID-19.

2. Materials and Methods

2. 1. Participants

Forty student athletes (football players and futsal players in university) of Imam Khomeini International University (weight: 73.2±4.91 kg, height: 174.80±5.15 cm, age: 22.22±00 years, BMI: 24.21±1.01 kg/m^2), who were recovered from COVID-19 were selected using both convenience and purposive sampling methods. They were studied in two pretest and post-test phases and randomly assigned to four groups: 1. The aerobic exercise + caffeine supplementation (AE+CAF) (N=10), 2. The aerobic exercise + placebo (AE+PEL) (N=10), 3. The aerobic Exercise (AE) (N=10), and 4. The control group (CONT) (N=10).

2. 2. Protocols

The participants voluntarily provided their medical history and personal information by completing medical history questionnaires [34] after agreeing to participate in the study. They were asked to sign an informed consent form indicating their willingness to participate and confirming they understood the study's objectives and procedures. Participants were included in the study if they met the following criteria: Having sports experience competing (football players and futsal players) at the university level prior to the COVID-19 pandemic; being free from specific underlying diseases as determined by a medical history

questionnaire; not taking medications, sports supplements, or alcoholic beverages on a regular basis; not participating in sports or exercise training due to the COVID-19 pandemic; having been infected with COVID-19 up to 6 months prior to participating in the research study according to Huang et al. (2021) [7] and were excluded from the study if any of the following occurred: irregular participation in the training program, failure to participate honestly (inconsistencies could indicate dishonesty) in study procedures, injuries that prevented completing the training program.

Cognitive performance and balance were assessed prior to the intervention as part of the initial evaluation. The Vienna Test System NEURO produced by SCHUHFRIED in Austria [35] was used to evaluate cognitive performance. A cognitive (COG) test examines attention, concentration and reaction speed in subjects. The COG test is performed using software, a keyboard with two metal handles and a display screen. It is based on Roelkh's (1991) model of concentration, which defines concentration as having three components: energy, execution and accuracy. This model helps the examiner accurately evaluate the subject's level of attention, concentration, comprehension and precision. The COG test procedure presents four images in a row above a single image. The subject must identify which of the four upper images matches the lower image within 1.2 sec. The COG test outcomes include: correct choice duration (accuracy), correct refusals (processing speed measure), correct choice duration (concentration index) [36].

The Good-Balance machine produced in Finland was used to evaluate participants' balance. The Good-balance device consists of a force platform with integrated sensors and software that measures and analyzes the forces and movements of the human body during balance. The device can be used for a variety of balance assessments, including postural sway, single-limb stance, and dynamic balance (Traveled length (mm)) and static balance (Covered area (mm)) tests. The device provides real-time feedback on balance performance and generates reports that can be used to track progress over time [37].

The intervention consisted of 12 sessions of aerobic exercise over four weeks. Following the intervention, participants were re-evaluated using the same cognitive and balance tests administered during the initial evaluation. This follow-up evaluation assessed any changes from baseline in cognitive performance and balance.

2. 3. Aerobic exercise

The aerobic exercise program consisted of four weeks of treadmill running three times per week, with an intensity between 60%-75% of each subject's maximum heart rate (MHR). Each training session included a warm-up, main training program, and cool-down. Heart rate was monitored during training using a Polar heart rate monitor (Pulsar med 3p, manufactured in Germany). If participants experienced any symptoms such as chest pain, shortness of breath, dizziness, fainting, or changes in complexion, the exercise was stopped and they were evaluated by the research team. MHR is calculated as MHR=210−age [38].

2. 4. Caffeine supplementation

Caffeine supplements made by the Nitro mass company and matching maltodextrin placebos were purchased from a pharmacy. The active dose was 0.5 mg caffeine per kg body weight, with matching placebo pills.

Supplements were identically packaged and randomly assigned to participants. Participants consumed their assigned supplement, either 0.5 mg caffeine/kg or placebo, 30 min before exercise. This regimen continued for four weeks, with participants blinded to whether they received active supplement or placebo [39].

2. 5. Statistical analysis

The normality of the data was assessed using the Shapiro-Wilk test. An analysis of covariance test and the Bonferroni post-hoc test were performed to analyze differences between groups. All statistical analyses were conducted using IBM SPSS V26 software, with statistical significance set at ($P<0.05$). Demographic data was compared between groups using ANOVA test. Figures were generated using Microsoft Excel 2016.

3. Results

Participant characteristics are shown in Table 1. No significant differences were observed for demographic characteristics of participants ($P>0.05$). Demographic data was compared between groups using ANOVA test.

Table 1. Participant demographic characteristics.

Variable groups	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)
AE+CAF	22.20±2.44	176.00±4.57	75.13±2.80	24.25±0.77
AE+PEL	22.40±1.89	175.20±6.16	72.88±6.95	23.70±1.51
AE	22.80±1.93	174.80±4.04	74.73±3.69	24.45±1.05
CONT	21.50±1.77	173.20±5.92	72.14±5.26	24.46±0.57

AE+CAF: Aerobic exercise + caffeine supplementation, AE+PEL: Aerobic exercise + Placebo, AE: Aerobic exercise, CONT: Control

Table 2 shows the Mean±SD of cognitive performance and balance scores in the pre-test and post-test for four groups: 1. AE+CAF, 2. AE+PEL, 3. AE, 4. CONT. The Shapiro-Wilk test results indicated that the distribution of pre-test and post-test data in each group was normal, with ($P>0.05$). Additionally, homogeneity of variance was confirmed.

Based on the fulfillment of these assumptions, an analysis of covariance (ANCOVA) was conducted to determine the differences in post-test scores while controlling for pre-test scores. Analysis of covariance revealed significant differences in mean cognitive performance and balance indices between the four groups at post-test ($P< 0.001$).

The Bonferroni Post hoc tests showed significant differences in cognitive performance, dynamic balance and static balance between AE+CAF versus AE+PEL and AE versus CONT for Correct choice duration: ($F_{3,35}=19.81$, $P=0.000$, $\eta^2=0.60$), ($F_{3,35}=19.81$, $P=0.040$, $\eta^2=0.18$); Correct choices made: ($F_{3,35}=31.80$, $P=0.000$, $\eta^2=0.73$), ($F_{3,35}=31.80$, $P=0.000$, $\eta^2=0.38$); Correct refusals: ($F_{3,35}=45.54$, $P=0.000$, $\eta^2=0.79$), ($F_{3,35}=45.54$, $P=0.000$, $\eta^2=0.46$); Dynamic balance: ($F_{3,35}=82.99$, $P=0.000$, $\eta^2=0.87$), ($F_{3,35}=82.99$, $P=0.000$, $\eta^2=0.72$); and Static balance: ($F_{3,35}=48.28$, $P=0.000$, $\eta^2=0.80$), ($F_{3,35}=48.28$, $P=0n002$, $\eta^2=0.56$) respectively.

Also, there was significant differences in mean cognitive performance and balance indices between AE+CAF versus CONT ($P< 0.001$) and AE+CAF versus AE ($P< 0.001$). It appeared that AE+CAF exhibited better cognitive performance, dynamic

balance and static balance compared to the other groups. Figure 1 shows the results of analysis covariance and the Bonferroni post hoc test in cognitive performance (A) and balance (B).

**Table 2.** Changes in cognitive performance and balance between groups

Variable	Groups	Stages	
		Pre-test Mean±SD	Post-test Mean±SD
Cognitive performance Correct choice duration (Sec)	AE+CAF	1.34±0.07	1.14±0.04
	AE+PEL	1.35±0.06	1.29±0.05
	AE	1.37±0.05	1.27±0.06
	CONT	1.34±0.06	1.33±0.08
Cognitive performance Correct choices made (Number)	AE+CAF	25.10±2.42	34.20±1.75
	AE+PEL	24.40±2.41	28.90±3.38
	AE	23.50±2.12	28.50±1.17
	CONT	24.10±2.68	24.60±3.03
Cognitive performance Correct refusals (Number)	AE+CAF	23.00±1.49	34.70±2.40
	AE+PEL	22.70±1.76	28.90±2.99
	AE	23.10±1.44	28.00±3.09
	CONT	21.30±2.31	20.60±1.57
Dynamic balance Traveled length (mm)	AE+CAF	1768.60±122.21	1190.50±63.09
	AE+PEL	1701.70±64.29	1471.60±53.59
	AE	1754.20±120.59	1397.10±104.04
	CONT	1737.80±125.44	1733.70±118.32
Static balance Covered area (mm)	AE+CAF	19.10±2.42	10.40±1.83
	AE+PEL	20.30±4.16	15.50±2.63
	AE	19.00±1.69	14.20±1.61
	CONT	18.90±3.72	19.00±2.90

AE+CAF: Aerobic exercise + caffeine supplementation, AE+PEL: Aerobic exercise + Placebo, AE: Aerobic exercise, CONT: Control

4. Discussion

The COVID-19 pandemic has had a substantial effect on athletes and sports enthusiasts globally. Athletes recovering from COVID-19 may experience delayed recovery and reduced performance due to respiratory issues and potential long-term health consequences. The pandemic has also resulted in the cancellation or deferral of numerous athletic events, disrupting the training and competition schedules of student-athletes which has not only impacted their physical development, but also their mental health and wellbeing. The uncertainty and disruption caused by the pandemic have added stress and anxiety to an already demanding and competitive environment, highlighting the necessity for improved support and resources for athletes and sports programs [40, 41, 42, 43]. Therefore, the objective of the current study was to investigate the effect of aerobic exercise and caffeine supplementation on the cognitive performance and balance of student athletes recovered from COVID-19.
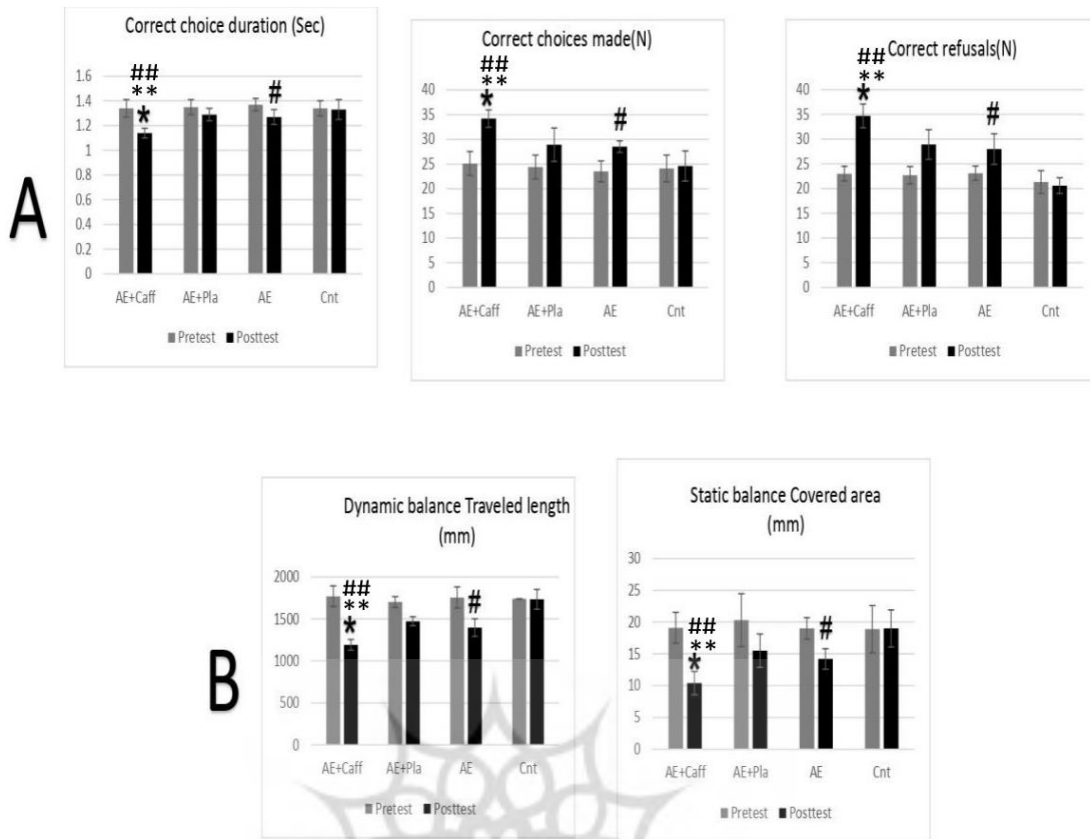
* Significant difference between AE+CAF and the AE+PEL (*P*<0.05); # Significant difference between AE and CONT (*P*<0.05); ** Significant difference between AE+CAF and CONT (*P*<0.05); ## Significant difference between AE+CAF and AE (*P*<0.05); AE+CAF: Aerobic exercise + caffeine supplementation; AE+PEL: Aerobic exercise + Placebo; AE: Aerobic exercise; CONT: Control.

Figure 1. Results of the Bonferroni post-hoc test in cognitive performance (A) and balance (B)

The results of the current study showed that there is a significant difference between AE+CAF and AE+PEL, AE and CONT, AE+CAF and CONT and also AE+CAF and AE in cognitive performance. In other words, it was shown that both aerobic exercise and aerobic exercise with caffeine supplementation have a positive impact on cognitive performance. It appeared that the aerobic exercise + caffeine supplementation group exhibited better cognitive performance compared to the other groups. Several mechanisms potentially underlie these effects. Aerobic exercise likely improves cognition by upregulating neurotransmitters such as dopamine and norepinephrine, increasing brain-derived neurotrophic factor and gray matter volume, which are pivotal for learning and memory [44]. In this regard, previous studies have shown that aerobic exercise [45, 46] and caffeine supplementation [47, 48] have a positive effect on cognitive performance. These results are consistent with the current study.

However, not all studies have shown that aerobic exercise benefits all aspects of cognitive performance [21]. Factors including exercise intensity, duration [49], timing relative to cognitive tasks [50], and individual differences [51] may influence effectiveness. Similarly, parameters relating to caffeine consumption such as dosage, timing, genetics and age could

determine its efficacy [52].

The findings of this study also showed a significant difference between AE+CAF and AE+PEL, AE and CONT, AE+CAF and CONT and also AE+CAF and AE in static and dynamic balance. In other words, it was shown that both aerobic exercise and aerobic exercise with caffeine supplementation had a positive effect on static and dynamic balance. AE+CAF seemed to have better balance compared to other groups.

Studies have shown that aerobic exercise improves balance in patients with osteoporosis [53] and diabetes [54], these results are consistent with the current study. Evidence suggests that physical activity improves muscle strength and power, increases neural flexibility, enhances cardiovascular performance, and reduces inflammation, all of which play a unique role in balance improvement [55].

However, some studies have found that aerobic exercise alone is insufficient to improve balance [56, 57], which may be associated with differences in exercise intensity, duration, frequency and participants' gender [58]. In addition to aerobic exercise, it has been shown that caffeine also improves balance [59, 60], these results are consistent with the current study. A major part of this efficacy is associated with caffeine's effects on muscle activation, which may improve balance through its effects on muscle activation and force production [60]. However, some studies have shown that caffeine has no effect on balance, in which case this lack of efficacy may be due to the dose, timing of ingestion and gender of the participants [61].

Finally, the current study showed that aerobic exercise with caffeine supplementation can improve cognitive performance and balance of student athlete recovered from COVID-19, but it had some limitations, such as a restricted number of eligible participants, because the COVID-19 outbreak had just recently been brought under control at that time (late spring-2022), but concerns about infection and the SARS-CoV-2 virus restrictions still existed, which restricted the number of participants.

In addition, the research was constrained by time limitations such that the aerobic exercise and caffeine supplement interventions could not be extended beyond four weeks. A 4-week training program was deemed feasible given the time constraints and other commitments of the student-athlete participants. While longer training periods are often recommended to induce significant adaptations, extending the interventions beyond four weeks was not practicable within the constraints of the study. The 4-week duration therefore represented a compromise between feasibility and optimal training duration to balance the aims of the research with the realities of the study context and participant population. The relatively short intervention period may have limited the magnitude of physiological and performance changes observed but permitted an initial investigation of the effects of interest within the practical constraints of the research design. Going forward, longer training periods should be considered to maximize the likelihood of beneficial adaptations and performance gains.

Therefore, further investigations are needed to identify optimal exercise intensities, appropriate doses and timings of caffeine supplementation ingestion and their effects on the cognitive and balance performance of athletes recovered from COVID-19.

5. Conclusion

Based on the findings of this investigation, it appears that aerobic exercise with caffeine supplementation may be an efficacious means to improve the cognitive and balance performance of athletes recuperating from COVID-19. However, the physiological characteristics of each student-athletes must be cognizant of their sensitivity to caffeine supplementation ingestion and take precautions.

Conflict of interest

The authors declared no conflicts of interest.

Authors' contributions

All authors contributed to the original idea, study design.

Ethical considerations

The authors have completely considered ethical issues, including informed consent, plagiarism, data fabrication, misconduct, and/or falsification, double publication and/or redundancy, submission, etc. The study procedure was approved by ethical committee of Qazvin medical sciences university (Ref no: IR.QUMS.REC.1401.171). The research was performed in accordance with the ethical standards of the Helsinki Declaration (1964).

Data availability

The dataset generated and analyzed during the current study is available from the corresponding author on reasonable request.

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