Heliyon 10 (2024) e35025

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

The effect of caffeine supplementation on muscular strength and endurance: A meta-analysis of meta-analyses

Hossein Taghizadeh Bilondi [a], Hanieh Valipour [a], Sahar Khoshro [a], Parsa Jamilian [b], Alireza Ostadrahimi [c,*], Meysam Zarezadeh [a,c,**]

[a] Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran
[b] School of Pharmacy and Bioengineering, Keele University, Staffordshire, UK
[c] Nutrition Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

ARTICLE INFO

Keywords:
Caffeine
Ergogenic aid
Muscle strength
Muscle endurance
Umbrella meta-analysis

ABSTRACT

Background: Caffeine is commonly used as an ergogenic aid to increase strength and endurance in athletes. The results of meta-analyses in this regard are still conflicting. Therefore, the current umbrella meta -analysis was conducted to determine the effects of caffeine supplementation on muscle strength and endurance as a clear and final conclusion.
Methods: Relevant studies were searched in international databases including PubMed, Scopus, and Web of Science until August 15, 2022. Meta-analysis studies examining the effects of caffeine supplementation on muscle strength and endurance were included in this study. Random effects model was used to perform meta-analysis. Additional analyses including subgroup and sensitivity analyzes were performed.
Findings: In general, 9 meta-analyses were included in the study. The results showed that caffeine supplementation led to a significant increase in muscle strength (SMD = 0.18, 95 % CI: 0.14, 0.21; $p < 0.001$) and muscle endurance (SMD = 0.30, 95 % CI 0.21, 0.38; $p < 0.001$).
Conclusion: Meta -analysis showed the significant effects of caffeine consumption on muscle strength and muscle endurance. Due to the lack of evidence, further studies are needed in the women's population.

1. Introduction

Dietary supplements are widely used by athletes at all levels of sports. Athletes use these supplements for various reasons, including improving health and performance, and providing micro- and macronutrients [1]. One of the common sports supplements among athletes is caffeine, which is popular due to its ergogenic effects on increasing performance [2]. Caffeine is widely found in drinks such as tea, coffee, and sodas, as well as in a wide variety of nutritional supplements known as "pre-workouts" [3–5]. Recently, a study has shown that 74 % of competitive athletes use caffeine [6]. Studies show that as a result of caffeine consumption, performance increases in both endurance and short-term, high-intensity exercise [7–9]. Some of the benefits attributed to the caffeine include improved endurance and muscle strength, increased concentration, mental alertness, and reduced fatigue [3]. Caffeine affects various organs (e.

* Corresponding author. School of Nutrition and Food Sciences, Attar-Neishaburi St., Golgasht Alley, Azadi Blvd., Tabriz, Iran.
** Corresponding author. Faculty of Nutrition and Food Sciences, Tabriz University of Medical Sciences, Attar-Neishaburi St., Golgasht Alley, Azadi Blvd., Tabriz, Iran.
E-mail addresses: ostadrahimi@tbzmed.ac.ir (A. Ostadrahimi), zarezadehm@tbzmed.ac.ir, Meysam.za93@gmail.com (M. Zarezadeh).

https://doi.org/10.1016/j.heliyon.2024.e35025
Received 25 July 2023; Received in revised form 21 July 2024; Accepted 22 July 2024
Available online 25 July 2024
2405-8440/

g., central nervous system, Na+/K+, ATPase activity, adenosine receptors, intracellular calcium and/or plasma catecholamine concentration, maximizing nitric oxide concentration), therefore it may be effective as an ergogenic aid to deal with decreased exercise performance and increase power output during the day [10,11].

Muscular endurance is "the ability of a muscle or muscle group to perform repeated contractions against a load for an extended period" [12]. Muscular strength is "the capacity to exert force under a particular set of biomechanical conditions" [13]. Muscle strength is very important for health, low levels of it cause loss of function, cancer and mortality [14–16]. Muscle strength plays an important role in sports such as shot put, and weight lifting [7]. The one-repetition maximum (1RM) test is commonly used to measure muscular strength [13].

In a meta-analysis study conducted by Grgic et al. [17], it was shown that caffeine improves muscle strength and endurance. While in the meta-analysis conducted by Polito et al. [18], the results showed that caffeine does not have a significant effect on muscle strength. Additionally, another randomized, double-blind, crossover study concluded that caffeine had no effect on muscle strength or endurance compared to a placebo in 9 healthy resistance-trained young men. There is disagreement among studies that have evaluated the effect of caffeine on exercise performance. A type of study that systematically compiles and evaluates numerous systematic reviews and meta-analyses on a particular research topic is called an umbrella review [19]. So far, only one umbrella meta-analysis article has examined the effect of caffeine on exercise performance. However, one of the limitations of this study is the small number of meta-analyses on muscle strength and endurance (2 articles for muscular endurance and 4 articles for muscular strength). Participants in the previous umbrella meta-analysis mostly included men (91.2 % for muscular endurance and 91.1 % for muscular strength), and there were no meta-analyses with only female participants. Therefore, the results may not necessarily be generalizable to women. Considering that several new meta-analyses have been published recently, including two meta-analyses exclusively in female athletes [20,21], this umbrella meta-analysis was carried out with the aim of investigating the effects of caffeine supplementation on muscle strength and endurance for clear, definitive and final conclusions to be drawn.

2. Methods

2.1. Search strategy

This study is reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [22]. A search was conducted in international scientific databases including PubMed, Scopus, and Web of Science to find relevant published articles up to August 15, 2022. An additional search was also done on Google Scholar. The following MeSH and keywords were used to develop a search strategy (caffeine OR coffee) AND Endurance(OR)Performance(OR)"athletic performance"(OR)"muscle strength"(OR)"resistance exercise"(OR)"resistance training"(OR)"strength training" (OR)"muscle endurance"(OR)"muscular endurance"(OR)"Endurance Training"(OR)"Physical Endurance") OR ("Muscle Strength") OR ("Athletic Performance") AND ("meta-analysis") OR ("meta"). After completing this part of the search process, in order to minimize the loss of articles, we examined the reference list of the included studies and added the articles that met the inclusion criteria. In this study, only English-language articles were considered. The protocol of the study has been registered on PROSPERO (CRD42023430574), an international database of systematic review protocols managed by the Centre for Reviews and Dissemination at the University of York, England [23].

2.2. Eligibility criteria

The inclusion criteria were applied using the Participant-Intervention-Comparison-Outcome (PICO) process as follows:

(1) Participants: both healthy men and women; (2) Intervention: studies examining the acute effect of caffeine consumption on muscle strength or muscle endurance; (3) Comparison: control or placebo group; (4) Outcome: muscular strength and/or muscular endurance.

Studies having abovementioned characteristics and providing effect size (ES) and corresponding confidence interval (CI) for the effect of caffeine on strength and endurance were included in the umbrella meta-analysis. Original studies, congress abstracts, narrative reviews and systematic reviews without data synthesis were excluded from the study.

2.3. Study selection

The articles found from the databases were entered into "Endnote20″ software and were initially evaluated in terms of duplication. After removing the duplicates, the titles of all the articles were reviewed, and finally, the remaining articles were included in the study by reviewing the abstracts and then the full text of the published articles. Reasons for exclusion were recorded at each stage. Two independent reviewers (HT and SKH) performed this process. Any discrepancies in the study selection and exclusion process were resolved in consultation with a third reviewer (MZ).

2.4. Data extraction

One reviewer (HT) collected data on the studies' characteristics in excel format using a predesigned checklist, which was then double-checked by another reviewer (SKH).

Data extracted from each study include the first author's name, publication year, country, gender, number of included studies, number of participants, supplementation dosage, type of caffeine, time of caffeine consumption, test of muscular strength or muscular endurance, and effect size (ES) and 95 % confidence intervals (95 % CIs).

The data for one included study [24] were presented as a figure (ES and CI). Get Data Graph Digitizer software was used to extract the data for this study.

2.5. Methodological quality and assessment of the certainty

Quality assessment was performed by two reviewers (HT and SKH), independently. Consensus was reached with assist of third reviewer (MZ) to resolve disagreements. In order to assess the methodological quality of published meta-analyses, the validated Assessing the Methodological Quality of Systematic Reviews 2 (AMSTAR2) checklist was used.

The AMSTAR2 checklist had 16 items. Response options for each item include "yes" or "partial yes" or "no" or "no meta-analysis". Based on the final score of this checklist, the quality of the articles was classified as "Critically low quality," "low quality," "moderate quality," and "high quality" [25]. The AMSTAR 2 checklist requires evaluating each item by responding with 'yes,' 'no,' 'cannot answer,' or 'not applicable.' Out of these possible answers, only the 'yes' answer counts as a point in the total score for the assessed review. Based on the summary point scores, the meta-analyses were categorized as high quality (at least 80 % of the items were satisfied), moderate quality (between 40 % and 80 % of the items were satisfied), or low quality (less than 40 % of the items were satisfied), as performed previously [26–28].

2.6. Data synthesis and statistical analysis

The overall effect sizes were calculated using effect sizes (ESs) and confidence intervals (CIs). These statistical measures represent the magnitude and precision of the observed effect, respectively.To assess heterogeneity, the I^2 statistics and Cochrane Q test were employed, where $p > 0.1$ and $I^2 > 50$ %, respectively, were considered as high heterogeneity. When significant heterogeneity was present (Iˆ2 > 50 % or $p < 0.1$), a random-effects model was employed to perform the meta-analysis, using the restricted maximum likelihood method (REML). Otherwise, a fixed-effects model was used. The caffeine dose, exercise tests, gender and quality of articles were used to conduct subgroup analysis to identify possible sources of heterogeneity.

To determine whether the pooled effect size changes when a single study is removed, a sensitivity analysis was used. This analysis involved removing one study at a time from the meta-analysis and recalculating the pooled effect size to assess the impact of each

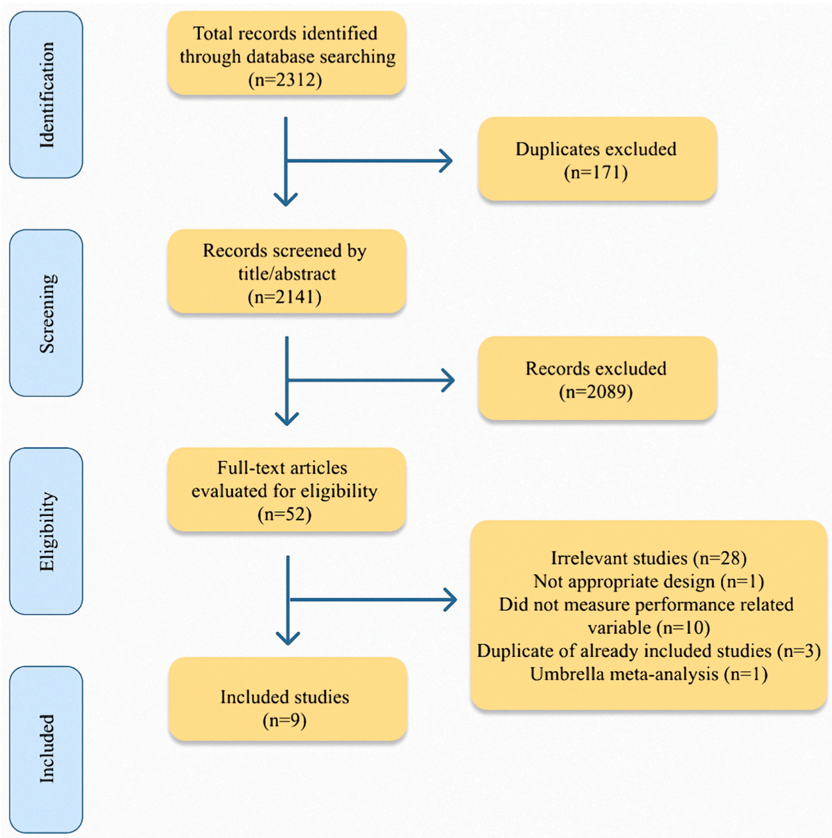

Fig. 1. The PRISMA flow chart.

individual study on the overall
result. Egger's and Begg's tests were used to assess the small-study effect. Begg's test is a rank-correlation test that assesses the association between the effect estimates and their variances, which can indicate the presence of publication bias [29]. Egger's test is a linear regression approach that regresses the standardized effect estimates against their precision (the inverse of the standard error) to detect asymmetry in the funnel plot, which may suggest publication bias [30]. By visual inspection, the funnel plot was evaluated for publication bias. An analysis of trim and fill was performed if any publication bias or small-study effect was detected. The tests for publication bias assessment were not performed if the number of observations was <8. STATA software (version 16, Stata Corporation, College Station, TX, US) was used to conduct the meta-analysis. When $P < 0.05$, values were considered statistically significant.

3. Results

3.1. Study selection and study characteristics

In the initial search, a total of 2312 results were obtained. To avoid duplication, 172 articles that appeared in more than one database were excluded. The remaining 2140 articles underwent screening of titles and abstracts, after which 2098 articles were excluded as they did not meet the inclusion criteria (Fig. 1). After reading the full-text of 52 articles, 10 meta-analysis studies were found that met the inclusion criteria. One of the articles that reported ES as weighted mean difference (WMD) was excluded from the meta-analysis [11].

Four studies [18,20,24,31] assessed both muscular strength and muscular endurance. In total, 9 studies evaluated muscular strength [13,18,20,21,24,29,31–34], and 4 studies evaluated muscular endurance [18,20,24,31], meeting the inclusion criteria based on the PICO framework. Of the 2463 participants who participated in the nine studies, 1628 were in the muscular strength group and 835 were in the muscular endurance group. The characteristics of these included studies are summarized in Table 1. Nine included studies were published between 2010 and 2022. The average dose of caffeine prescribed in the studies was between 1.56 mg/kg and 5.74 mg/kg and the average duration of caffeine supplementation was 50–60 min before exercise. The location of the studies was as follows: five in Australia [13,20,31,32,34], one in Brazil [18], one in Spain [21], one in Tunisia [33], and one in the United States [24].

Table 1
Summary of the studies included in the umbrella meta-analysis.

Reference	Number of included studies (Strength/ endurance)	Location	sample size (Strength/ endurance)	Caffeine dose (mg/kg)/ caffeine form	Timing of caffeine ingestion (min befor exercise)	Muscular Strength/ endurance test	Quality assessment scale and outcome
Grgic et al. (2022) [17]	8 Strength/7 endurance	Australia	141 Strength/ 122 endurance	1.56 (Capsules/ solution/gel)	60	Muscular endurance (assessed by repetitions to fatigue) and strength in the 1RM test/hand grip strength.	yes (Pedro) 8/ 10 high
Grgic et al. (2022) [35	16 Strength	Australia	353 Strength	4.14 (Capsules/ drink)	59.06	hand grip strength	yes (Rob2) 16/ 16 some concern
Delleli et al. (2022) [31]]	5 Strength	Tunisia	62 Strength	4.1 (Capsules)	60	hand grip strength	yes (Pedro) 5/5 high
Grgic et al. (2021) [36]	6 Strength/8 endurance	Australia	125 Strength/ 77 endurance	5 (NR)	56.25	Muscular endurance (assessed by repetitions to fatigue) and strength in the 1RM test.	yes (Pedro) 6/8 high
Gomez et al. (2021) [21]	3 Strength	Spain	47 Strength	2.56 (Capsules/ energy drink)	50	hand grip strength	yes (Pedro) 3/3 high
Grgic et al. (2018) [37]	10 Strength	Australia	133 Strength	5.5 (NR)	57	knee extensor/knee flexors/ elbow flexors/ankle plantar	yes (Pedro) 9/ 10 high
Grgic et al. (2018) [13]	11 Strength	Australia	145 Strength	4.5 (Capsules/ liquid/gel)	58.5	1RM test	yes (Pedro) 11/ 11 high
Polito et al. (2016) [38]	5 Strength/ 17endurance	Brazil	46 Strength/ 248 endurance	5 (Capsules/ liquid)	60	Muscular endurance (assessed by repetitions to fatigue) and strength in the 1RM test.	yes (Pedro) 16/ 17 high
Warren et al. (2010) [24]	27 Strength/ 23endurance	usa	576 Strength/ 388 endurance	5.74 (NR)	NR	MVC and muscular endurance	yes (Pedro) 32/ 34 high

Abbreviations: NR = Not reported; ROB 2 = Risk of bias assessment for randomized trials; PEDro = Physiotherapy Evidence Database scale for rating the quality of randomized controlled trials.

3.2. Quality assessment

Out of the 9 articles reviewed, 5 were classified as high quality and 4 as moderate quality, according to the criteria outlined in the AMSTAR2 tool, which evaluates the methodological rigor of systematic reviews and meta-analyses (Table 2).

3.3. The effects of caffeine on muscular strength

Overall, 9 studies (1628 participants) reported the effect of caffeine supplementation on muscle strength as standardized mean difference (SMD). Considerable variability was observed among studies examining the effect of caffeine consumption on muscle strength, with ES ranging from 0.09 to 0.395 (Fig. 2A). Only 1 of the 9 studies did not show a significant effect of caffeine supplementation on muscle strength. In contrast, 8 other studies showed positive and beneficial effects of caffeine on muscle strength compared to placebo. Combining the findings of these studies using a random effects model, it was found that caffeine supplementation significantly increased muscle strength (SMD = 0.18, 95 % CI: 0.14, 0.21; $p < 0.001$). There was significant heterogeneity between studies. ($I^2 = 0.0$ %, $p = 0.789$), which subgroup analysis showed that gender is the source of it (Table 3). Subgroup analysis also showed that caffeine supplementation had a greater effect on increasing muscle strength in studies with a dose of less than 5 g/kg, in women, in arm strength training tests, and in high-quality studies (Table 3). There was no evidence that study-specific exclusion affected the overall effect size based on sensitivity analysis. The Begg's and Egger's tests indicated that there was no evidence of a small study effect (respectively $P = 0.0935$ and $P = 0.3013$).

However, the funnel plot showed a diffusion bias. A trim and fill analysis was performed using 11 studies (two imputed studies) and as a result no significant difference in results was observed (SMD = 0.171, 95 % CI: 0.136, 0.206; $p < 0.05$) (Fig. 2B).

3.4. Effects of caffeine on muscular endurance

Overall, 4 studies (835 participants) reported the effect of caffeine supplementation on muscle strength as SMD.

The ES range of the studies varied from 0.21 to 0.275. Overall, caffeine supplementation had a positive effect on muscle endurance and the studies showed no significant heterogeneity (SMD = 0.30, 95 % CI 0.21, 0.38; $p < 0.001$, $I^2 = 34.6$ %, $p = 0.205$) (Fig. 3). The effect size was not affected by the sensitivity analysis.

4. Discussion

Multiple factors happen to make our muscular system work properly; muscular strength and endurance could be assessed by hand grip and one-repetition maximum (1RM) and hand grip respectively [33,34]. Caffeine causes changes in myocyte activity due to its effect on the neural system and its receptors [40]. Caffeine has been shown to increase motor unit recruitment, which may represent an increase in activation and attenuate exercise-induced reduction in voluntary activation [41]. Additionally, larger muscles, have a greater motor unit recruitment capability with caffeine intake than smaller muscles. Caffeine may also enhance muscular strength by altering the capacity of calcium release through the sensitization of calcium channels, inducing calcium discharge [41,42].

Caffeine's inhibition of calcium currents involves mobilization of intracellular calcium, inhibition of phosphodiesterases, and antagonism of adenosine receptors [43]. Caffeine affects calcium release by sensitizing calcium channels, triggering the mobilization of calcium from intracellular stores, and affecting calcium influx through voltage-operated calcium channels (VOCCs) [43,44]. Caffeine affects calcium release and GABAergic transmission. One study found it inhibited calcium current, weakly inhibited sodium current, and had no effect on chloride current [45]; while, *Kramer* et al. found that caffeine stimulates calcium-induced calcium release (CICR) in many cell types, including neurons, and that it stimulates CICR presynaptically, leading to fast inhibition of glutamate-activated currents [41,42,44].

Caffeine induces intracellular calcium release in peripheral and central neurons [46]. The methylxanthine caffeine binds to the ryanodine receptors and — when used at a low concentration—enhances slow after hyperpolarization (sIAHP) in CA1 pyramidal neurons [47]. Neurons respond to depolarizing stimuli with a rise in the concentration of free cytosolic calcium—which is initiated by Ca^{2+} entry through voltage-gated calcium channels [48]. Caffeine has also been used to show that ryanodine-sensitive Ca^{2+} stores contain releasable Ca^{2+} at rest [49]. Prolonged exposure of caffeine depleted the caffeine-sensitive stores of releasable Ca^{2+}; the degree of this depletion depended on caffeine concentration [50]. In noradrenergic neurons, caffeine's major effect was to induce CICR [51]. In this study, an attempt was made to examine the results of nine other meta-analysis studies that investigated the effect of caffeine on myocyte strength and endurance during isometric activity. We analyzed the results of included studies following their qualification.

The results of this umbrella meta-analysis study following the review of nine studies demonstrate that caffeine effects on isometric activities are present, however, the effects are low. *Polito* et al. reported the lowest overall effect and on the other hand, *Gomez* et al. reported the highest overall effect which was related to the effect of caffeine on hand grip in a female population [38,52]; The reported overall caffeine effect range from the remaining studies were close to overall caffeine effect in this study. Throughout the involved studies, caffeine was consumed in capsule or liquid form; it was consumed on average 50–60 min before the start of the isometric exercise test. *Grgic* et al. divided 16 studies into two categories of low dose and high dose according to the consumed caffeine—1 to 3 mg/kg was considered as a low dose and 5–7 mg/kg as a high dose—They concluded that its consumption, both in low and high doses, is associated with an increase in muscle strength [35]. In *Polito* et al. study, the effectiveness of caffeine was greater in those who consumed more than 6 mg/kg of caffeine than those who consumed 4 mg/kg or less, and this effectiveness was greater in muscular endurance than muscular strength [38]. Our results similarly displayed a significant caffeine efficacy at both low and high doses.

Table 2
Results of assess the methodological quality of meta-analysis.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Quality assessment
Grgic et al, (2022) [17]	YES	YES	YES	YES	NO	NO	YES	YES	YES	NO	YES	YES	YES	YES	NO	NO	**69 % Moderate quality**
Grgic et al, (2022) [35]	NO	YES	YES	YES	NO	NO	YES	YES	YES	YES	NO	YES	YES	YES	NO	YES	**69 % Moderate quality**
Delleli et al, (2022) [31]	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	**100 % High quality**
Grgic et al, (2021) [21]	YES	YES	YES	YES	NO	NO	YES	YES	YES	YES	YES	NO	YES	YES	YES	YES	**81 % High quality**
Gomez et al, (2021) [21]	YES	YES	YES	partial yes	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES	**88 % High quality**
Grgic et al, (2018) [37]	YES	NO	YES	YES	YES	NO	NO	YES	YES	NO	YES	YES	YES	YES	YES	YES	**75 % Moderate quality**
Grgic et al, (2018) [13]	YES	NO	YES	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	YES	YES	YES	**88 % High quality**
Polito et al, (2016) [38]	YES	NO	YES	YES	YES	YES	NO	YES	YES	NO	YES	YES	YES	YES	YES	YES	**81 % High quality**
Warren et al, (2010) [39]	YES	NO	YES	YES	NO	NO	NO	YES	YES	YES	YES	YES	YES	YES	YES	YES	**75 % Moderate quality**

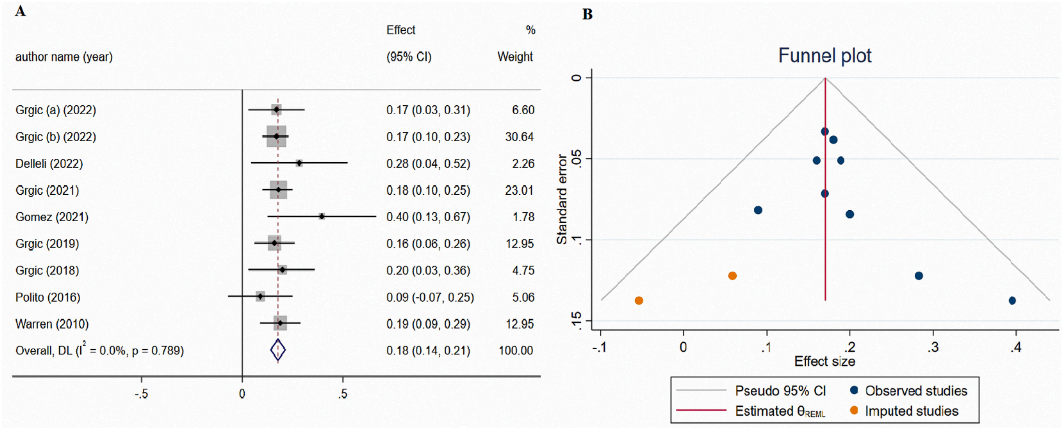

Fig. 2. The Forest plot (A) and the funnel plot (B) of effect of caffeine supplementation on strength.

Table 3
Subgroup analyses for the effects of caffeine on muscular strength and endurance.

	Effect size, n	ES (95%CI)	P-value	I2 (%)	P-heterogeneity
Caffeine on muscular strength					
Overall	9	0.18(0.14–0.22)	<0.001	0	0.789
Dosage(mg/kg)					
<5	5	0.18(0.13–0.24)	<0.001	0	0.517
≥5	4	0.34(0.24–0.44)	<0.001	0	0.752
Gender					
Both	7	0.17(0.13–0.21)	<0.001	0	0.909
Female	2	0.25(0.05–0.44)	0.013	55.9	0.132
Test type					
1 RM	3	0.17(0.11–023)	<0.001	0	0.561
Hand grip srength	3	0.23(0.11–0.36)	<0.001	36.8	0.206
Other test	3	0.17(0.11–0.24)	<0.001	0	0.921
Quality					
High	5	0.19(0.12–0.26)	<0.001	8.6	0.358
Moderate	4	0.17(0.13–0.22)	<0.001	0	0.982
Caffeine on muscular endurance					
overall	4	0.30(0.21–0.38)	<0.001	34.6	0.205
Dosage(mg/kg)					
<5	2	0.22(0.10–0.34)	<0.001	0	0.76
≥5	2	0.34(0.24–0.44)	<0.001	33.1	0.222
Quality					
High	2	0.35(0.25–0.46)	<0.001	14.9	0.278
Moderate	2	0.24(0.14–0.34)	<0.001	0	0.518

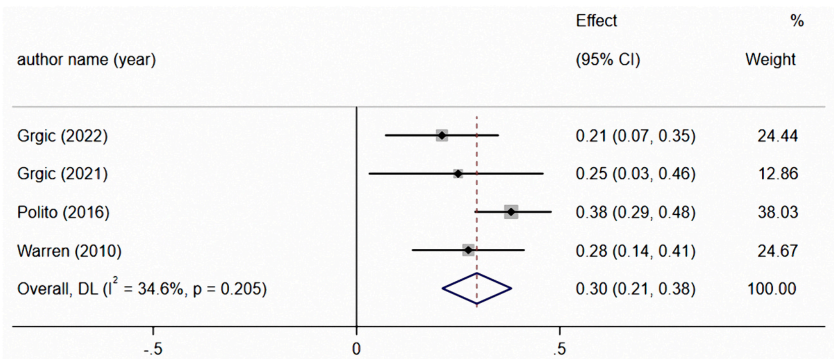

Fig. 3. The Forest plot of effect of caffeine supplementation on endurance.

Hand grip and 1RM were used to test the muscular strength and endurance [13,31,35–39,52,53]. The overall caffeine effect of the studies that used hand grip was higher than that of the studies that used 1RM, however, after examining the studies in separate subgroups based on the isometric test used, the results indicate significance effect for both subgroups. Two out of the nine studies reviewed investigated the effect of caffeine on the female population; a moderate overall caffeine effect was reported in those studies, which was higher than the overall effect calculated from the full set of studies [52,36]. On the other hand, *Dellili* et al., reported a moderate caffeine effect on muscular power in an isometric exercise test in their study on 58 males and 4 females [31]. Even though reviewed meta-analysis studies believed that caffeine affects muscular power during an isometric activity but *Astorino* et al., following investigating the effect of caffeine consumption on 22 trained males claimed an insignificant muscular power enhancement while, muscular endurance increases upon consumption; according to *Ali* et al., caffeine ingestion did not have an effect on countermovement jump height [54,55]; this means that caffeine did not improve the height of the jump in this particular test. However, other studies have shown that caffeine can be ergogenic for aerobic and muscle endurance, muscle strength, as well as sprint and speed performance [56]. Some of the included studies, in addition to examining the performance of upper body muscles, assessed the performance of lower body muscles influenced caffeine as well, they claimed that this supplement has a low effect and, in some cases, insignificant on muscular power, however, *Dellili* et al. a high effect following the caffeine consumption before a combat simulator [31]. Only two studies considered habitual caffeine intake—considering the possibility of tolerance formation after chronic caffeine consumption [53, 36].

Therefore, it seems that designing more studies to investigate the participants in separate gender-based groups and taking into account more factors—specific physical conditions—can form a better understanding of the effect of caffeine on the myocyte's function. We count the dissimilarity of the investigated populations in terms of gender and geographical distribution in the included studies as our most important limitation. The lack of similar studies in different races and ages is quite noticeable, so we strongly suggest the design of similar multicenter studies that, in addition to examining young individuals, also examines the effect of caffeine on middle-aged and elderly individuals. The other limitation that we faced was the lack of attention to the human body's physiological changes—hormonal changes in the menstrual cycle. New Studies can develop our knowledge by observing the effect of caffeine during a menstrual period or before and after menopause.

Suggestions for future research:

Despite the existing research, there is a need for additional studies specifically analyzing the effects of caffeine in female populations. These studies should carefully account for factors such as menstrual cycle phase and the use of hormonal contraceptives to fully elucidate any potential sex-specific differences or moderating effects on caffeine's ergogenic properties.

5. Conclusion

It seems that muscles are affected by caffeine through an increase in intracellular calcium. Therefore, muscular strength and endurance are improved by the consumption of caffeine. The present study shows that athletes' performance is enhanced by caffeine in different doses. However, significant limitations still remain and undoubtedly handling these limitations helps to form a deeper understanding. Paying attention to age and hormonal changes as two determining factors in designing similar studies are recommended.

Funding

None.

Data availability statement

The data supporting the findings of this study are available within the article and its supplementary materials. Any additional data or materials can be requested from the corresponding author.

CRediT authorship contribution statement

Hossein Taghizadeh Bilondi: Writing – original draft, Methodology, Data curation, Conceptualization. **Hanieh Valipour:** Writing – review & editing, Conceptualization. **Sahar Khoshro:** Methodology, Conceptualization. **Parsa Jamilian:** Investigation, Conceptualization. **Alireza Ostadrahimi:** Writing – original draft, Methodology, Conceptualization. **Meysam Zarezadeh:** Methodology, Formal analysis, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e35025.

References

[1] R.J. Maughan, et al., IOC consensus statement: dietary supplements and the high-performance athlete, Br. J. Sports Med. 52 (7) (2018) 439–455.
[2] W.H. Rivers, H.N. Webber, The action of caffeine on the capacity for muscular work, J. Physiol. 36 (1) (1907) 33–47.
[3] M.A. Heckman, J. Weil, E. Gonzalez de Mejia, Caffeine (1, 3, 7-trimethylxanthine) in foods: a comprehensive review on consumption, functionality, safety, and regulatory matters, J. Food Sci. 75 (3) (2010) R77–R87.
[4] C. Alves, R.V.B. Lima, Dietary supplement use by adolescents, J. Pediatr. 85 (2009) 287–294.
[5] L.M. Burke, Caffeine and sports performance, Appl. Physiol. Nutr. Metabol. 33 (6) (2008) 1319–1334.
[6] J. Del Coso, G. Muñoz, J. Muñoz-Guerra, Prevalence of caffeine use in elite athletes following its removal from the World Anti-Doping Agency list of banned substances, Appl. Physiol. Nutr. Metabol. 36 (4) (2011) 555–561.
[7] L.M. Burke, Caffeine and sports performance, Appl. Physiol. Nutr. Metabol. 33 (6) (2008) 1319–1334.
[8] M. Doherty, P.M. Smith, Effects of caffeine ingestion on exercise testing: a meta-analysis, Int. J. Sport Nutr. Exerc. Metabol. 14 (6) (2004) 626–646.
[9] M.S. Ganio, et al., Effect of caffeine on sport-specific endurance performance: a systematic review, J. Strength Condit Res. 23 (1) (2009) 315–324.
[10] R. Sun, et al., Effects of caffeine ingestion on physiological indexes of human neuromuscular fatigue: a systematic review and meta-analysis, Brain Behav 12 (4) (2022) e2529.
[11] T.T. Ferreira, J.V.F. da Silva, N.B. Bueno, Effects of caffeine supplementation on muscle endurance, maximum strength, and perceived exertion in adults submitted to strength training: a systematic review and meta-analyses, Crit. Rev. Food Sci. Nutr. 61 (15) (2021) 2587–2600.
[12] R.T. Kell, G. Bell, A. Quinney, Musculoskeletal fitness, health outcomes and quality of life, Sports Med. 31 (12) (2001) 863–873.
[13] J. Grgic, et al., Effects of caffeine intake on muscle strength and power: a systematic review and meta-analysis, Sports Nutr. Rev. J. 15 (1) (2018) 11.
[14] P.A. Brill, et al., Muscular strength and physical function, Med. Sci. Sports Exerc. 32 (2) (2000) 412–416.
[15] J.R. Ruiz, et al., Muscular strength and adiposity as predictors of adulthood cancer mortality in men, Cancer Epidemiol. Biomarkers Prev. 18 (5) (2009) 1468–1476.
[16] J.R. Ruiz, et al., Association between muscular strength and mortality in men: prospective cohort study, Br. Med. J. 337 (7661) (2008) a439.
[17] J. Grgic, Exploring the minimum ergogenic dose of caffeine on resistance exercise performance: a meta-analytic approach, Nutrition 97 (2022).
[18] M.D. Polito, et al., Acute effect of caffeine consumption on isotonic muscular strength and endurance: a systematic review and meta-analysis, Sci. Sports 31 (3) (2016) 119–128.
[19] L. Belbasis, et al., Environmental risk factors and multiple sclerosis: an umbrella review of systematic reviews and meta-analyses, Lancet Neurol. 14 (3) (2015) 263–273.
[20] J. Grgic, J. Del Coso, Ergogenic effects of acute caffeine intake on muscular endurance and muscular strength in women: a meta-analysis, Int. J. Environ. Res. Publ. Health 18 (11) (2021).
[21] A. Gomez-Bruton, et al., Does acute caffeine supplementation improve physical performance in female team-sport athletes? Evidence from a systematic review and meta-analysis, Nutrients 13 (10) (2021).
[22] M.J. Page, et al., The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, Br. Med. J. 372 (2021) n71.
[23] J.H. Schiavo, PROSPERO: an international register of systematic review protocols, Med. Ref. Serv. Q. 38 (2) (2019) 171–180.
[24] G.L. Warren, et al., Effect of caffeine ingestion on muscular strength and endurance: a meta-analysis, Med. Sci. Sports Exerc. 42 (7) (2010) 1375–1387.
[25] B.J. Shea, et al., Amstar 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both, Br. Med. J. (2017) 358.
[26] J. Grgic, et al., Wake up and smell the coffee: caffeine supplementation and exercise performance-an umbrella review of 21 published meta-analyses, Br. J. Sports Med. 54 (11) (2020) 681–688.
[27] B.T. Johnson, et al., Methodological quality of meta-analyses on the blood pressure response to exercise: a review, J. Hypertens. 32 (4) (2014) 706–723.
[28] L. Monasta, et al., Early-life determinants of overweight and obesity: a review of systematic reviews, Obes. Rev. 11 (10) (2010) 695–708.
[29] C.B. Begg, M. Mazumdar, Operating characteristics of a rank correlation test for publication bias, Biometrics 50 (4) (1994) 1088–1101.
[30] A. Sabag, et al., Timing of moderate to vigorous physical activity, mortality, cardiovascular disease, and microvascular disease in adults with obesity, Diabetes Care 47 (5) (2024) 890–897.
[31] S. Delleli, et al., Acute effects of caffeine supplementation on physical performance, physiological responses, perceived exertion, and technical-tactical skills in combat sports: a systematic review and meta-analysis, Nutrients 14 (14) (2022) 2996.
[32] M. Egger, et al., Bias in meta-analysis detected by a simple, graphical test, Br. Med. J. 315 (7109) (1997) 629–634.
[33] A.F. Widodo, et al., Isotonic and isometric exercise interventions improve the hamstring muscles' strength and flexibility: a narrative review, in: Healthcare, MDPI, 2022.
[34] J.K. De Witt, et al., Isometric midthigh pull reliability and relationship to deadlift one repetition maximum, J. Strength Condit Res. 32 (2) (2018) 528–533.
[35] J. Grgic, Effects of caffeine on isometric handgrip strength: a meta-analysis, Clinical Nutrition ESPEN 47 (2022) 89–95.
[36] J. Grgic, J. Del Coso, Ergogenic effects of acute caffeine intake on muscular endurance and muscular strength in women: a meta-analysis, Int. J. Environ. Res. Publ. Health 18 (11) (2021) 5773.
[37] J. Grgic, C. Pickering, The effects of caffeine ingestion on isokinetic muscular strength: a meta-analysis, J. Sci. Med. Sport 22 (3) (2019) 353–360.
[38] M. Polito, et al., Acute effect of caffeine consumption on isotonic muscular strength and endurance: a systematic review and meta-analysis, Sci. Sports 31 (3) (2016) 119–128.
[39] G.L. Warren, et al., Effect of caffeine ingestion on muscular strength and endurance: a meta-analysis, Med. Sci. Sports Exerc. 42 (7) (2010) 1375–1387.
[40] N. Dittrich, et al., Effects of caffeine chewing gum on exercise tolerance and neuromuscular responses in well-trained runners, J. Strength Condit Res. 35 (6) (2021) 1671–1676.
[41] B. Ferreira Viana, et al., Caffeine increases motor output entropy and performance in 4 km cycling time trial, PLoS One 15 (8) (2020) e0236592.
[42] C. Reggiani, Caffeine as a tool to investigate sarcoplasmic reticulum and intracellular calcium dynamics in human skeletal muscles, J. Muscle Res. Cell Motil. 42 (2) (2021) 281–289.
[43] L. Karhapää, K. Törnquist, Effects of caffeine on the influx of extracellular calcium in GH4C1 pituitary cells, J. Cell. Physiol. 171 (1) (1997) 52–60.
[44] R.H. Kramer, R. Mokkapatti, E.S. Levitan, Effects of caffeine on intracellular calcium, calcium current and calcium-dependent potassium current in anterior pituitary GH3 cells, Pflügers Archiv 426 (1–2) (1994) 12–20.
[45] F.-L. Zhao, S.-G. Lu, S. Herness, Dual actions of caffeine on voltage-dependent currents and intracellular calcium in taste receptor cells, Am. J. Physiol. Regul. Integr. Comp. Physiol. 283 (1) (2002) R115–R129.
[46] A. Verkhratsky, A. Shmigol, Calcium-induced calcium release in neurones, Cell Calcium 19 (1) (1996) 1–14.
[47] A. Tedoldi, et al., Calcium-induced calcium release and type 3 ryanodine receptors modulate the slow afterhyperpolarising current, sIAHP, and its potentiation in hippocampal pyramidal neurons, PLoS One 15 (6) (2020) e0230465.
[48] J. Hongpaisan, et al., Multiple modes of calcium-induced calcium release in sympathetic neurons II: a [Ca2+] i-and location-dependent transition from endoplasmic reticulum Ca accumulation to net Ca release, J. Gen. Physiol. 118 (1) (2001) 101–112.
[49] V.M. Sandler, J.-G. Barbara, Calcium-induced calcium release contributes to action potential-evoked calcium transients in hippocampal CA1 pyramidal neurons, J. Neurosci. 19 (11) (1999) 4325–4336.
[50] Y. Usachev, et al., Caffeine-induced calcium release from internal stores in cultured rat sensory neurons, Neuroscience 57 (3) (1993) 845–859.
[51] H. Kawano, et al., Calcium-induced calcium release in noradrenergic neurons of the locus coeruleus, Brain Res. 1729 (2020) 146627.
[52] A. Gomez-Bruton, et al., Does acute caffeine supplementation improve physical performance in female team-sport athletes? Evidence from a systematic review and meta-analysis, Nutrients 13 (10) (2021) 3663.
[53] J. Grgic, Exploring the minimum ergogenic dose of caffeine on resistance exercise performance: a meta-analytical approach, Nutrition (2022) 111604.

[54] A. Ali, et al., The influence of caffeine ingestion on strength and power performance in female team-sport players, J Int Soc Sports Nutr 13 (2016) 46.
[55] T.A. Astorino, R.L. Rohmann, K. Firth, Effect of caffeine ingestion on one-repetition maximum muscular strength, Eur. J. Appl. Physiol. 102 (2) (2008) 127–132.
[56] J. Grgic, A comprehensive assessment of caffeine's effects on components of countermovement jump performance, Biol. Sport 39 (3) (2022) 515–520.