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SYSTEMATIC REVIEW

Effects of Creatine Monohydrate on Endurance Performance in a Trained Population: A Systematic Review and Meta-analysis

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Abstract

Background There is robust evidence that creatine monohydrate supplementation can enhance short-term high-intensity exercise in athletes. However, the effect of creatine monohydrate supplementation on aerobic performance and its role during aerobic activities is still controversial.

Objective The purpose of this systematic review and meta-analysis was to evaluate the supplementation effects of creatine monohydrate on endurance performance in a trained population.

Methods The search strategy in this systematic review and meta-analysis was designed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and PubMed/MEDLINE, Web of Science, and Scopus databases were explored from inception until 19 May, 2022. Only human experimental trials, controlled with a placebo group, evaluating the effects of creatine monohydrate supplementation on endurance performance in a trained population were analyzed in this systematic review and meta-analysis. The methodological quality of included studies was evaluated using the Physiotherapy Evidence Database (PEDro) scale.

Results A total of 13 studies satisfied all the eligibility criteria and were included in this systematic review and meta-analysis. The results for the pooled meta-analysis showed a non-significant change in endurance performance after creatine monohydrate supplementation in a trained population ($p = 0.47$), with a trivial negative effect (pooled standardized mean difference = −0.07 [95% confidence interval −0.32 to 0.18]; $I^2 = 34.75\%$). Further, after excluding the studies not evenly distributed around the base of the funnel plot, the results were similar (pooled standardized mean difference = −0.07 [95% confidence interval −0.27 to 0.13]; $I^2 = 0\%$; $p = 0.49$).

Conclusions Creatine monohydrate supplementation was shown to be ineffective on endurance performance in a trained population.

Clinical Trial Registration The study protocol was registered in the Prospective Register of Systematic Review (PROSPERO) with the following registration number: CRD42022327368.

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Key Points

Creatine monohydrate seems ineffective when the primary purpose is to improve endurance performance.

Creatine monohydrate inefficacy to improve running endurance performance could be associated with its capability to increase body mass.

Creatine monohydrate could improve aerobic performance in sports modalities where the increment in body mass does not increase the energy cost of exercise, and strength is an essential factor for the sport.

1 Introduction

Creatine (Cr) is a non-protein amino acid endogenously synthesized primarily in the liver and kidneys through several enzyme processes from arginine, glycine, and methionine [1, 2]. Creatine is predominantly stored in skeletal muscle (~ 95%), with ~ 66% of intramuscular Cr stored as phosphocreatine (PCr), and the remaining as free Cr [3]. However, only 60–80% of muscle Cr and PCr stores are saturated in a regular diet [3]. Hence, dietary supplementation of creatine monohydrate (CrM) could help to increase muscle Cr and PCr by 20–40% [4, 5].

There are two main strategies to increase muscle Cr and PCr concentration following CrM ingestion: rapid or slow loading. The rapid loading consists of four daily dosages of 5 g of CrM (or 0.3 g/kg body mass) for 5–7 days [4, 5]. After reaching the maximum saturation of muscle Cr, a maintenance dose of CrM (3 g/day or 0.03 g/kg body mass) is recommended in order to sustain a high Cr concentration [3]. In contrast, the slow loading protocol consists of ingesting the maintenance dose (3 g/day or 0.03 g/kg body mass) for at least 28 days [4].

Creatine monohydrate is an ergogenic aid with considerable evidence concerning sports performance improvement [6–9]. Specifically, large effectiveness in optimizing power and strength performance has been shown in athletes after the ingestion of this supplement [10–12]. Nevertheless, the effectiveness of CrM on endurance performance in a trained population is still unclear. Previously, it has been hypothesized that CrM could improve endurance performance via greater shuttling of adenosine triphosphate (ATP) from mitochondria [3]. The Cr/PCr system could improve aerobic capacity by maintaining ATP availability during aerobic exercise [13]. Therefore, additional energy availability could be provided by resynthesizing PCr from Cr in the muscle cell's mitochondria [13–15]. Furthermore, hydrogen cations are utilized in this process to produce ATP through adenosine diphosphate rephosphorylation. Hence, CrM may act as a proton buffer, helping to delay fatigue [16]. In addition, this supplement could enhance endurance performance by increasing glycogen storage [17]. Furthermore, it is well known that supplementation with CrM could increase body mass [18], and the increase in body mass could negatively influence endurance performance [19, 20]. In light of these relevant physiological pathways influencing endurance performance, athletes need to be aware of the effectiveness of this ergogenic aid in improving or impairing endurance performance.

A recent meta-analysis showed a negative effect of Cr supplementation on the maximum rate of oxygen consumption (VO_{2max}) [21]. However, in that review, the analysis was conducted in a trained and untrained population and the only endurance outcome measured was VO_{2max}. To the best of the authors' knowledge, none of the previous systematic reviews and meta-analyses (SRMAs) analyzed CrM effectiveness on endurance performance, specifically in a trained population. Therefore, this SRMA aims to evaluate CrM supplementation's influence on endurance performance in a trained population.

2 Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [22] was followed in order to evaluate the effects of CrM supplementation on endurance performance in a trained population. Before starting the search strategy, the study protocol was registered in the Prospective Register of Systematic Review (PROSPERO) with the following registration number: CRD42022327368.

2.1 Literature Search

The search was independently conducted by two authors (JFL and NT), and disagreements were solved by third-party adjudication (ASG). Studies were identified by searching PubMed/MEDLINE, Web of Science, and Scopus databases from inception until 19 May, 2022. Records were identified using the following Boolean search: ((“creatine monohydrate” OR “oral creatine” OR “creatine supplementation” OR “Cr supplementation”) AND (endurance AND aerobic) AND (athlete OR trained OR elite OR competitive)). Moreover, so as to detect any missed study in the literature search, the snowball strategy [23] was used.

2.2 Inclusion and Exclusion Criteria

The a priori inclusion criteria to select the articles for this SRMA were: (i) CrM supplementation; (ii) trained population (trained/developmental, highly trained/national level, and/or elite/international level [24]); and (iii) endurance performance measurements (VO_{2max}, peak oxygen consumption (VO_{2peak}), individual anaerobic/lactate threshold, stages, time trial and time to exhaustion) involving the following tests: 6-km terrain run, continuous treadmill test, Leger shuttle run test, incremental test (rowing ergometer or cycle ergometer), maximal discontinuous incremental running test, 1000-m rowing test, 2000-m rowing test, 2500-m rowing test, and 400-m swimming test; (iv) human experimental trial; (v) controlled with a placebo group; (vi) original and peer-reviewed studies written in the English language.

Studies were excluded when: (i) CrM was combined with other supplements (except when the data for each supplement were given separately); (ii) volunteers in the studies were not considered as a trained population; (iii) there was no placebo group for the comparison of the results; and (iv) studies had no pre- and post-exercise data.

2.3 Text Screening

Two authors (JFL and NT) conducted the process independently, and potential discrepancies between reviewers were resolved by consensus with a third author (ASG). The first step of the process was to screen abstracts and titles in order to efficiently reduce the number of studies not meeting the inclusion and exclusion criteria. Subsequently, the same researchers screened the full texts to determine which experimental trials were relevant to be included in the SRMA.

2.4 Data Extraction and Study Coding

The following data from all studies satisfying inclusion and exclusion criteria were extracted: study authors and publication year, study design, participant's sex, participant's age, supplementation dose, duration of supplementation protocol, supplementation form, body mass (pre- and post-data), and endurance test outcomes (pre- and post-data). When there were no numerical data available, and the data were expressed in images (e.g., graphs), Image J software® (National Institutes of Health, Bethesda, MD, USA) was used in order to calculate mean and standard deviation values by measuring the pixel length of each magnitude. Finally, all the information was carefully reviewed and added to a spreadsheet (Microsoft Excel; Microsoft Corporation, Washington, DC, USA).

Most of the investigations included in the SRMA showed more than one relevant outcome measuring endurance performance. When more than one outcome per study was included in a meta-analysis, the final results could be affected because one effect size was given for each outcome [25]. Therefore, with the aim of reducing possible bias, the "MAd" package in R software (R Foundation for Statistical Computing, Vienna, Austria) was utilized to obtain a unique effect size estimate for each study [26]. This package needs a within-study correlation to give an accurate effect size to each study; hence, the within-study correlation was 0.70, the same Trexler et al. previously used [27].

2.5 Quality Assessment of Included Studies

Two independent researchers (JFL and ASG) conducted the process, and potential discrepancies between reviewers were resolved through discussion. The methodological quality of included studies was evaluated using the Physiotherapy Evidence Database (PEDro) scale [28]. This scale consists of 11 items, but only items from 2 to 11 can be rated. When an item receives a positive answer, it is rated with 1 point, whereas with a negative answer it is rated 0 points. Therefore, the maximum possible score on this scale is 10 points. A high PEDro score means that there is a low risk of bias, while a low PEDro score means a high risk of bias. The PEDro scale was assessed as excellent quality (a score of 9 or 10 points), good quality (a score between 6 and 8 points), fair quality (a score between 4 and 5 points), or poor quality (a score of 3 points or lower) [29].

2.6 Statistical Analysis

The statistical analyses were performed using R software's "metafor" package (R Foundation for Statistical Computing, Vienna, Austria). Every study included in the SRMA received a weighted estimation of a standardized mean difference (SMD) and variance calculated as Hedges' G [30], using the inverse variance random-effects model by the DerSimonian and Laird method [31]. In order to obtain the variance, the correlation coefficient used was 0.70, following Rosenthal's recommendation [32]. The calculation of the effects of CrM supplementation versus placebo on endurance performance was measured using the SMD with a 95% confidence interval (95% CI [lower bound to–upper bound]), and the significance was set at $p < 0.05$. The SMD was classified as trivial (when the SMD was < 0.2); small (when the SMD was between 0.2 and 0.3); moderate (when the SMD was between 0.4 and 0.8); and large (when the SMD was > 0.8), following the Cohen criteria [33].

The heterogeneity among studies was evaluated using the I^2 statistic, and ranked as low (when $I^2 < 25\%$), moderate (when $I^2 = 25$–75%), or considerable (when $I^2 > 75\%$) risk of heterogeneity [34]. The I^2 statistic was calculated based upon the restricted maximum likelihood estimation of tau-square.

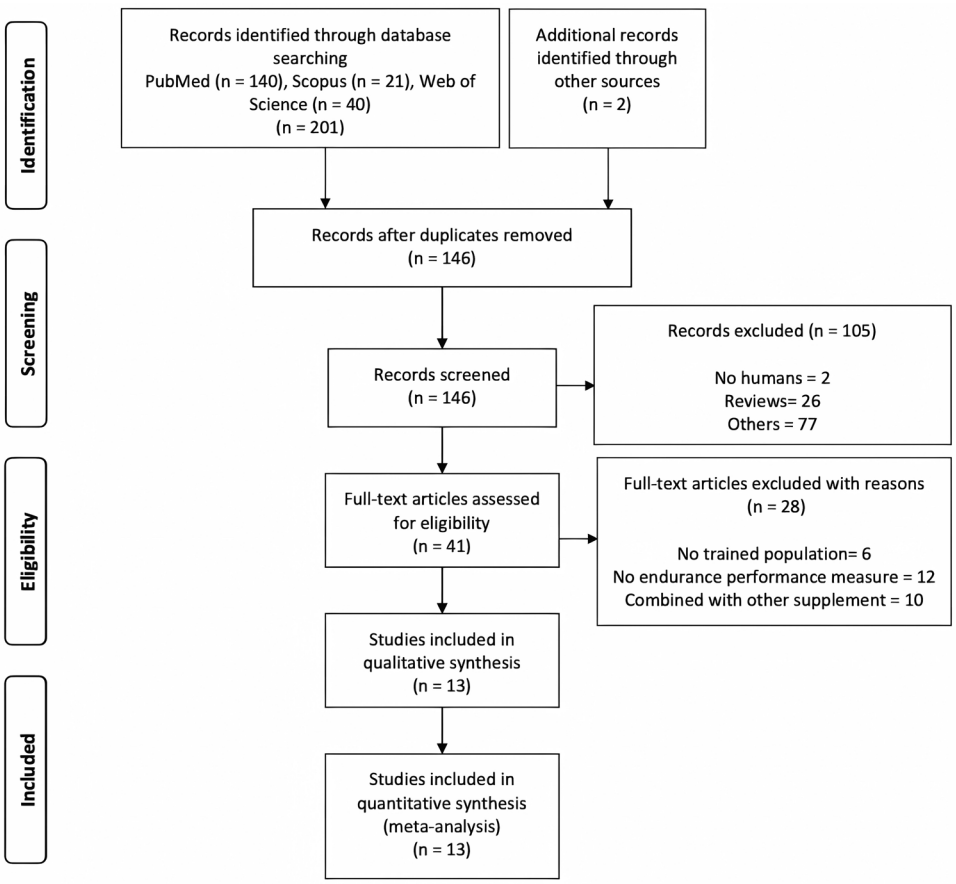

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram

In order to determine the potential publication bias of the pooled data from each study, funnel plot asymmetry was visually evaluated. Moreover, funnel plot asymmetry was evaluated through Egger's regression test [35] and with Duval and Tweedie's trim and rill method [36]. The meta-analysis was repeated after excluding studies not evenly distributed around the base of the funnel plot in order to reduce publication bias.

3 Results

3.1 Literature Search

A total of 201 records were found through the database search and two [37, 38] were identified through the snowball strategy. Subsequently, duplicates were removed, including 146 unique records in the SRMA. Titles and abstracts were screened and 105 unrelated studies were eliminated. Consequently, 41 eligible studies were included for the full-text screening. Finally, 13 articles were considered to be included in this SRMA, involving 277 participants [37–49]. Figure 1 displays the information concerning the PRISMA flow diagram.

All relevant information regarding studies meeting the inclusion criteria is summarized in Table 1. Nine studies reported a loading supplementation protocol [37–39, 41, 44–48], while six studies reported a maintenance supplementation protocol [40, 42, 43, 45, 48, 49]. Two studies started with a loading protocol and continued with the maintenance protocol [45, 48]. In the studies that completed the loading supplementation protocol, ingested dosages ranged from 5 g [39] to 30 g per day [47]. In the maintenance supplementation protocol, the dose intake varied from 2 g [49] to 10 g per day [45]. Both supplementation duration protocols ranged from 5 days [37, 38, 41, 44] to 70 days [42].

Concerning the body mass change, five studies showed a significant body mass increase after CrM supplementation [39, 40, 43–45], while three studies observed no change in body mass after a period of CrM ingestion [37, 42, 48]. Five studies included in this SRMA did not provide data regarding body mass change [38, 41, 46, 47, 49].

Endurance performance was assessed through the following tests: 6-km terrain run [39], continuous treadmill test [39], Leger shuttle run test [40, 47], incremental exercise test in a rowing ergometer [41, 42], incremental exercise test in a cycle ergometer [43, 45, 46], maximal discontinuous incremental running test [44], maximal

Table 1 Summary of the studies included in the systematic review and meta-analysis

Study	Participants	Supplementation protocol		Duration (days)	Body mass change	Test	Outcome	Effect
		Loading	Maintenance					
Balsom et al. (1993) [39]	18 well-trained male individuals (EG: age 25.6 years; PLA: age 27.3 years)	5 g/day	-	6	Increase	6-km terrain run	Time trial (min)	↓
						Continuous treadmill test	VO_{2peak} (mL/kg/min)	↔
Chilibeck et al. (2007) [40]	19 male rugby players (EG: age 27.2 ± 2.8 years; PLA: age 26.4 ± 3.0 years)	–	0.1 g/kg/day	56	Increase	Leger shuttle run test	Stages (#)	↔
Chwalbinska-Moneta et al. (2003) [41]	16 elite male rowers (EG: age 22.5 ± 0.5 years; PLA: age 25.3 ± 1.7 years)	20 g/day	–	5	Not reported	Incremental test (rowing ergometer)	4-mmol/L lactate threshold (W)	↔
							Individual threshold (W)	↑
							Time to exhaustion (s)	↑
Fernández-Landa et al. (2020) [42]	28 elite male rowers (age 30.43 ± 4.64 years)	–	0.04 g/kg/day	70	No change	Incremental test (rowing ergometer)	Individual anaerobic threshold (W)	↔
							4-mmol/L lactate threshold (W)	↔
							8-mmol/L lactate threshold (W)	↑
Hickner et al. (2010) [43]	12 endurance-trained male individuals (age 27.30 ± 1.00 years)	–	3 g/day	28	Increase	Incremental test (cycle ergometer)	VO_{2peak} (L/min)	↔
Izquierdo et al. (2002) [44]	19 trained handball players (EG: age 20.8 ± 5.0 years; PLA: age 23.6 ± 5.0 years)	4 × 5 g/day	–	5	Increase	Maximal discontinuous incremental running test	Time to exhaustion (s)	↔
Lawrence et al. (1997) [37]	20 male and female trained rowers (EG: age 21.1 ± 2.0 years; PLA: age 24.2 ± 3.7 years)	4 × 5 g/day	–	5	No change	2500-m time trial (rowing ergometer)	Time trial (min)	↑
							VO_{2peak} (L/min)	↔
Murphy et al. (2000) [45]	18 team sport players (age 24.00 ± 3.00 years)	4 × 5 g/day (7 days)	2 × 5 g/day (21 days)	28	Increase	Incremental test (cycle ergometer)	Time to exhaustion (s)	↔
							VO_{2max} (L/min)	↔
Nelson et al. (2000) [46]	37 trained male and female individuals (age 21–27 years)	4 × 5 g/day	–	7	Not reported	Incremental test (cycle ergometer)	VO_{2peak} (L/min)	↔
Ostojic (2004) [47]	20 male soccer players (EG: age 16.9 ± 1.5 years; PLA: age 16.2 ± 2.3 years)	3 × 10 g/day	–	7	Not reported	Leger shuttle run test	Time to exhaustion (s)	↔
Rossiter et al. (1996) [38]	38 competitive oarsmen and oarswomen (age 22.7 ± 4.2 years)	0.25 g/kg/day	–	5	Not reported	1000-m time trial (rowing ergometer)	Time trial (s)	↑

Table 1 (continued)

Study	Participants	Supplementation protocol		Duration (days)	Body mass change	Test	Outcome	Effect
		Loading	Maintenance					
Syrotuik et al. (2001) [48]	22 trained rowers (age 23.00 years)	0.3 g/kg (5 days)	0.03 g/kg (35 days)	40	No change	2000 m time trial (rowing ergometer)	VO_{2max} (L/min)	↔
							Time trial (s)	↔
Thompson et al. (1996) [49]	10 female swimming athletes	–	2 g/day	42	Not reported	400 m swimming time trial	Time trial (s)	↔

EG experimental group, *min* minutes, *PLA* placebo group, *s* seconds, VO_{2max} maximum rate of oxygen consumption, VO_{2peak} peak oxygen consumption, *W* watts, ↑ creatine monohydrate supplementation statistically improved over PLA, ↓ creatine monohydrate supplementation statistically compared with over PLA, ↔ creatine monohydrate supplementation was not statistically different from PLA, # number

2500-m rowing ergometer test [37], 1000-m time trial in a rowing ergometer [38], 2000-m rowing test [48], and 400-m swimming time trial [49].

Four studies reported significant improvements in endurance test outcomes after CrM supplementation. One study noticed an increase in the individual threshold [41]. In addition, the study conducted by Fernández-Landa et al. [42] reported an improvement in the 8-mml/L lactate threshold. The remaining two studies observed greater results in time trials [37, 38]. Otherwise, only one study showed negative effects on endurance performance outcomes. Balsom et al. study participants had impaired time trial results after CrM ingestion [39]. Finally, $VO_{2max/peak}$ [37, 39, 43, 45, 46, 48], individual anaerobic/lactate threshold [41, 42], time trial [48, 49], stages [40], and time to exhaustion [44, 45, 47] remained unchanged after the supplementation protocol.

3.2 Study Quality

The PEDro scale mean score for the included studies was 7.69, considered as good quality. Four studies [40–42, 44] were classified as excellent quality, eight investigations [37, 39, 43, 45–48]) were categorized as good quality, and one study [38] was classified as fair quality. The PEDro scale is shown in Table 2.

3.3 Pooled Effect Estimate

The I^2 test found no significant heterogeneity between studies ($p = 0.19$). Nevertheless, the I^2 statistic observed a moderate risk of heterogeneity ($I^2 = 34.75\%$). The visual analysis of the funnel plot indicated asymmetry showing publication bias (Fig. 2); however, no significant results were found in the Egger's regression test for funnel plot asymmetry ($df = 11$; $p = 0.70$), and Duval and Tweedie's trim and fill method did not identify missing studies on either side of the plot. After excluding the studies not evenly distributed around the base of the funnel plot, the heterogeneity between studies was drastically reduced, showing a low risk of heterogeneity ($I^2 = 0\%$; $p = 0.89$). Egger's regression test showed no funnel plot asymmetry ($df = 9$; $p = 0.90$) and Duval and Tweedie's trim and fill method did not identify missing studies on either side of the plot after the bias correction. Funnel plots are displayed in Fig. 2.

The results for the pooled meta-analysis showed a non-significant change in endurance performance after CrM supplementation in a trained population ($p = 0.47$), with a trivial negative effect (pooled SMD = −0.07 [95% CI −0.32 to 0.18]). Following the exclusion of the studies not evenly distributed around the base of the funnel plot, the results were similar (pooled SMD = −0.07 [95% CI −0.27 to 0.13]; $p = 0.49$). Forest plots are shown in Fig. 3.

Table 2 Physiotherapy Evidence Database (PEDro) scale ratings of the included studies

Study	1	2	3	4	5	6	7	8	9	10	11	Total
Balsom et al. (1993) [39]	Yes	0	0	1	1	1	1	1	1	1	1	8
Chilibeck et al. (2007) [40]	Yes	1	0	1	1	1	1	1	1	1	1	9
Chwalbinska-Moneta et al. (2003) [41]	Yes	1	0	1	1	1	1	1	1	1	1	9
Fernández-Landa et al. (2020) [42]	Yes	1	1	1	1	1	1	1	1	1	1	10
Hickner et al. (2010) [43]	Yes	0	0	1	1	1	1	1	1	1	1	8
Izquierdo et al. (2002) [44]	Yes	1	0	1	1	1	1	1	1	1	1	9
Lawrence et al. (1997) [37]	Yes	0	0	1	1	1	1	1	1	1	1	8
Murphy et al. (2000) [45]	Yes	0	0	1	1	1	1	1	1	1	1	8
Nelson et al. (2000) [46]	Yes	1	0	0	1	1	1	0	1	1	1	7
Ostojic (2004) [47]	Yes	1	0	1	1	0	0	1	1	1	1	7
Rossiter et al. (1996) [38]	Yes	0	0	0	1	0	0	1	1	1	1	5
Syrotuik et al. (2001) [48]	Yes	0	0	1	1	0	0	1	1	1	1	6
Thompson et al. (1996) [49]	Yes	1	0	0	1	0	0	1	1	1	1	6

1, eligibility criteria were specified; 2, volunteers were randomly allocated to groups; 3, allocation was concealed; 4, the groups were similar at baseline regarding the most important prognostic indicators; 5, blinding of all participants; 6, blinding of all therapists who administered the therapy; 7, blinding of all assessors who measured at least one key outcome; 8, measures of one key outcome were obtained from 85% of participants initially allocated to groups; 9, all participants for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome were analyzed by "intention to treat"; 10, the results of between-group statistical comparisons are reported for at least one key outcome; 11, the study provides both point measures and measures of variability for at least one key outcome

4 Discussion

Thirteen studies satisfied the inclusion criteria to assess the effect of CrM supplementation on endurance performance. All of the participants ($n=277$) in the analyzed studies followed a slow or rapid CrM supplementation protocol in order to assure fully saturated muscle PCr and Cr storage. The primary aim of this SRMA was to examine and summarize the current scientific literature regarding the effectiveness of CrM supplementation on endurance performance in a trained population. The main finding was that CrM supplementation had no effects on endurance performance in a trained population. In addition, the meta-analysis results revealed no significant change ($p=0.57$) with a trivial negative effect (pooled SMD = −0.07 [95% CI −0.32 to 0.18]; $I^2=34.75\%$) in endurance performance compared with placebo. In addition, so as to reduce publication bias, the same analysis was carried out after excluding two studies [41, 43] not evenly distributed around the base of the funnel plot. After excluding those studies, the result of the meta-analysis was similar (pooled SMD = −0.07 [95% CI −0.27 to 0.13]; $p=0.49$; $I^2=0\%$).

The results found in the current SRMA differ from those in the Gras et al. meta-analysis [21], where a negative influence of Cr on endurance capacity (measured as VO_{2max}) was found. In contrast, the results of this SMRA showed no effect of CrM on endurance performance (measured as VO_{2max}/VO_{2peak}, individual anaerobic/lactate threshold, time trial, and time to exhaustion). Another considerable

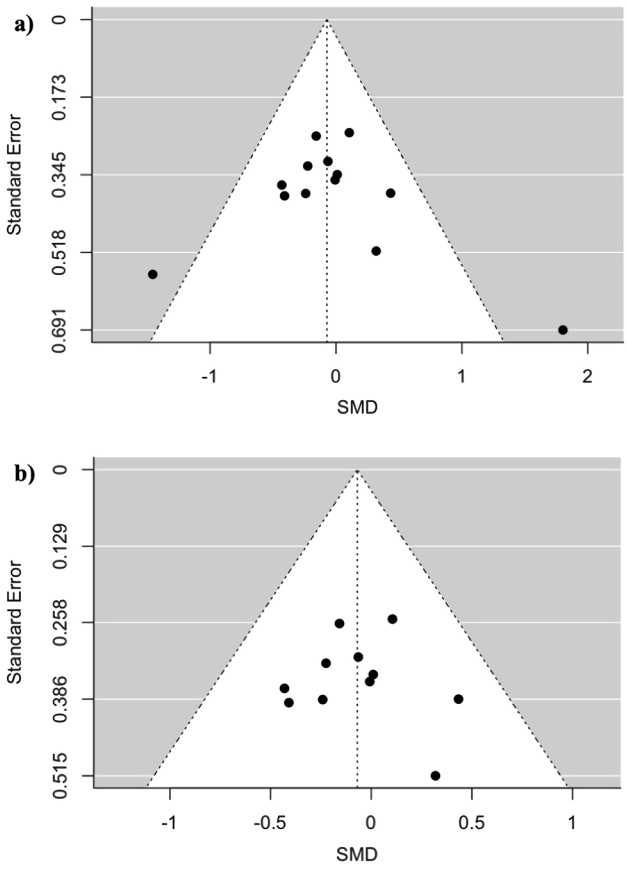

Fig. 2 Funnel plot of included studies, **a** before excluding studies not evenly distributed around the base of the funnel plot and **b** after excluding studies not evenly distributed around the base of the funnel plot. *SMD* standardized mean difference

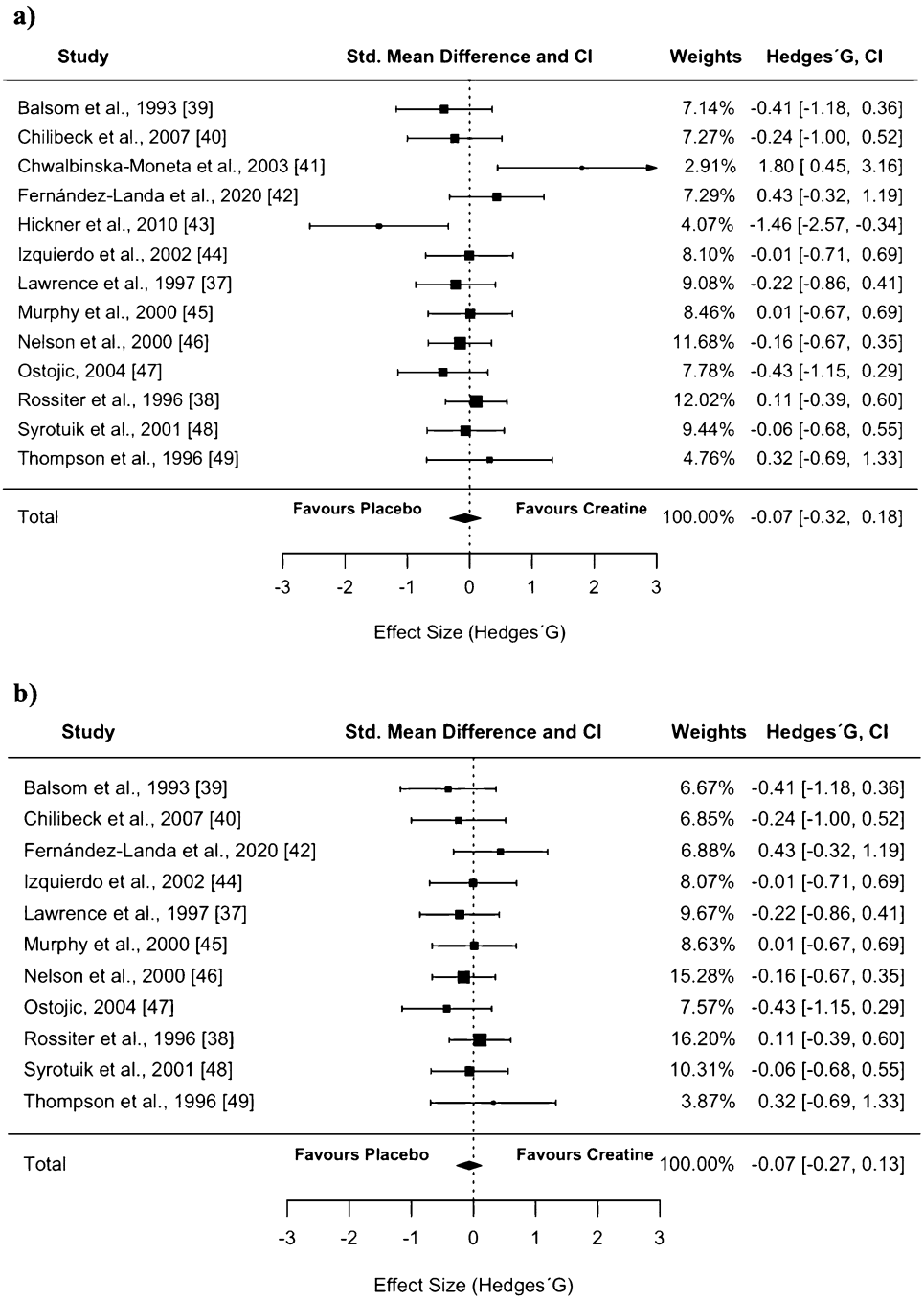

Fig. 3 Pooled meta-analysis of included studies, **a** before excluding studies not evenly distributed around the base of the funnel plot and **b** after excluding studies not evenly distributed around the base of the funnel plot. *CI* confidence interval, *Std.* standardized

difference between reviews was the inclusion criteria applied to the population. In the Gras et al. meta-analysis [21], all young and healthy participants were included, while in this meta-analysis, only trained populations met the inclusion criteria. The results of both meta-analyses showed that this supplement could differently influence trained and untrained populations.

In this systematic review, some endurance outcomes of analyzed studies were improved after CrM ingestion. All studies with significant improvements in the measured outcomes (individual threshold [41], 8-mmol/L lactate threshold [42], time trial [37, 38], and time to exhaustion [41]) were found when a rowing ergometer test was carried out. The enhancement of performance was only found in rowers. Rowing is considered an endurance sport because of its high demand for aerobic energy, which ranges from 70 to 86% of the total energy demands [50]. However, upper and lower body strength also plays a key role in achieving the maximum performance and has been established as one

of the most important rowing performance predictors [51]. In this context, CrM has shown effectiveness in improving upper and lower body strength [6, 52]. That might be the main reason for the improvement in the tests carried out in rowing ergometers by these athletes compared with the remaining trained population included in the SRMA. Moreover, the increase in the Cr/PCr system after CrM ingestion shuttling additional ATP from mitochondria [3, 13] and the capability of this supplement to increase muscle glycogen storage [17] may also have had a positive influence on endurance performance. However, one study showed a significant impairment in an endurance performance outcome [39]. In order to find an explanation for these findings, Balsom et al. [39] suggested that the impairment could have been related to the increase in body mass in the group that ingested CrM.

Although four studies found positive effects on endurance performance and only one found adverse effects, the meta-analysis showed a non-significant negative effect after the CrM supplementation (pooled SMD = −0.07; $p = 0.57$). Specifically, the studies with a larger negative effect size (SMD > −0.20) in the meta-analysis [37, 39, 40, 43, 47] were generally associated with a body mass increase after CrM ingestion. In three studies [39, 40, 43], participants increased their body mass, while one [47] did not report body mass change data, and only one study [37] did not find changes in that parameter. More precisely, results from Balsom et al. [39] and Chilibeck et al. [40], both carried out on running performance tests (6-km terrain run [39] and Leger shuttle run test [40]), could have been more affected by a body mass increase. In these studies, the impairment of endurance performance might be explained by an increase in body weight, which could augment energy costs during running [53]. Otherwise, the three studies showing higher positive effects on endurance performance (effect size > 0.20) did not report changes in body mass [41, 42], or the body mass was not measured [49]. This shows that the results of this SRMA could be considered a negative interaction between endurance performance and the CrM supplementation-induced increase in body mass.

Even though it previously has been hypothesized that CrM could improve endurance performance by shuttling additional ATP from mitochondria through the Cr/PCr system [3, 13], the ingestion of this ergogenic aid should not be the most appropriate to enhance aerobic capacity. One explanation for this result might be the action of CrM at the peripheral muscle level. This supplement is well known for its effectiveness in enhancing muscle hypertrophy and increasing the recruitment of fast-twitch muscle fibers [54]. Therefore, these changes in skeletal muscle could negatively affect endurance performance. Another reason explaining why this supplement is ineffective in enhancing endurance performance could be associated with the capacity for CrM to augment body mass. The increase in body mass could negatively influence endurance performance raising the energy cost during exercise, mainly during running [53]. However, in events where the effect of body mass does not increase the energy cost of exercise (e.g., rowing in a rowing ergometer) and strength is an essential factor for the sport (e.g., rowing), it might be a good option to ingest CrM so as to enhance endurance performance.

5 Conclusions

The result obtained in this SRMA showed that CrM supplementation was ineffective, regardless of the supplementation protocol, at improving endurance performance in a trained population. Considering that this supplement is one of the most popular ergogenic aids in the sports field, athletes, coaches, nutritionists, dietitians, and sports scientists should be aware of the finding of the current SRMA when the primary purpose is to improve endurance performance.

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Authors' Contributions JFL designed and conceived the systematic review and meta-analysis. JFL wrote the first draft of the manuscript. JFL, NT, and ASG conducted the literature search. JFL, NT, and ASG selected the articles for inclusion in the review. JFL and ASG assessed the quality of the included studies. JFL conducted the statistical analysis. JFL, ASG, NT, VS, and SMO revised the original manuscript. All authors read and approved the final manuscript.

Declarations

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Conflicts of Interest/Competing Interests Julen Fernández-Landa, Asier Santibañez-Gutierrez, Nikola Todorovic, Valdemar Stajer, and Sergej M. Ostojic have no conflicts of interest that are directly relevant to the content of this article.

Ethics Approval This project was performed in accordance with PRISMA guidelines.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Availability of Data and Material Data for the current analysis are available upon request and can be obtained by contacting the corresponding author.

Code Availability Not applicable.

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