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Influence of Branched-Chain Amino Acid Ingestion on Creatine Kinase Post of Eccentric Exercise on Recovery: A Systematic Review and Meta-Analysis

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HIGHLIGHTS

- BCAA supplementation reduces exercise-induced muscle damage markers.
- Meta-analysis shows significant reduction in EIMD with BCAA intake.
- Subgroup analysis reveals dosage and exercise type influence BCAA effectiveness.
- BCAA administration reduces creatine kinase levels in trained and untrained individuals.

Abstract: The objective of this systematic review and meta-analysis was to investigate whether the administration of branched-chain amino acids (BCAAs) reduces exercise-induced muscle damage (EIMD) markers following eccentric exercise (EE) compared to a placebo (PL). The Cochrane bias risk tool and NutriGrade scale were used to critically evaluate the included studies. Forest plots were used to visualize the standardized mean differences (SMD) and p-values. The included studies were randomized controlled trials with either a placebo or crossover randomized design. The assessment of EIMD markers was compared between the intervention (BCAA) and placebo situations at 0, 24, 48, 72, and 96 hours after the EE protocol. Subgroup analyses were conducted to assess the effects of BCAA intake on creatine kinase concentration based on follow-up times (immediately, 24 hours, 48 hours, 72 hours, 96 hours), dosage (≥ 10 g/day, < 10 g/day), administration duration (≥ 1 week, < 1 week), exercise type (aerobic, anaerobic), and training status (trained, untrained). The intervention situation showed a significant reduction in indirect markers of EIMD compared to the placebo situation ($p = 0.001$; $I2 = 81\%$). Subgroup analyses indicated that BCAA administration had a significant reducing effect on creatine kinase levels in trials with a dosage of ≥ 10 g/day, anaerobic exercise, trained individuals, and an ingestion duration of less than 1 week. The findings of this study suggest that BCAA administration reduces EIMD markers following chronic EE in both trained and untrained individuals. BCAA administration reduces creatine kinase activity at 48 hours, 72 hours, and overall post-EE compared to a placebo.

Keywords: Branched chain amino acid; Exercise-induced muscle damage; Eccentric exercise; Creatine kinase concentration.

INTRODUCTION

Athletes regularly engage in physical activity to maximize the potential benefits of muscle contraction. The significance and advantages of regular physical activity in maintaining overall health and preventing aging are well recognized. However, intense and sudden exercise can lead to soreness in the skeletal muscles in the hours and days following the exercise, known as delayed-onset muscle soreness (DOMS) [1]. DOMS is characterized by muscle damage resulting from eccentric exercise, which includes injury to the myocyte membranes, inflammation cytokine influx to the injured area, and increased production of inflammation markers. DOMS-induced soreness can lead to decreased performance and muscle strength gains for up to 20 days [2].

In a study by Shimomura and coauthors [2], it was suggested that administration of branched-chains amino acids (BCAAs) before squats exercise reduced DOMS in the hours following the exercises. Furthermore, the beneficial effects of BCAA intake in inhibiting of both EIMD and DOMS were observed in an exercise schedule involving cycling and trained long-distance runners. However, a study by Jackman and coauthors [3] found no significant decrease in DOMS or inflammatory markers following high-intensity exercises with BCAA administration, except when evaluated with extended knees. Therefore, the effective effects of BCAA administration on EIMD and DOMS were less pronounced in exercises with higher intensities. Stock and coauthors conducted a study to assess the combined effects of leucine administration and carbohydrate beverages on delayed onset muscle soreness (DOMS) and plasma markers of exercise-induced muscle damage (EIMD) during the recovery period following squat exercises. However, no significant influences were observed before and after eccentric exercise (EE) [4,5]. Moreover, the mixture of proteins (types of free amino acid comprising BCAAs) and carbohydrates nutrient supplemented pre and post of EE had not any influences on EIMD, strengths loss and DOMS [6]. Thus, mixture of BCAA with other anti-inflammations supplements may be advantageous for decreasing EIMD and DOMS. Furthermore, the supplementation of a protein mixture (containing free amino acids including BCAAs) and carbohydrates before and after eccentric exercise did not show any effects on EIMD, strength loss, or DOMS [6]. Therefore, it is suggested that a combination of BCAAs with other anti-inflammatory supplements may prove beneficial in reducing EIMD and DOMS. Mantuano and coauthors [7] examined the effects of a 12-week oral supplementation of branched-chain amino acids (BCAAs) on aged mice. The BCAAs, known for their muscle-building properties, were given to 17-month-old mice in the form of a drink. Some mice received additional compounds to enhance the absorption of BCAAs. The results showed that the supplemented mice had improved muscle strength and size compared to adult mice. The muscles of the treated mice also showed better contractile properties and increased levels of a protein associated with muscle growth. These findings suggest that BCAAs-based supplements, especially those with enhanced bioavailability, could be beneficial for treating sarcopenia. Khemtong and coauthors [8] investigated the impact of BCAAs supplementation on various factors in collegiate basketball players during a 72-hour recovery period after a COD exercise protocol. Participants were randomly assigned to receive either BCAAs or a placebo. The results showed that creatine kinase levels increased immediately after exercise and peaked at 24 hours, while muscle soreness remained elevated for the entire 72-hour period. Arterial stiffness decreased after exercise in both groups. There was a slight decrease in interleukin-6 levels in the BCAAs group. Overall, the study found no significant benefits of BCAAs supplementation on muscle damage, soreness, neuromuscular performance, or arterial stiffness for basketball players following COD exercises.

In an effort to mitigate the detrimental effects of exercise-induced muscle damage (EIMD), several investigations have explored various approaches. These include cold water immersion [9], administration of antioxidants [10], ergogenic aids [11], nonsteroidal anti-inflammation drugs (NSAIDs) [12] and nutritional interventions [13]. Among these interventions, nutritional administration of branched-chain amino acids has shown promising effectiveness in reducing EIMD, particularly after intense eccentric exercise [14]. Previous studies have also highlighted the potential therapeutic benefits of BCAAs in post-damaging EE recovery [15].

Notably, studies examining recovery from strenuous endurance EE have provided evidence supporting the use of BCAAs in reducing muscle damage and expediting the recovery process [16–19]. BCAAs, namely valine, leucine, and isoleucine, are three of the nine essential amino acids required for protein synthesis in humans. Structurally similar, BCAAs are metabolized through a common catabolic pathway, ultimately entering the Krebs cycle to synthesize adenosine triphosphates (ATPs) [20]. BCAAs account for approximately 36% of the essential amino acids found in skeletal muscle proteins [20,21].

During EE, skeletal muscle mitochondria catabolize BCAAs through a two-step process. Initially, BCAAs are transaminated into α-keto acids via the branched-chain amino transferases (BCAT) enzymes. These α-keto acids remain in the pool of organ amino acids. Subsequently, the alpha-keto acids undergo further metabolism by branched-chain α-keto acid dehydrogenases (BCKDs) to generate products that enter the

Krebs cycle and are utilized for muscle protein synthesis [1]. BCKD compounds play a critical role in BCAA metabolism and are activated through dephosphorylation [2]. However, BCKD activity is somewhat reduced in skeletal muscles due to increased action of BCKD-kinase deactivating enzymes. Consequently, BCAAs metabolized into α-keto acids during EE are more likely to be utilized for synthesizing skeletal muscle proteins post-exercise [22].

Within the context of EE, skeletal muscles oxidize a greater fraction of BCAAs compared to other amino acids [23]. Eccentric muscle contractions induce the highest degree of delayed onset muscle soreness (DOMS), characterized by the soreness experienced in skeletal muscles during or after EE, typically peaking 1 to 2 days following exercise [24]. Controlled EE involves strenuous muscle contractions that result in the catabolism of muscle proteins and cause micro-injuries to muscle fibers.

METHODS

Strategy of Search

This meta-analysis was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). An electronic search was performed from the inception of the study up until July 2022 using various databases, including PubMed, Scopus, ISI Web of Science, and Google Scholar. The search utilized a combination of keywords and their variations, such as "branched-chain amino acids," "exercise-induced muscle damage," "sports," "creatine kinase," "training," "physical activity," and "delayed-onset muscle soreness." Additionally, terms such as "controlled trial," "recovery," "muscle damage," and "cross-over design" were included to refine the search results. The reference lists of identified studies were also examined to identify additional relevant investigations.

Criteria of Eligibility

The selected investigations for screening in this study involved human participants who were administered with BCAA prior to eccentric exercise (EE) or both pre and post EE. The inclusion criteria for the screening process were as follows:

- The investigations followed a randomized design with participants assigned to either a BCAA ingestion group or a placebo (PL) group.
- Measurement of serum creatine kinase levels was included as an outcome measure.
- BCAA supplementation was administered both before and after EE, and the ingestion protocol was repeated on subsequent days following EE.
- Participants could be of any gender and involved in various sports training situations. There were no limitations on the type of EE or the type of placebo utilized.
- Investigations involving multiple nutrient ingestions, such as BCAA in combination with other nutrients, were not included in the study.

Selection of investigations

Two independent authors were responsible for selecting the investigations to be included in the study. They reviewed the titles and abstracts of the investigations obtained through the search strategies. All investigations that were deemed relevant by either of the authors were retrieved for further assessment. Standardized forms were used to determine the eligibility of the investigations for inclusion in the study, following the criteria set forth in the study protocol. In case of any disagreements between the authors, they were resolved through discussion and consensus. If a consensus could not be reached, a third reviewer was consulted to make the final decision.

Data extraction

Two independent reviewers conducted the data extraction using a customized data extraction sheet. Any discrepancies or differences in the extracted data were resolved through consensus between the reviewers. The data extraction process involved extracting relevant information on methodological details, eligibility criteria, intervention descriptions (including specific details of the BCAA ingestion protocol), comparison groups, and outcome measures from each included investigation.

Measures of treatment influence

The mean differences and standard deviations were calculated for continuous outcomes in each investigation. If the continuous outcomes were measured on different scales, standardized mean differences were used. The primary focus was to extract information related to changes from the pre-intervention baseline (mean change scores), although most investigations reported follow-up scores.

In cases where there was no evidence of heterogeneity (P>0.05), a fixed-effects model was used for the meta-analysis. However, if there was significant heterogeneity detected, the results were assessed using random-effects models.

To examine the potential influence of BCAA ingestion on creatine kinase levels, subgroup analyses were conducted. The meta-analysis was performed based on different follow-up times (immediately, 24 hours, 48 hours, 72 hours, 96 hours), dosage categories (≥ 10 g/day, < 10 g/day), duration of ingestion (≥ 1 week, < 1 week), exercise types (aerobic or anaerobic), and training status (trained or untrained).

NutriGrade

To assess the overall quality of the meta-analysis regarding the efficacy of BCAA ingestion on creatine kinase, we employed the NutriGrade rating system [25]. NutriGrade is a rating system that assigns a score from 0 to 10 to evaluate the quality of meta-analyses conducted in the field of nutrition. It considers the following components:

- Bias risk (3 scores): Assessing the risk of bias in the included studies.
- Precision (1 score): Evaluating the precision of the effect estimates.
- Heterogeneity (1 score): Examining the degree of heterogeneity among the studies.
- Directness (1 score): Determining the extent to which the evidence directly addresses the research question.
- Publication bias (1 score): Assessing the potential bias introduced by selective publication of studies.
- Funding bias (1 score): Considering the influence of funding sources on the results.
- Study design (2 scores): Evaluating the quality of the included investigations.

Based on the scores assigned to each component, NutriGrade categorizes the evidence validity into four categories:

- High (≥ 8 scores)
- Moderate (6-7.9 scores)
- Low (4-5.9 scores)
- Very low (≤ 3.9 scores) [24].

RESULTS

Searching findings

The electronic search initially identified 80 relative investigations. After removing duplicate studies, a thorough review of titles and abstracts was conducted, resulting in 75 investigations. Following the screening process based on the eligibility criteria, 25 investigations remained. Finally, 10 investigations were included in the meta-analysis, comprising a total of 21 effect sizes for creatine kinase levels, involving 526 participants. It should be noted that some trials had participants who dropped out during the study. The age of the individuals ranged from 20 to 42 years, and all investigations included male participants except for one study that exclusively involved females [26] (n = 14). Figure 1 and Table 1 provide an overview of the reasons for excluding and selecting investigations.

The included investigations were published between 2007 and 2020. The number of participants who completed the assessments was 277 in the intervention group and 249 in the control group for creatine kinase levels. The duration of BCAA ingestion varied from one day to 18 days across the investigations. All 10 trials examined the influence of BCAA on creatine kinase levels.

In terms of measuring creatine kinase, most investigations evaluated follow-up times immediately and at various intervals (5, 10, 15, 30, and 60 minutes, and 1, 2, 24, 48, and 72 hours) after EE. Data were extracted for measurements taken in minutes, hours, and subsequent days after EE. All 10 trials included an immediate post-EE follow-up, with nine trials reporting follow-up times below 24 hours, eight trials at 48 hours, six trials

at 72 hours, and three trials at 96 hours post-EE. Additionally, the participants in all investigations were trained, except for four investigations that included untrained individuals [23,26–28].

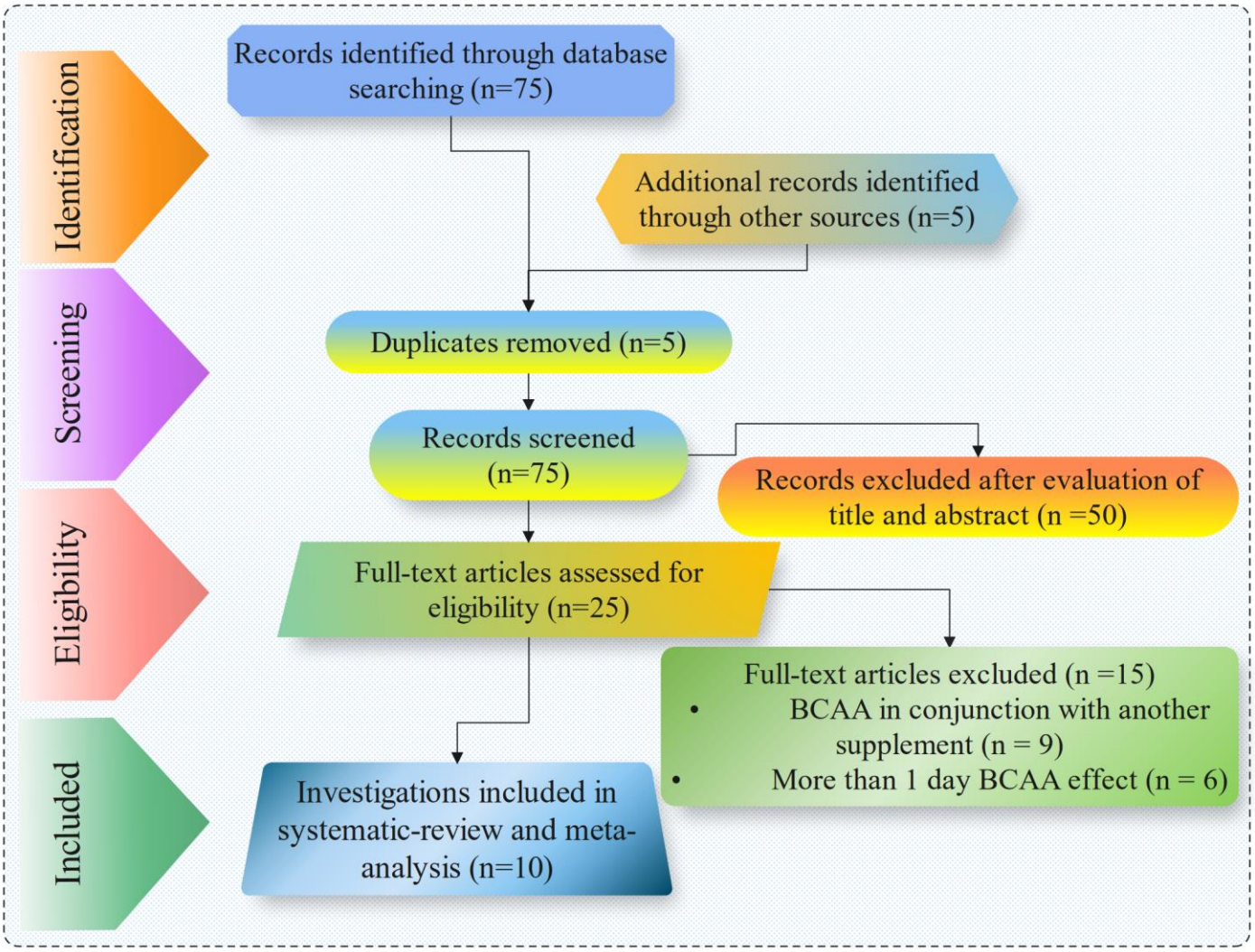

Figure 1. Flow diagram of investigation selection process based on PRISMA.

Table 1. Characteristics of the included investigations

Author (year)	Investigation Design Characteristics						Average age (y)	Sample Size		Exercise type	Muscle damage indices
	Design	Country	Training status	BCAA dose (mg/d)	Duration (d)	Gender		BCAA	Control		
Koba et al. (2007) #	RP	Japan	T	3	1	M	21	4	4	aerobic	^
Jackman et al. (2010) #	RP	UK	U	7.3	3	M	21	20	20	aerobic	^
Ramin et al. (2011)	RP	Iran	T	32	7	M	22.6	10	9	resistance	CK
Ramin et al. (2011)	RP	Iran	T	15	7	M	22.6	10	9	resistance	CK, LDH
Knechtle, et al. (2012)	RP	Switzerland	T	0.25	1	M	42.4	14	14	aerobic	CK
Howatson, et al. (2012)	CP	UK	T	10	9	M	23	6	6	resistance	CK
Ra et al. (2013)	CP	Japan	U	3.2	14	M	22.9	9	9	resistance	CK, LDH
Mohamad-Panahi et al. (2013)	RP	Iran	U	15	7	M	20.1	10	10	aerobic	CK, LDH
Fouré et al. (2015)	RP	France	U	7	1	M	22	13	13	resistance	CK
Osmond et al. (2019)	RP	USA	U	15	7	M & F	23.5	7	7	resistance	CK
Lim et al. (2020)	CP	Korea	T	3	8	M	33.8	17	17	resistance	CK

CK: Creatine kinase; LDH: Lactate dehydrogenase; RP: randomized controlled trial; CP: cross-over investigations; M: male; F: Female; D: Days; Y: years; T: trained; U: untrained
Excluded from meta-analysis ^ inaccessible data

Results of quality measurements

The quality assessment of bias is presented in Table 2. Overall, all investigations reported random allocation of individuals. However, only two investigations provided information on the methods used for generating random sequences. One investigation reported allocations concealment. Regarding bias risk, all investigations had low risk in terms of incomplete outcome and selective outcome reporting. However, when it came to blinding of individuals and personnel, as well as outcome measurement, all investigations had either high or unclear bias risk, except for two investigations that reported low risk in these aspects. Lastly, most investigations had a medium risk of bias, while one article had a low risk [26].

Findings from BCAA ingestion influences on serum creatine kinase

Based on the analysis of 21 trials, it was found that BCAA ingestion had a significant overall effect in reducing creatine kinase levels (WMD = -80.749 IU/L, 95% CI: -129.185 to -32.313; P = 0.001) (Figure 2). However, considerable heterogeneity was observed among the investigations (Cochran's Q test = 129.24, P = 0.000, I2 = 80.6%) (Table 3). To further investigate the potential influence of BCAA ingestion on creatine kinase levels, subgroup analyses were conducted based on follow-up times (immediately, 24, 48, 72, and 96 hours), dosage (≥ 10 g/day, < 10 g/day), ingestion duration (≥ 1 week, < 1 week), exercise type (aerobic, anaerobic), and training status (trained or untrained) (Table 3). The subgroup analyses revealed that BCAA ingestion had a significant decreasing effect on creatine kinase levels in trials with a dosage of ≥ 10 g/day, anaerobic exercise, trained participants, and ingestion duration of less than 1 week.

Sensitivity analysis

No significant changes were observed in the Meta-Analysis findings when any of the investigations were removed from the analysis in terms of serum creatine kinase levels, as determined by sensitivity analysis. The funnel plots for creatine kinase levels exhibited symmetry (Figure 3), and the findings of the Begg's test did not indicate evidence of publication bias in the investigations evaluating the influence of BCAA administration on creatine kinase concentration (Begg's test, P = 0.123).

NutriGrade

The total quality score for the findings, as measured by the NutriGrade scoring system, was 5.5 for creatine kinase. This score indicates a low level of confidence in the estimation of the influence, suggesting that more studies may be needed to provide substantial evidence and potentially change the estimation of the influences.

Table 2. Cochrane Risk of Bias Measurements

Investigation	Random Sequences Generation	Concealment of Allocation	Personnel and Participants Blinding	Outcomes assessment Blinding	Incomplete outcomes data	Selective outcomes reporting	Other sources of bias	Total Bias Risk
Koba et al. (2007)	U	H	H	H	L	L	L	High
Jackman et al. (2010)	U	U	H	H	L	U	L	High
Ramin et al. (2011)	L	U	L	U	L	L	L	Medium
Knechtle, et al. (2012)	U	U	U	H	L	H	L	Medium
Howatson, et al. (2012)	U	U	U	H	L	L	L	Medium
Ra et al. (2013)	U	U	U	H	L	L	L	Medium
Mohamad-Panahi et al. (2013)	U	U	U	H	L	H	L	Medium
Fouré et al. (2015)	U	U	U	H	L	L	L	Medium
Osmond et al. (2019)	L	L	L	L	L	L	L	Low
Lim et al. (2020)	U	U	L	L	L	L	L	Medium

Table 3. Subgroup Analysis to Measure the Influence of BCAA Administration on Creatine Kinase

Sub grouped by	No. of trials	Influence size[1]	95% CI		I^2 (%)	p for heterogeneity	significance
Creatine Kinase							
Follow ups							
immediately	4	-13.944	-74.802	46.915	32.5	0.218	0.653
24 hours	6	-98.213	-200.251	3.825	62.3	0.021	0.059
48 hours	5	-227.649	-273.188	-182.110	0.0	0.750	**0.000**
72 hours	3	-36.461	-62.489	-10.433	0.0	0.455	**0.006**
96 hours	3	-3.8e+03	-1.0e+04	2616.394	68.6	0.041	0.246
Total	21	-80.749	-129.185	-32.313	80.6	0.000	**0.001**
Dose							
≥ 10 g/day	9	-110.575	-171.292	-49.857	89.7	0.245	**0.000**
< 10 g/day	12	-11.952	-80.027	56.123	20.2	0.000	0.731
Exercise type							
Aerobic	8	-88.213	-100.251	3.825	62.3	0.021	0.110
Anaerobic	13	-127.649	-173.188	-82.110	0.0	0.750	**0.000**
Training status							
Trained	10	-100.622	-164.049	-37.196	90.3	0.000	**0.002**
Untrained	11	-44.707	-94.989	5.576	80.6	0.374	0.081
Duration							
≥ 1 week	9	-79.056	-175.959	17.848	50.2	0.042	0.110
< 1 week	12	-84.314	-145.839	-22.788	87.4	0.000	**0.007**

[1]Calculated by random influences model.

CI = confidence interval; BCAA = branched chain amino acid

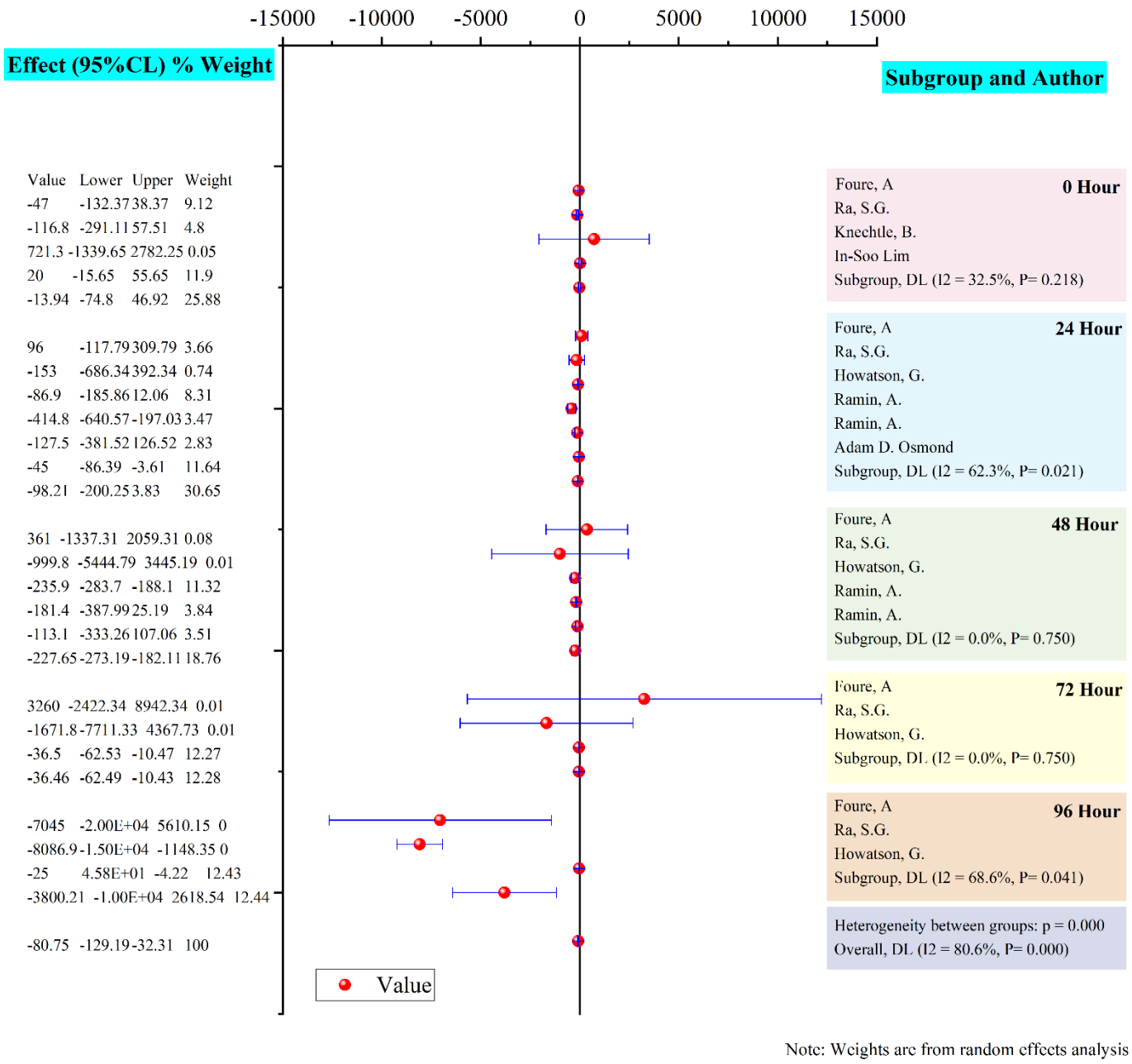

Figure 2. Forest plot of the influence of BCAA ingestion on creatine kinase concentration subgrouped by investigation follow ups, WMD = weighted mean difference; CI = confidence interval.

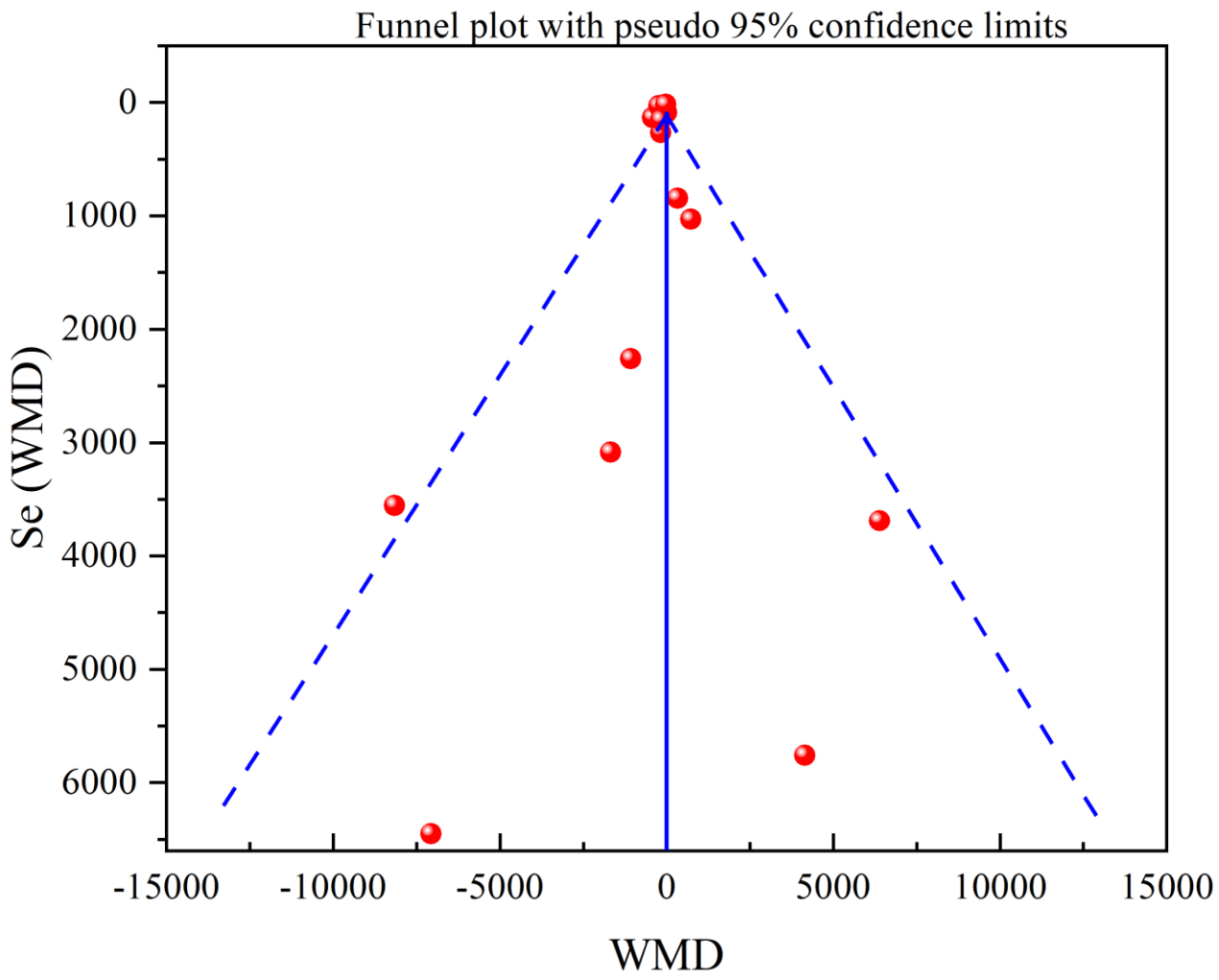

Figure 3. Funnel plot for measuring publication bias in creatine kinase

DISCUSSION

The aim of the current Meta-Analysis was to investigate whether BCAA administration during exercise-induced muscle damage (EIMD) could reduce the levels of an indirect indicator, specifically creatine kinase, compared to a placebo (PL). It was hypothesized that BCAA administration would lead to decreased creatine kinase levels after exercise, particularly at the 48 and 72-hour follow-ups. The analysis suggests that BCAA administration is effective in reducing muscle damage during chronic exercise in both trained and untrained young males and females.

As mentioned in the results section, the strong evidence from this investigation suggests that BCAA administration effectively reduces muscle damage, as indicated by the levels of the muscle enzyme creatine kinase. BCAA administration leads to reduced creatine kinase levels compared to placebo trials at 48 and 72 hours after exercise, as well as overall compared to all trials. However, it is important to note that the observed outcomes may also be influenced by calorie intake during physical activity, regardless of the specific macronutrient composition, as it can reduce the need for muscle protein oxidation. It should be acknowledged that fat intake during exercise was not specifically examined in this study. The findings regarding creatine kinase response in this investigation align with the results reported by Coombes and McNaughton [29] and Saunders and coauthors [30], who investigated the effects of BCAAs or protein administration during endurance exercise. It is worth considering that the inter-individual variation in creatine kinase response is typically quite large, resulting in wide standard deviations (SD) and making it more challenging to achieve statistically significant differences. To mitigate the potential bias of outlier data on group responses, many of the included studies in this analysis utilized a repeated bouts design. By including multiple bouts of exercise, which can have effects lasting up to 4 months, a wider variability among the studies is introduced, but it also strengthens the overall design. However, an analysis of the order of trials revealed no significant differences in creatine kinase response in the included studies. The mean difference in creatine kinase peak levels between the first and third trials was 91.35 U/L. Given that these differences, as well as those observed at

other follow-up times, could have occurred by chance ($p>0.05$), it is suggested that the influence of repeated bouts on creatine kinase response was not a significant source of heterogeneity in the current review.

While the specific mechanisms underlying the reduction in exercise-induced muscle damage (EIMD) with BCAA administration were not investigated in this study, there are several hypotheses that attempt to explain this phenomenon. One hypothesis suggests that when BCAAs are ingested prior to aerobic exercises, they can elevate levels of human growth hormone (HGH) and testosterone, creating a more favorable metabolic environment. Both BCAA supplementation and the presence of alpha-ketoisocaproate (a keto leucine analog) have been shown to inhibit protein metabolism in vitro. Additionally, increased leucine concentrations have been associated with improved action of eukaryotic initiation factor 4F, which plays a crucial role in protein synthesis.

Furthermore, it has been observed that a reduction in amino acids within the free muscle pools, which can occur during chronic exercise, can serve as signals to enhance the degradation of muscle proteins, thereby replenishing the amino acid pools. By maintaining elevated levels of BCAAs through administration, the signaling for muscle damage may be inhibited. The reduction in protein breakdown and subsequent decrease in cell membrane leakage are believed to contribute to the improvement in EIMD indices observed during BCAA supplementation.

It is important to note that these hypotheses provide potential explanations for the observed effects of BCAA administration on EIMD but require further investigation to confirm their validity.

Creatine kinase, as a surrogate marker for exercise-induced muscle damage (EIMD), is indicative of the presence of damage and gaps in the sarcolemma, which leads to the leakage of the cytosolic enzyme into the bloodstream [27]. The sarcolemma, or muscle cell membrane, is likely to undergo various degrees of lipolysis as a result of an imbalance in calcium homeostasis [13,31], often caused by exercise-induced injury. The literature on EIMD consistently demonstrates higher levels of inter-individual variability in creatine kinase as a marker, although the variability in some studies was relatively small, likely due to the trained status of the participants. The higher conditioning of these individuals has likely resulted in a repeated bouts effect [32], where conditioning exercise bouts (in this case, prior to exercise) lead to a reduction in the damage index in subsequent bouts [32].

This repeated bouts effect is further supported by the lower creatine kinase responses observed in both the BCAA and placebo (PL) groups post-exercise, compared to the damage responses observed in untrained individuals [33,34]. Despite this overall homogeneity, the creatine kinase responses were lower in the BCAA group, suggesting that the integrity of the cell membranes was better maintained compared to the PL group. The damage responses following exercise are known to be biphasic in nature: an initial response caused by mechanical stresses during exercise, followed by secondary, temporary inflammatory responses over the subsequent hours and days [29,35]. The subsequent inflammatory response increases the uptake of proteins required for use as a calorie source and plays a role in myocyte signaling and subsequent muscle remodeling [36]. While we cannot definitively support these hypotheses, it seems plausible that the increased bioavailability provided by BCAA supplementation enhanced these responses and thereby reduced secondary muscle damage.

The main limitation of this meta-analysis is that the reported outcomes in the Results section are not well supported by the data from the included studies. Additionally, the included studies have small sample sizes, resulting in wide confidence intervals and lack of statistical significance [23,28]. The main results of the paper are based on only three studies [23,37,38], and further research with larger sample sizes is needed to obtain more statistically robust results. Therefore, caution should be exercised when interpreting the outcomes of this meta-analysis.

The second limitation of the current meta-analysis is the high heterogeneity reported. Several factors may contribute to this high heterogeneity and the inconclusive outcomes that have been described. While creatine kinase is considered an important marker of muscle damage, it is not the only indicator of exercise-induced muscle damage, particularly during aerobic exercise. Moreover, psychological fatigue induced by chronic self-regulation can increase the perception of effort and decrease performance following endurance training. Many studies have suggested that both peripheral and central factors play a significant role in muscle damage, and the relative contribution of each factor may vary depending on the type of exercise [39,40].

Other factors that may contribute to the inconsistency in outcomes include variations in the proportions of valine, isoleucine, and leucine, differences in BCAA production, and variations in the categorization of BCAAs across different countries. All of these factors can contribute to the heterogeneity observed in the results. Furthermore, the included studies in the present meta-analysis examined various doses of BCAA supplementation, ranging from 0.25 g/day [41] to 32 g/day [42], which can also contribute to the variability in outcomes.

CONCLUSIONS

In conclusion, the findings from this meta-analysis provide valuable insights into the utilization of branched-chain amino acid (BCAA) administration for improving recovery from exercise-induced muscle damage (EIMD). The results suggest that overall BCAA administration is beneficial in alleviating EIMD that occurs after strenuous exercise and muscle damage.

Further research is needed to investigate the optimal dosage and frequency of BCAA administration for achieving optimized recovery, considering various dosages and different exercise strategies. Additionally, it is important to explore other relevant factors associated with recovery after exercise-induced muscle damage, such as inflammatory markers, muscle performance, and neuromuscular functions. These factors play a crucial role in the recovery process, and further investigations are warranted to evaluate the effects of various therapeutic recovery strategies on these outcomes.

Overall, this study highlights the potential benefits of BCAA administration in enhancing recovery from exercise-induced muscle damage, but further research is required to fully understand the optimal strategies for maximizing recovery and improving overall muscle health.

Conflicts of Interest: The author declare no conflict of interest.

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