# ROLE OF WHEY PROTEIN IN POST-WORKOUT RECOVERY

*FUNÇÃO DA PROTEÍNA DE SORO DE LEITE NA RECUPERAÇÃO PÓS-TREINO*

*EL PAPEL DE LA PROTEÍNA DE SUERO DE LECHE EN LA RECUPERACIÓN POST-ENTRENAMIENTO*

**Review Article**
***Artigo de Revisão***
***Artículo de Revisión***

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## ABSTRACT

Introduction: Evidence indicates that whey protein supplementation may accelerate tissue repair and be useful for exercise-induced muscle injury (EIMD) by accelerating recovery and elevating protein synthesis and blood amino acids. However, the potential role of whey protein after EIMD in humans is inconsistent. Objective: Find the effective role of whey protein in post-exercise recovery from EIMD. Methods: Scopus, Medline, and Google scholar, were systematically searched until March 2022. To assess the risk of bias, the Cochrane collaboration tool was applied. Weighted mean differences (WMD), 95% confidence intervals (CI), and random effect models to calculate the total effect. Results: The result of the review indicated that the decreasing impact of whey protein intake is significant on creatine kinase (CK) [WMD = -19.11 IU.L-1, CI: -36.200, -2.036; P = 0.028]. The effect of whey protein supplementation on lactate dehydrogenase (LDH) concentration indicated that the impact of whey protein on changing LDH levels is significant. In addition, subgroup analysis showed significant decreases in CK and LDH based on post-exercise follow-up times, whey protein dosage, test duration, supplementation time, exercise types, and training status. Conclusion: The results showed the efficacy of whey protein in decreasing CK and LDH levels among adults in general and in subgroup analysis. Therefore, whey protein could have an effective role in the post-exercise recovery of EIMD. **Level of evidence II; Therapeutic studies – review of results.**

**Keywords:** Whey Proteins; Creatine Kinase; Soft Tissue Injuries; Exercise.

## *RESUMO*

*Introdução: As evidências indicam que a suplementação de proteína de soro de leite pode acelerar a reparação tecidual e, portanto, ser útil para as lesões musculares induzidas pelo exercício (EIMD), acelerando a recuperação, além de elevar a síntese proteica e os aminoácidos sanguíneos. Entretanto, o papel potencial da proteína de soro de leite após a EIMD em humanos, é inconsistente. Objetivos: Encontrar a função efetiva da proteína de soro de leite na recuperação pós exercício de EIMD. Métodos: Scopus, Medline e Google scholar foram sistematicamente pesquisados até março de 2022. Para avaliar o risco de viés, foi aplicada a ferramenta de colaboração Cochrane. Diferenças médias ponderadas (WMD), intervalos de confiança de 95% (CI) e modelos de efeito aleatório foram utilizados para o cálculo do efeito total. Resultados: O resultado da revisão indicou que o impacto decrescente do consumo de proteína de soro de leite é significativo na creatina quinase (CK) [WMD = -19,11 IU.L-1, CI: -36,200, -2,036; P = 0,028]. O efeito da suplementação proteica do soro de leite na concentração de desidrogenase láctica (LDH) indicou que o impacto da proteína do soro de leite na mudança dos níveis de LDH é significativo. Além disso, a análise dos subgrupos mostrou diminuição significativa na CK e LDH, com base nos tempos de acompanhamento após o exercício, dosagem da proteína do soro de leite, duração dos testes, tempo de suplementação, tipos de exercício e status de treinamento. Conclusão: Os resultados mostraram a eficácia da proteína de soro de leite na diminuição dos níveis de CK e LDH entre adultos, em geral e na análise dos subgrupos. Portanto, a proteína do soro de leite poderia ter uma função eficaz na recuperação pós exercício de EIMD.* ***Nível de evidência II; Estudos terapêuticos – revisão dos resultados.***

***Descritores:*** *Proteínas do Soro do Leite; Creatina Quinase; Lesões dos Tecidos Moles; Exercício Físico.*

## *RESUMEN*

*Introducción: Las pruebas indican que la suplementación con proteína de suero de leche puede acelerar la reparación de los tejidos y, por lo tanto, ser útil para las lesiones musculares inducidas por el ejercicio (EIMD) al acelerar la recuperación, así como elevar la síntesis de proteínas y los aminoácidos en sangre. Sin embargo, el papel potencial de la proteína de suero después de la EIMD en los seres humanos, es inconsistente. Objetivos: Encontrar el papel efectivo de la proteína de suero de leche en la recuperación posterior al ejercicio de EIMD. Métodos: Se realizaron búsquedas sistemáticas en Scopus, Medline y Google scholar hasta marzo de 2022. Para evaluar el riesgo de sesgo, se aplicó la herramienta de colaboración Cochrane. Para calcular el efecto total se utilizaron diferencias medias ponderadas (WMD), intervalos de confianza (CI) del 95% y modelos de efectos aleatorios. Resultados: El resultado de la revisión indicó que el impacto decreciente de la ingesta de proteína de suero es significativo en la creatina quinasa (CK) [WMD = -19,11 UI.L-1, IC: -36,200, -2,036; P = 0,028]. El efecto de la suplementación con proteína de suero en la concentración de lactato deshidrogenasa (LDH) indicó que el impacto de la proteína de suero en el cambio de los niveles de LDH es significativo. Además, el análisis de subgrupos mostró disminuciones significativas de la CK y la LDH en función de los tiempos de seguimiento tras el ejercicio, la dosis de proteína de suero, la duración de la prueba, el tiempo de* *suplementación, los tipos de ejercicio y el estado de entrenamiento. Conclusión: Los resultados mostraron la eficacia de la proteína de suero en la disminución de los niveles de CK y LDH entre los adultos en general y en el análisis de subgrupos. Por lo tanto, la proteína de suero podría tener un papel eficaz en la recuperación posterior al ejercicio de EIMD.* ***Nivel de evidencia II; Estudios terapéuticos – revisión de resultados.***

***Descriptores*****:** *Proteína de Suero de Leche; Creatina Quinasa; Traumatismos de los Tejidos Blandos; Ejercicio Físico.*

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## INTRODUCTION

Muscle cells begin a reactions cascade after exercise which lead to complicated action and reaction between degradation and synthesis of protein.[1] Thereby, when protein turnover is increased, catabolism exceeds anabolism, therefore, breakdown of proteins leads to muscle atrophy and degeneration.[2] This conversion in protein structure lead to take down muscles function and exercise induced-muscle damage (EIMD).[3] EIMD is related to increased plasma creatine kinase (CK) and lactate dehydrogenase (LDH) concentrations, delayed onset muscle soreness (DOMS), and decreases in subsequent exercise performance.

In relevance to nutrients intervention, some recovery improving nutrients include vitamins, antioxidants, carbohydrates, branched--chain amino acids (BCAA), beta Hydroxy beta-methylbutyric acid (HMB) and proteins[4] have been examined. Proteins, especially when content is high in BCAA, have the potential to inhibit proteolysis and motivate protein synthesis. This combined effect on breakdown and synthesis could lead to a positive balance of net protein, enhanced contractile function, therewith ameliorating recovery, especially after EIMD. Quality and digestive features of proteins may also regulate these impacts. Synthesis of muscles proteins has been proved to be higher by whey proteins administration when compared with casein.[5] Documents for the whey protein administration role in muscle function recovery after exercise have low publications.[6] Some researchers indicated no advantage of whey proteins administration for melioration of muscles functions, EIMD and DOMS[7] and some of them reported an unexpected effect on muscle damage and soreness indices.[8] The current review assessed indices of EIMD and DOMS, as well as CK and LDH amongst trained and untrained participants.

## METHODS

### Searching

Current meta analysis performed based on PRISMA. From inception to March 2022 a computerized search was done applying various databases consist of ISI Web of Science, PubMed, Scopus and Google Scholar searching.

### Criteria of Eligibility

Papers were elected based on the PICOS, including: The Population, Interventions, Comparison, Outcomes (EIMD and DOMS markers including CK and LDH concentration that performed as randomised controlled trial (RCTs)).

Inclusion criteria for including RCTs in the current meta-analysis were: 1) design of RCT for original studies, 2) Subjects intake whey protein for supplementation, 3) reporting CK and LDH as muscle damage indices, 4) recording data as mean ± SD of CK and LDH in both intervention and placebo groups. RCTs excluded in current meta analysis based on: 1) using combination of whey protein in supplementation group only ; 2) trials nonrandomized and without control groups; 3) animal studies; 4) duplicate papers with same subjects.

### Quality of Studies

For evaluating the bias risk, Cochrane Collaboration items applied. The RCTs quality were evaluated by the following factors: generation of randomization sequence; concealment of allocation; participants and personnel blinding and rates of attrition. These factors gave high, low and unclear bias risk ranking.

### Analysis

For continuous measures of each trial mean and SD measured. Mean changes applied for measurements pooled on the diverse standards. Following formula were applied for studies with no mean change SD: change SD=square root [(SD after$^2$ + SD before$^2$) - (2×0.8×SD after SD before)]. Chi-squared ($\chi 2$) test applied for Heterogeneity of studies evaluation and calculated via $I^2$ statistic, that reports the total variation percentage among effect sizes that is imputable to heterogeneity instead of chance.

The weighted means difference (WMD) with 95 percent confidence interval (CI) was computed applying the random effect models for estimating overall impact. Also, according to follow-up measures post exercise, subgroup analysis was carried out, (immediately, < 1, 1, 2, 3 and 4 days post exercise), dosage of whey protein ,duration of studies, supplementation time, exercise type and status of training.

## RESULTS

### Findings from search and included studies overview

Computerized search found 247 related articles. After remove of duplicate articles, numerous titles and abstracts checking performed on 244 articles. Twenty-nine articles left after screening the inclusion and exclusion items. Finally, 14 articles included in meta-analysis, cocsist of 61 and 17 effects sizes for CK and LDH concentration, that assessed 432 and 144 subjects respectively. These participants covering numbers who dropout in several trials.[7,8]

In Figure 1 the papers published between 2010 to 2020. The participants that finished the assays was 221 participants in intervention and 211 in control group for CK levels and 73 participants in intervention and 71 in control group for LDH levels. The whey protein dosage was 15 to 100 gram/day and duration was 3 days to 12 weeks. RCT used in all studies except one study that applied randomized cross-over design. The whey protein effect on CK and LDH evaluated in five articles together. Raw data of two studies for CK were not available in the articles. An email was sent to the authors requesting raw data but we did not receive a response. Also, baseline measurements for LDH were not available in Hansen et al. study[9] and we excluded this study from meta-analysis.

For both index, most of the studies evaluated some follow-up time (immediately, 30 minutes, 1, 2, 3, 4, 6, 24, 48, 72 and 96 hours). We concentrated on outcomes recorded after exercise and subsequent days. Thirteen trials in 9 papers had follow-ups immediately post exercise; Twenty effects size in 6 papers provided < 24 hours follow-ups time; Fifteen trials in 11 studies had 24 hours follow-up times; Ten effects size in 7 papers recorded 48 hours follow-ups; 9 effects size in 7 papers presented 72 hours follow-ups and Six effects size in 4 papers provided 96 hours follow-ups post exercise.

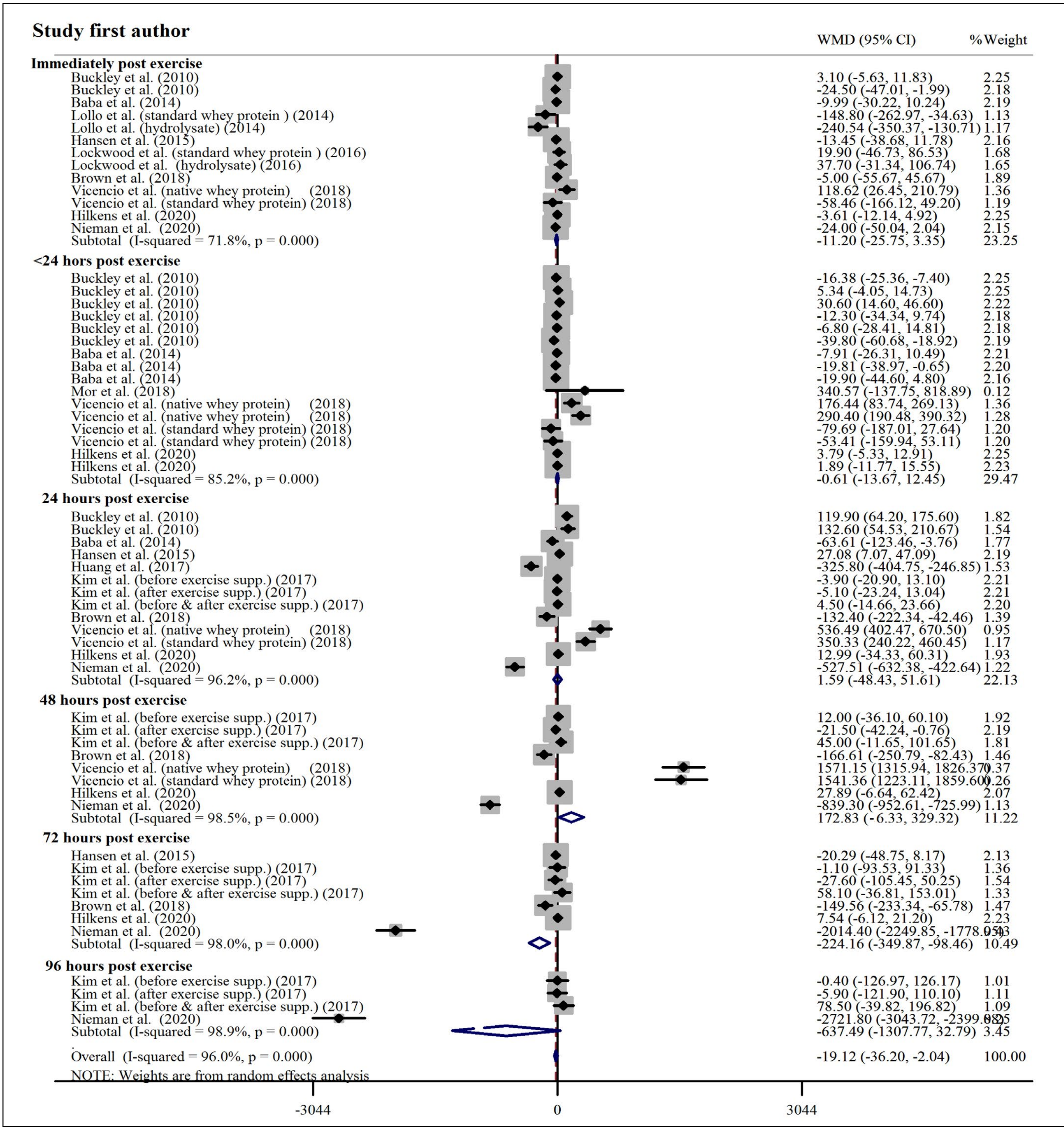


**Figure 1.** Forest plot of the effect of whey supplementation on CK subgrouped by follow up times after exercise. WMD = weighted mean difference; CI = confidence interval.

## Findings from whey supplementation effects on EIMD markers

### Whey administration effects on CK concentration

Based on meta-analysis on 61 effects size, totally, whey protein supplementation had significant decrease impact on CK level: (WMDs = -19.11 $IU.L^{-1}$, CI: -36.200, -2.036; P = 0.028). Significantly heterogeneity observed amongst the articles (Cochran's Q test= 1501.27, P = 0.000, $I^2$ = 96.0 %) (Figure 1).Subgroups analysis indicated that whey administration have a significant decrease impact on CK level in studies with 72 hours measures of CK post exercise, more than 50 gram/day whey intake, 3 days to 2 weeks trial duration, trials with post exercise time of administration, trials on trained subjects and trials with aerobic and combined anaerobic & aerobic type of exercise [9] (Table 1).

### Whey supplementation effects on LDH concentration

Whey protein supplementation effect on LDH levels evaluated in 17 trials and meta-analysis indicated that LDH level change was significant. Also considerable heterogeneity observed amongst the articles (Cochran's Q test = 64.91, P = 0.000, $I^2$ = 75.3%) (Figure 2). For evaluating of the whey protein administration impact on LDH levels is diverse based on subgroup meta-analysis, analysis conducted according to follow-up times post exercise, dosage of whey, duration of studies, time of administration, training status and type of exercise (Table 2).

**Table 1.** Subgroup Analysis to Assess the Effect of Whey protein on CK concentration.

| Subgrouped by | No. of trials | Effect size[1] | 95% CI | P Value | $I^2$ (%) |
|---|---|---|---|---|---|
| **Follow-ups after exercise** | | | | | |
| Immediately | 13 | -11.198 | -25.747 3.351 | 0.131 | 71.8 |
| <24 hours | 16 | -0.611 | -13.674 12.452 | 0.927 | 85.2 |
| 24 hours | 13 | 1.588 | -48.430 51.607 | 0.950 | 96.2 |
| 48 hours | 8 | 172.825 | -6.330 329.321 | 0.230 | 98.5 |
| 72 hours | 7 | -224.164 | -349.865 -98.462 | <0.001 | 98.0 |
| 96 hours | 4 | -637.486 | -1303.651 32.793 | 0.062 | 98.9 |
| **Dose of whey protein** | | | | | |
| <50 g/day | 36 | 19.508 | -0.014 39.002 | 0.055 | 94.1 |
| >50 g/day | 25 | -101.239 | -133.363 -69.116 | <0.001 | 97.3 |
| **Duration** | | | | | |
| Acute (single dose in 1 day) | 28 | -2.854 | -11.675 5.967 | 0.526 | 72.6 |
| 3 days to 2 weeks | 18 | -161.045 | -201.733 -120.358 | <0.001 | 98.1 |
| > 5 weeks | 15 | 117.124 | -64.445 369.804 | 0.152 | 97.0 |
| **Time of supplementation** | | | | | |
| before exercise | 4 | -2.077 | -17.751 13.597 | 0.795 | 0.0 |
| after exercise | 35 | -1.968 | -10.863 6.928 | 0.665 | 65.1 |
| before & after exercise | 22 | -39.120 | -71.640 -6.601 | 0.018 | 97.6 |
| **Train status** | | | | | |
| trained | 24 | -22.396 | -36.450 -8.341 | 0.002 | 85.2 |
| untrained | 37 | -8.875 | -37.549 19.800 | 0.544 | 97.3 |
| **Type of exercise** | | | | | |
| aerobic | 10 | -32.103 | -59.178 -5.028 | 0.020 | 89.0 |
| anaerobic | 44 | 11.212 | -7.330 35.094 | 0.332 | 91.8 |
| anaerobic & aerobic | 7 | -906.339 | -1.3e+03 -484.952 | <0.001 | 99.2 |

[1]Calculated by random effects model. CI = confidence interval.

**Table 2.** Subgroup Analysis to Assess the Effect of Whey protein on LDH concentration.

| Subgrouped by | No. of trials | Effect size[1] | 95% CI | P Value | $I^2$ (%) |
|---|---|---|---|---|---|
| **Follow-ups after exercise** | | | | | |
| Immediately | 3 | -8.783 | -24.107 6.541 | 0.261 | 76.4 |
| <24 hours | 5 | 10.718 | -4.798 19.795 | 0.212 | 29.4 |
| 24 hours | 3 | -10.428 | -17.469 -3.387 | 0.004 | 0.0 |
| 48 hours | 2 | -25.841 | -42.397 -9.286 | 0.002 | 44.9 |
| 72 hours | 2 | -20.415 | -89.456 48.627 | 0.562 | 90.4 |
| 96 hours | 2 | -28.318 | -96.427 39.791 | 0.415 | 82.9 |
| **Dose of whey protein** | | | | | |
| <50 g/day | 10 | 1.337 | -9.607 12.281 | 0.811 | 75.6 |
| >50 g/day | 7 | -15.604 | -27.044 -4.164 | 0.008 | 70.3 |
| **Duration** | | | | | |
| Acute (single dose in 1 day) | 1 | - | - | - | - |
| 3 days to 2 weeks | 13 | -6.869 | -15.618 1.880 | 0.124 | 66.4 |
| > 5 weeks | 3 | -11.053 | -26.549 4.442 | 0.162 | 76.4 |
| **Time of supplementation** | | | | | |
| after exercise | 15 | -5.131 | -13.814 3.552 | 0.247 | 74.9 |
| before & after exercise | 2 | -9.870 | -40.357 20.618 | 0.526 | 87.9 |
| **Train status** | | | | | |
| trained | 12 | -0.683 | -10.693 9.326 | 0.894 | 77.0 |
| untrained | 5 | -18.133 | -31.730 -4.537 | 0.090 | 66.2 |
| **Type of exercise** | | | | | |
| aerobic | 2 | 5.998 | -32.017 44.013 | 0.757 | 94.8 |
| anaerobic | 8 | 0.168 | -10.692 11.027 | 0.976 | 60.2 |
| anaerobic & aerobic | 7 | -15.604 | -27.044 -4.164 | 0.008 | 60.2 |

[1]Calculated by random effects model. CI = confidence interval.

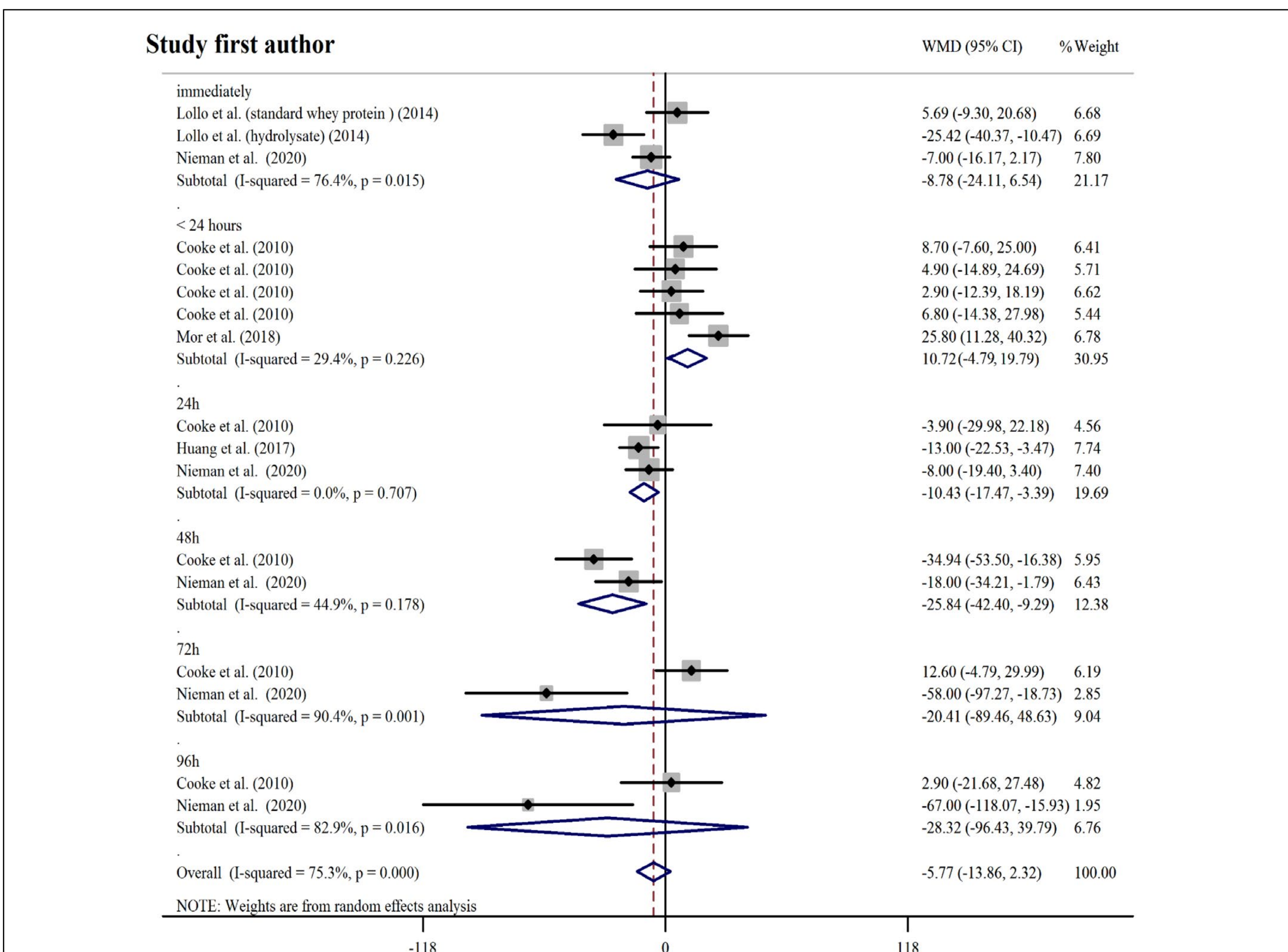


**Figure 2.** Forest plot of the effect of whey supplementation on LDH subgrouped by follow up times after exercise. WMD = weighted mean difference; CI = confidence interval.

## DISCUSSION

The serum level of relevant enzymes is index of the muscle tissue function and varies widely in both physiological and pathological situations. An increase in these enzymes may indicate an index of tissue damage and cellular necrosis following chronic and acute muscle damages. The outcomes of the previous meta-analysis, carried out on 14 randomized controlled trials, with a total of 432 and 144 adult participants for CK and LDH respectively, manifested useful outcomes of whey protein supplementation in diminishing overall CK levels during training protocols of various duration, but significant change in LDH concentration was not seen overally.

Recovery from an exercise can focus many variables, Saunders suggested that protein supplemented during exercise attenuated EIMD.[10] Whey is more effective at elevating protein synthesis and plasma amino acids due to its different amino acid profile (high purity of protein which contains abundant essential and BCAA) and kinetics of rapid absorption compared to regular protein supplements.[11]

## CONCLUSION

Whey protein consumption has a lowering effect on serum LDH in 24 and 48 hours post physical activity. Also, this effect was significant in 24 and 48 hours post physical activity for LDH. Moreover, lower serum levels of CK and LDH might depend on when the early site of muscle damage happened, exercise type, the training status of the participants and therefore the restriction of particular proteins leakage. Hereof, subgroup analysis demonstrated that RCTs with trained participants had a significant decrease in CK levels with whey protein consumption. So, whey protein consumption is more beneficial for untrained subjects. Herein, it should be noted that most of papers were specified by lack of data on dietary standardization, low sample sizes, and restricted evaluation of muscle performance and function.

The author declare no potential conflict of interest related to this article

**AUTHORS' CONTRIBUTIONS:** The work is conceived and executed by Chunlei Gu. The author is fully responsible for execution and writing of this manuscript.

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