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Exercise-Induced Muscle Damage in Soccer: A Systematic Review and Meta-Analysis of the Moderating Roles of Age, Assessment Timing, and Cardiorespiratory Fitness

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Abstract

Purpose: Soccer players frequently experience exercise-induced muscle damage (EIMD) due to the high-intensity, eccentric demands of training and match-play. This systematic review and meta-analysis aimed to quantify the pooled effect of soccer-specific exercise training on serum CK levels and to examine the moderating roles of post-exercise assessment timing (≤ 25 vs. > 25 hours), participant age (≤ 20 vs. > 20 years), and VO_2max (≤ 57 vs. > 57 mL/kg/min).

Method: A systematic search of PubMed/MEDLINE, Scopus, and Web of Science was conducted from inception to 2026. Twenty-nine eligible studies were included. Random-effects meta-analyses and subgroup analyses were performed.

Results: Exercise training significantly elevated CK levels (SMD = 0.553, 95% CI: 0.249 to 0.856; P = 0.001), with substantial heterogeneity (I^2 = 71.07%; τ^2 = 0.558). Subgroup analyses revealed that CK elevations were significant when measured within 25 hours post-exercise (SMD = 0.65, 95% CI: 0.27 to 1.04; P = 0.001) but not beyond 25 hours (SMD = 0.47, 95% CI: −0.06 to 0.99; P = 0.082). Younger players (≤ 20 years) demonstrated substantially larger effects (SMD = 1.26, 95% CI: 0.28 to 2.24; P = 0.012) compared to older players (> 20 years; SMD = 0.42, 95% CI: 0.13 to 0.70; P = 0.004). VO_2max showed the strongest moderating trend, with higher VO_2max (> 57 mL/kg/min; k = 5) associated with markedly larger CK elevations (SMD = 2.42, 95% CI: 0.61 to 4.24; P = 0.009) compared to lower VO_2max (≤ 57 mL/kg/min; SMD = 0.44, 95% CI: 0.16 to 0.72; P = 0.002), although this between-subgroup difference did not reach statistical significance (Q = 4.63, P = 0.099).

Conclusion: Soccer-specific training induces moderate-to-large CK elevations. VO_2max emerged as the most promising moderating factor and warrants further investigation with larger, well-controlled studies.

Keywords: Creatine kinase, exercise-induced muscle damage, soccer, meta-analysis, VO_2max, age, recovery.

Introduction

Soccer is the world's most popular sport, with over 270 million participants globally, and is characterized by high-intensity intermittent activities including repeated sprints, rapid accelerations, decelerations, changes of direction, and physical tackles (Bal, 2026). These demanding physical activities impose substantial mechanical and metabolic stress on players, frequently inducing skeletal muscle damage (Rezaei et al., 2026). The health benefits of regular physical exercise are well established (Ruegsegger & Booth, 2018); however, the balance between training load and recovery is critical, as excessive or prolonged muscle damage may impair performance, delay recovery, and increase susceptibility to overuse injuries (Brenner & Watson, 2024). Therefore, monitoring biomarkers of muscle damage has become an essential component of training load management in elite soccer, enabling coaches and sports scientists to optimize training prescription and minimize injury risk (Owen et al., 2026).

Exercise-induced muscle damage (EIMD) is characterized by sarcomere disruption, cytoskeletal disorganization, altered excitation-contraction coupling, and inflammatory responses (Stožer et al., 2020). In soccer, the eccentric nature of actions such as sprinting, cutting, tackling, and shooting predisposes players to repeated mechanical strain (McBurnie & Dos' Santos, 2022). Among available biomarkers, creatine kinase (CK) remains the most extensively validated indirect indicator of muscle membrane disruption, with serum concentrations directly correlating with the magnitude of myofiber damage (Bischof et al., 2024). CK release occurs following sarcolemma trauma, increased membrane permeability, and efflux of cytosolic proteins, making it a reliable marker for monitoring training load and recovery (Cosio Fernández, 2024). Importantly, CK elevation should be interpreted as a biomarker of muscle membrane disruption rather than a direct measure of clinical injury or functional impairment. Statistically significant increases in serum CK indicate that exercise has induced sarcolemma trauma and increased membrane permeability, but they do not necessarily translate into clinically meaningful muscle damage,

performance decrements, or impaired recovery. This distinction is critical because the clinical relevance of CK elevation depends on its magnitude, time course, and association with functional outcomes such as strength loss, range of motion restriction, and delayed-onset muscle soreness. Throughout this review, CK is therefore treated as a physiological indicator of EIMD, and its statistical significance is distinguished from its clinical and practical meaningfulness.

Considerable research has confirmed that match play and high-intensity training consistently elevate serum CK, with peak concentrations typically observed between 24 and 48 hours post-exercise (Abdulkader et al., 2025). In a study of elite rugby league players, McLellan et al. reported that CK increased significantly after match play, peaking at 24 hours (889.25 ± 238.27 U/L) and remaining elevated even at 120 hours post-match, indicating prolonged muscle damage and a sustained catabolic state. Similar findings have been reported in soccer (McLellan et al., 2010). Beattie et al. found that CK increased by 49% at 48 hours post-match in English Championship soccer players, and this increase was accompanied by a 4.2% reduction in countermovement jump height and alterations in force–time phase variables (2.4–7.4%), all of which were associated with the high physical demands of match play (Beattie et al., 2021). Recently, Tomassetti et al. also observed significant post-match elevations in CK-MB in competitive amateur soccer players. Importantly, elevated CK has been linked not only to acute muscle damage but also to subsequent performance impairment (Tomassetti et al., 2026). Likewise, another study demonstrated that in elite soccer players, a pre-training CK Z-score of +1 was associated with 3.1–5.5% reductions in high-speed running distance, accelerations, decelerations, explosive distance, and maximal speed (Malone et al., 2018). Collectively, these studies confirm that match play and high-intensity training induce substantial CK elevations and neuromuscular fatigue, a condition that can persist for several days and impair subsequent performance. However, despite consistent evidence that soccer-specific exercise elevates CK, the magnitude of this response varies considerably across studies, and the extent to which this

variability is explained by participant characteristics) and methodological factors remains unclear.

Despite extensive primary research, three critical gaps remain unaddressed. First, although individual characteristics such as age, training status, and cardiorespiratory fitness are plausible moderators of EIMD, they have rarely been systematically examined in soccer populations. Second, methodological heterogeneity, particularly regarding post-exercise assessment timing, has prevented consensus on optimal measurement windows; some studies assessed CK immediately post-exercise, others at 24–48 hours, and still others at 72 hours or beyond, contributing to substantial between-study heterogeneity. Third, VO_2max, a key indicator of aerobic fitness and training status, has been inconsistently reported, and its moderating role remains unclear. To date, no meta-analysis has simultaneously quantified the overall effect of soccer-specific exercise on CK while examining the independent moderating effects of age, measurement timing, and VO_2max within a single analytical framework. Addressing these gaps is essential to generate evidence-based benchmarks for training load management and injury prevention in soccer.

The hypotheses of this meta-analysis are grounded in three mechanistic considerations. First, because CK efflux peaks 24–48 hours post-exercise due to delayed membrane permeability and inflammatory signaling, we hypothesized that studies assessing CK within 25 hours would capture the ascending phase and show larger effects than those assessing beyond 25 hours. Second, younger players (≤20 years) may be more susceptible to EIMD due to incomplete neuromuscular maturation and lower training history, although this difference may be attenuated by variations in muscle mass and recovery kinetics. Third, players with higher VO_2max (>57 mL/kg/min) can sustain greater training intensities and total work volumes, potentially inducing more sarcolemma trauma, but this relationship may be confounded by enhanced recovery capacity and competitive level. We therefore hypothesized larger CK elevations in younger players and in those with

higher VO_2max, while acknowledging that these effects may be moderated by training status and training load.

Given these gaps, the present systematic review and meta-analysis provides a comprehensive quantitative synthesis of EIMD responses to soccer-specific exercise, identifying key moderators that explain the substantial heterogeneity across studies. By understanding who (age), when (measurement timing), and under what conditions (VO_2max and intervention duration) players are most susceptible to EIMD, we aim to generate evidence-based benchmarks for training load management and injury prevention. Specifically, this study was designed to:

(1) quantify the overall effect of soccer-specific exercise on serum CK using a random-effects meta-analysis;

(2) examine whether post-exercise assessment timing (≤ 25 h vs. > 25 h) moderates the CK response;

(3) investigate whether participant age (≤ 20 years vs. > 20 years) influences EIMD severity;

(4) evaluate whether VO_2max (≤ 57 vs. > 57 mL/kg/min) moderates CK responses.

Methods

Protocol Registration and PICOs Framework

This systematic review and meta-analysis was prospectively registered in the PROSPERO database (2025 CRD420251144680) to ensure transparency and minimize reporting bias. The study was conducted and reported in accordance with the PRISMA 2020 guidelines(Page et al., 2021), with all methodological steps documented to ensure reproducibility. The research question was structured using the PICOs framework (Population, Intervention, Comparator, Outcomes, and Study Design) to guide study selection, data extraction, and synthesis.

Eligibility Criteria

Studies were included in this systematic review if they met all of the following criteria: (1) study design: randomized controlled trials

(RCTs) with parallel or crossover designs, non-randomized controlled trials, and pre-post intervention studies with repeated measures, including both supervised exercise interventions and regular seasonal training programs; (2) population: soccer players of any age, sex, or competitive level (professional, semi-professional, amateur, collegiate, or youth), with no restrictions on baseline fitness status, playing position, or training history, and without acute musculoskeletal injuries or chronic metabolic disorders; (3) intervention: structured exercise training programs, including but not limited to aerobic training, resistance training, combined aerobic-resistance training, high-intensity interval training (HIIT), plyometric training, small-sided games, speed/agility training, technical drills, or regular in-season/off-season training regimens, with no minimum duration restriction applied; (4) comparators: control groups consisting of soccer players who underwent either an alternative training protocol, maintenance of regular training without additional structured intervention, passive rest or no-exercise control, or baseline pre-intervention values in pre-post study designs; (5) outcomes: reporting CK levels measured in blood samples (serum or plasma) using validated laboratory methods; and (6) publication: original full-text articles published in English in peer-reviewed journals. No restrictions were applied regarding geographical location, publication year, or competitive level of the participants.

Studies were excluded if they met any of the following criteria: (1) non-randomized study designs, including observational studies, cohort studies, case-control studies, cross-sectional studies, and pre-post studies without a control group, as well as non-randomized controlled trials lacking appropriate comparison groups; (2) non-original articles such as narrative reviews, scoping reviews, rapid reviews, meta-analyses, editorials, commentaries, letters to the editor, conference abstracts, and case reports; (3) studies without a control group or with non-exercise control interventions (pharmacological interventions, nutritional supplements without exercise, or passive interventions without structured training); (4) exercise interventions lasting less than 1 week or lacking sufficient detail on exercise prescription (intensity,

frequency, duration, or training modality) to enable replication or accurate categorization for subgroup analyses; (5) studies that did not report quantitative outcome data for CK measured in blood samples (serum or plasma), or reported outcomes in a format that prevented standardized mean difference (SMD) calculation for meta-analysis; (6) studies on animal models or populations other than soccer players; (7) studies with insufficient methodological detail or incomplete outcome reporting that precluded quality assessment (risk of bias evaluation) or data extraction; and (8) duplicate publications or studies reporting overlapping data from the same cohort, in which case only the most recent or most complete publication was retained.

Search Strategy

A comprehensive systematic search was developed to identify studies evaluating the effects of exercise training on CK levels in soccer players. The search strategy was structured around three conceptual areas: (1) soccer players ("soccer", "football", "football players", "association football"); (2) exercise intervention ("exercise training", "resistance training", "aerobic training", "combined training", "HIIT", "high-intensity interval training", "plyometric training", "small-sided games", "speed training", "agility training", "physical activity"); and (3) outcomes related to muscle damage ("creatine kinase", "CK", "muscle damage", "muscle injury", "exercise-induced muscle damage", "EIMD", "rhabdomyolysis"). Keywords and MeSH terms were combined using Boolean operators (AND, OR, NOT). Database-specific adaptations were applied as follows: for PubMed/MEDLINE, MeSH terms were combined with free-text words using the [tiab] field tag; for Scopus, TITLE-ABS-KEY was used; and for Web of Science, Topic (TS) search was applied.

Two independent investigators (M.M.R.A. and A.P.G.) searched PubMed/MEDLINE, Scopus, and Web of Science from inception to 2026. No language restrictions were applied during the search; however, only English-language full texts were included in the final analysis. Duplicate records were identified and removed using EndNote

2025 software (Clarivate Analytics, Philadelphia, PA, USA) with both automatic duplicate detection and manual verification by two reviewers. The specific number of duplicates removed at each stage is reported in the PRISMA flow diagram (***Fig. 1***). In addition to the electronic database search, we manually screened the reference lists of all eligible studies and relevant systematic reviews (backward citation tracking) and performed forward citation tracking via Google Scholar. No date or geographical restrictions were applied.

Study Selection Process

Following the literature search, study selection was performed in two stages using EndNote 2025 software. An experienced researcher initially removed duplicate records. Two independent reviewers then conducted title/abstract screening, followed by full-text screening of potentially eligible articles based on predefined inclusion and exclusion criteria. Disagreements were resolved through discussion or by consulting a third reviewer when consensus could not be reached. Inter-rater reliability was assessed using Cohen's kappa coefficient to evaluate agreement between reviewers during the screening process.

Data Extraction

After finalizing eligible studies through a two-stage review process, two reviewers extracted data independently using a standardized electronic form in Microsoft Excel. The form was pilot-tested on five randomly selected studies and revised accordingly. For each included study, the following data were extracted: (1) study characteristics (author, year, country, study design); (2) participant characteristics (sample size, age, sex, competitive level, baseline VO_2max values); (3) intervention details (exercise modality, frequency, intensity, duration in weeks, and supervision status); (4) comparator description (alternative training protocol, regular training without additional intervention, passive rest, or pre-post baseline measures); and (5) outcome data (mean, standard deviation [SD], and sample size for intervention and control groups at baseline and post-intervention) for CK. Additionally, we recorded the

timing of post-exercise blood sampling (≤ 25 hours vs. > 25 hours) to enable subgroup analyses. Where data were reported as median and range or interquartile range (IQR), we applied standard methods to estimate means and standard deviations.

Statistical Analysis

Meta-analyses were conducted using Comprehensive Meta-Analysis (CMA) software (version 4)(Loghman et al., 2023). Because of anticipated heterogeneity across studies in participant characteristics (age, competitive level, baseline VO_2max), training protocols (modality, intensity, duration), and assessment timing, the random-effects model with the Restricted Maximum Likelihood (REML) estimator was used as the primary analytical approach(Maestrini et al., 2026). Effect sizes were calculated as standardized mean differences (SMD) with 95% confidence intervals (CIs), using Hedges' g correction for small-sample bias. For studies reporting pre-post intervention data within the same group, we calculated the effect size using the correlation coefficient estimated from baseline and post-intervention values(Al-Aayedi et al., 2026; Wahib et al., 2026). When multiple time points or intervention groups were reported, we selected post-intervention data and the highest intensity/dose group for primary analysis, with sensitivity analyses including alternative groups to test the robustness of the findings. Studies were weighted using the inverse variance method, which assigns greater weight to studies with smaller standard errors (larger sample sizes). Forest plots were generated to visualize individual and pooled effect sizes with 95% CIs for CK. Statistical significance was set at a two-tailed $p < 0.05$ for primary analyses.

Heterogeneity Assessment

Heterogeneity was assessed using Cochran's Q test (significance set at $p < 0.10$), τ^2 (between-study variance estimated via the REMLmethod), and the I^2 statistic, which was categorized as low (0–25%), moderate (25–50%), substantial (50–75%), or considerable (75–100%) according

to conventional thresholds. When substantial heterogeneity was present ($I^2 > 50\%$), predefined subgroup analyses(Farzizadeh et al., 2026). Additionally, 95% prediction intervals (PIs) were calculated to estimate the expected range of true effects in future studies, providing a clinically meaningful measure of anticipated variability in individual study effects, particularly for outcomes with substantial or considerable heterogeneity (Huedo-Medina et al., 2006).

Publication Bias and Sensitivity Analysis

Publication bias was assessed using funnel plots, Egger's linear regression test, and Begg's rank correlation test ($p < 0.10$ considered indicative of asymmetry). When asymmetry was detected, we applied the trim-and-fill method to adjust pooled effect estimates (Viechtbauer, 2007). Sensitivity analyses included leave-one-out analysis to evaluate the influence of individual studies and the Classic Fail-Safe N test to determine the number of null studies required to render the observed effect non-significant. A Fail-Safe $N > 5k + 10$ (where k = number of studies) was considered robust. Leave-one-out forest plots were generated using Python (v3.11) with matplotlib (v3.8.0)(Willis & Riley, 2017).

Subgroup Analyses

To explore potential sources of heterogeneity and examine the influence of predefined moderators on effect estimates, subgroup analyses were conducted for CK using mixed-effects models, with random effects within subgroups and fixed effects for between-subgroup comparisons. We examined the following categorical moderators: post-exercise assessment timing (≤ 25 hours vs. > 25 hours), participant age (≤ 20 years vs. > 20 years), and VO_2max levels (≤ 57 vs. > 57 mL/kg/min). We assessed statistical significance of subgroup differences using the Q-between statistic (Qb), with $p < 0.05$ considered indicative of significant differences. Subgroup analyses with fewer than three studies ($k < 3$) were not performed and were instead summarized narratively. All analyses were performed using CMA.

Results

Study selection

A systematic search of PubMed/MEDLINE, Scopus, and Web of Science yielded 363 records, of which 96 duplicates were removed, leaving 267 records for title and abstract screening. Following the exclusion of 194 irrelevant records, 73 reports were sought for full-text retrieval, but 11 could not be obtained, resulting in 62 articles assessed for eligibility. Of these, 33 were excluded due to being non-original studies (n = 4), non-English full texts (n = 2), animal studies (n = 9), lacking an exercise intervention (n = 6), not reporting muscle damage outcomes (n = 8), or not involving soccer players (n = 3). Cohen's kappa was 0.81, indicating substantial agreement between reviewers. Ultimately, 29 single studies contributing 34 independent datasets met the inclusion criteria and were included in the systematic review and meta-analysis (Fig. 1).

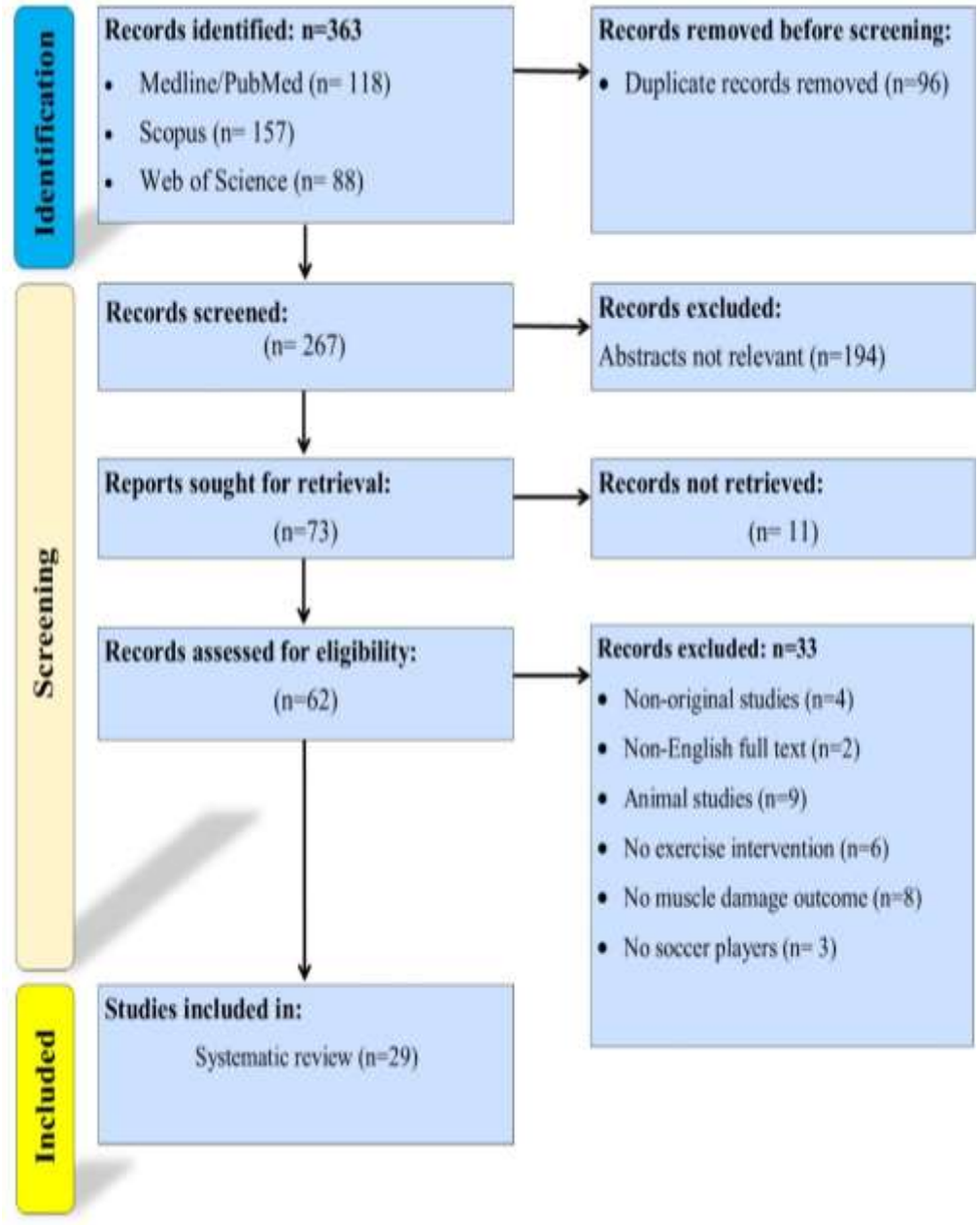

Fig. 1. PRISMA 2020 flow diagram illustrating the study selection process for the systematic review and meta analysis.

Study characterization

A total of 29 studies were included in this review, all of which investigated recovery and muscle damage responses in soccer or soccer-relevant team-sport populations. The majority of studies employed randomised controlled trial (RCT) designs, including parallel-group (Andersson et al., 2008; Bell et al., 2016; Bieuzen et al., 2012; Capó et al., 2014; Deminice et al., 2013; Dos Reis et al., 2014; Simpson et al., 2019), crossover (Abaïdia et al., 2019; Bishop et al., 2002; Bouzid et al., 2018; Fullagar et al., 2016; Goulart et al., 2020; Kritikos et al., 2021; Machado et al., 2010; Poulios et al., 2025; Wang et al., 2026; Abbey & Rankin, 2011; Barnes et al., 2012; Gurton et al., 2025; Hamlin et al., 2012; Pointon & Duffield, 2012; Russell et al., 2017; Horgan et al., 2024), and counterbalanced crossover protocols (Bishop et al., 2002; Draganidis et al., 2013; Russell et al., 2017). A smaller number utilised quasi-experimental pre-post designs (Farkhari Babak et al., 2020) or cross-sectional genetic association designs (Pimenta et al., 2011). Sample sizes were generally small, with most studies recruiting between 8 and 27 participants, and only Wang et al. (2026) exceeding 30 participants (n=36). This limitation is acknowledged across the literature and represents a consistent methodological constraint. The study populations were predominantly male, with only Andersson et al. (2008), Bowtell et al. (2016), and Goulart et al. (2020) focusing exclusively on female players, and Gurton et al. (2025) employing a mixed-sex cohort. Participants ranged from recreational and amateur players (Abaïdia et al., 2019; Bishop et al., 2002; Fullagar et al., 2016; Wang et al., 2026) to semi-professional (Bell et al., 2016) and elite professionals, with competitive levels spanning regional divisions, national leagues, and Premier League academies (Andersson et al., 2008; Bieuzen et al., 2012; Bouzid et al., 2018; Draganidis et al., 2013; Goulart et al., 2020; Pimenta et al., 2011; Russell et al., 2017; Simpson et al., 2019). Age ranged from approximately 17 to 38 years, and where reported, maximal oxygen uptake (VO_2max) values typically fell between 48 and 60 mL/kg/min, reflecting a well-trained to elite aerobic capacity.

Regarding the interventions examined, the studies encompassed a broad spectrum of recovery modalities and exercise protocols designed to induce muscle damage. Nutritional interventions included carbohydrate (Bishop et al., 2002), whey and soy protein (Kritikos et al., 2021), creatine (Deminice et al., 2013; Simpson et al., 2019), caffeine (Machado et al., 2010), quercetin (Abbey & Rankin, 2011), DHA (Capó et al., 2014), and tart cherry supplementation (Bell et al., 2016). Physical recovery strategies comprised cold water immersion (Bouzid et al., 2018; Farkhari Babak et al., 2020; Pointon & Duffield, 2012; Horgan et al., 2024), hot water immersion (Horgan et al., 2024), whole-body cryotherapy (Russell et al., 2017), compression garments (Hamlin et al., 2012), active recovery (Andersson et al., 2008; Abaïdia et al., 2019), low-level laser therapy (Dos Reis et al., 2014), and electrical blood-flow stimulation (Bieuzen et al., 2012). Other interventions included sleep hygiene (Fullagar et al., 2016), protein–carbohydrate recovery drinks (Fabre et al., 2022), and sodium bicarbonate (Gurton et al., 2025). Exercise protocols used to induce muscle damage varied considerably, including the Loughborough Intermittent Shuttle Test (LIST) (Bishop et al., 2002; Bouzid et al., 2018; Farkhari Babak et al., 2020), repeated-sprint protocols (Abbey & Rankin, 2011; Gurton et al., 2025; Russell et al., 2017), small-sided games (Wang et al., 2026; Bowtell et al., 2016), resistance exercise (Draganidis et al., 2013; Machado et al., 2010; Horgan et al., 2024), speed-endurance maintenance training (Kritikos et al., 2021; Poulios et al., 2025), and simulated match-play activities (Bell et al., 2016; Barnes et al., 2012; Fabre et al., 2022; Hamlin et al., 2012; Pointon & Duffield, 2012). In a subset of studies, the exercise stimulus was derived from actual competitive matches (Andersson et al., 2008; Fullagar et al., 2016; Goulart et al., 2020) or regular training sessions (Capó et al., 2014; Simpson et al., 2019), providing greater ecological validity. The intensity and duration of these protocols were carefully controlled in experimental settings, although several studies acknowledged that single acute bouts may not fully represent the cumulative demands of chronic training or congested fixture schedules.

The primary biomarker of muscle damage assessed across the vast majority of studies was serum CK, measured in 26 of the 29 included investigations. Studies that measured CK included Abaïdia et al. (2019), Andersson et al. (2008), Bell et al. (2016), Bieuzen et al. (2012), Bouzid et al. (2018), Deminice et al. (2013), Dos Reis et al. (2014), Draganidis et al. (2013), Fullagar et al. (2016), Kritikos et al. (2021), Machado et al. (2010), Pimenta et al. (2011), Poulios et al. (2025), Wang et al. (2026), Barnes et al. (2012), Bowtell et al. (2016), Fabre et al. (2022), Hamlin et al. (2012), Horgan et al. (2024), and Pointon & Duffield (2012). Notably, three studies did not measure CK: Capó et al. (2014) and Goulart et al. (2020) assessed only inflammatory markers (IL-6, TNF-α, CRP) without muscle damage biomarkers, while Simpson et al. (2019) focused exclusively on airway inflammation (FeNO) and lung function. Additional markers included lactate dehydrogenase (LDH) (Bieuzen et al., 2012; Deminice et al., 2013; Machado et al., 2010; Farkhari Babak et al., 2020), aspartate aminotransferase (AST) (Machado et al., 2010; Farkhari Babak et al., 2020; Pointon & Duffield, 2012), myoglobin (Horgan et al., 2024), α-actin (Pimenta et al., 2011), and muscle-specific microRNA-1 (miR-1) (Fabre et al., 2022). Perceptual measures of muscle damage, such as delayed-onset muscle soreness (DOMS), were frequently employed alongside biochemical markers (Bell et al., 2016; Draganidis et al., 2013; Kritikos et al., 2021; Poulios et al., 2025; Hamlin et al., 2012; Fabre et al., 2022; Russell et al., 2017). Inflammatory responses were commonly evaluated through interleukin-6 (IL-6) (Bell et al., 2016; Bishop et al., 2002; Capó et al., 2014; Pimenta et al., 2011; Abbey & Rankin, 2011; Fabre et al., 2022; Horgan et al., 2024), tumour necrosis factor-alpha (TNF-α) (Bell et al., 2016; Bishop et al., 2002; Capó et al., 2014; Deminice et al., 2013; Fabre et al., 2022; Horgan et al., 2024), C-reactive protein (CRP) (Bell et al., 2016; Deminice et al., 2013; Draganidis et al., 2013; Fullagar et al., 2016; Goulart et al., 2020; Pointon & Duffield, 2012), and interleukin-1 receptor antagonist (IL-1ra) (Fabre et al., 2022; Horgan et al., 2024). Functional performance assessments, including countermovement jump (CMJ),

sprint times, repeated-sprint ability (RSA), isokinetic strength, and agility tests, were routinely used as indirect indicators of recovery from muscle damage. Timing of biomarker measurements varied considerably, with most studies collecting samples immediately post-exercise and at intervals ranging from 1 hour to 72 hours post-intervention. However, a notable limitation was the short follow-up duration in several studies, with some only assessing outcomes up to 1 hour (Bishop et al., 2002; Deminice et al., 2013) or 24 hours (Bieuzen et al., 2012; Dos Reis et al., 2014; Hamlin et al., 2012; Pointon & Duffield, 2012; Wang et al., 2026) post-exercise, potentially missing the peak muscle damage response, which typically occurs between 24 and 48 hours.

In terms of conclusions and methodological limitations, the reviewed studies consistently reported that muscle damage biomarkers, particularly CK, were elevated following all forms of intense or intermittent exercise, with peak responses generally observed between 24 and 72 hours post-exercise (Abaïdia et al., 2019; Andersson et al., 2008; Bell et al., 2016; Bouzid et al., 2018; Draganidis et al., 2013; Fullagar et al., 2016; Kritikos et al., 2021; Poulios et al., 2025; Wang et al., 2026; Barnes et al., 2012; Fabre et al., 2022; Russell et al., 2017). However, the effectiveness of various recovery interventions in reducing CK or accelerating its clearance was highly inconsistent. While some strategies, such as CWI (Bouzid et al., 2018), tart cherry supplementation (Bell et al., 2016), protein–carbohydrate combinations (Fabre et al., 2022), and compression garments (Hamlin et al., 2012), showed promising effects on functional recovery and perceived soreness, their impact on CK levels was frequently non-significant or trivial. Importantly, several studies noted a dissociation between biochemical markers and functional performance (Bouzid et al., 2018; Bell et al., 2016; Pointon & Duffield, 2012), suggesting that reductions in CK do not necessarily translate to improved neuromuscular recovery. Studies that did not measure CK (Capó et al., 2014; Goulart et al., 2020; Simpson et al., 2019) were unable to draw conclusions regarding muscle damage directly. Common limitations across the literature

included small sample sizes , lack of blinding , absence of female participants , single acute exercise bouts rather than chronic training models, and insufficient control of dietary or circadian factors (Abaïdia et al., 2019; Andersson et al., 2008; Bell et al., 2016; Bieuzen et al., 2012; Bishop et al., 2002; Bouzid et al., 2018; Capó et al., 2014; Deminice et al., 2013; Dos Reis et al., 2014; Draganidis et al., 2013; Fullagar et al., 2016; Goulart et al., 2020; Kritikos et al., 2021; Machado et al., 2010; Pimenta et al., 2011; Poulios et al., 2025; Wang et al., 2026; Abbey & Rankin, 2011; Barnes et al., 2012; Bowtell et al., 2016; Fabre et al., 2022; Farkhari Babak et al., 2020; Gurton et al., 2025; Hamlin et al., 2012; Horgan et al., 2024; Pointon & Duffield, 2012; Russell et al., 2017; Simpson et al., 2019). These methodological constraints highlight the need for larger, well-controlled trials with extended follow-up periods to better elucidate the role of muscle damage markers in recovery and to establish evidence-based guidelines for soccer practitioners.

Meta-analysis findings

The meta-analysis of 34 datasets from 29 studies demonstrated that exercise training significantly affected serum CK concentrations in soccer players (***Fig. 2***). Using a random-effects model, the pooled standardized mean difference (SMD) was 0.553 (95% CI: 0.249 to 0.856; P = 0.001), indicating a moderate-to-large positive effect. However, substantial between-study heterogeneity was detected (τ^2 = 0.558, I^2 = 71.069%), and the 95% prediction interval, ranging from −1.001 to 2.106, suggested that the true effect may vary considerably across different populations and training contexts.

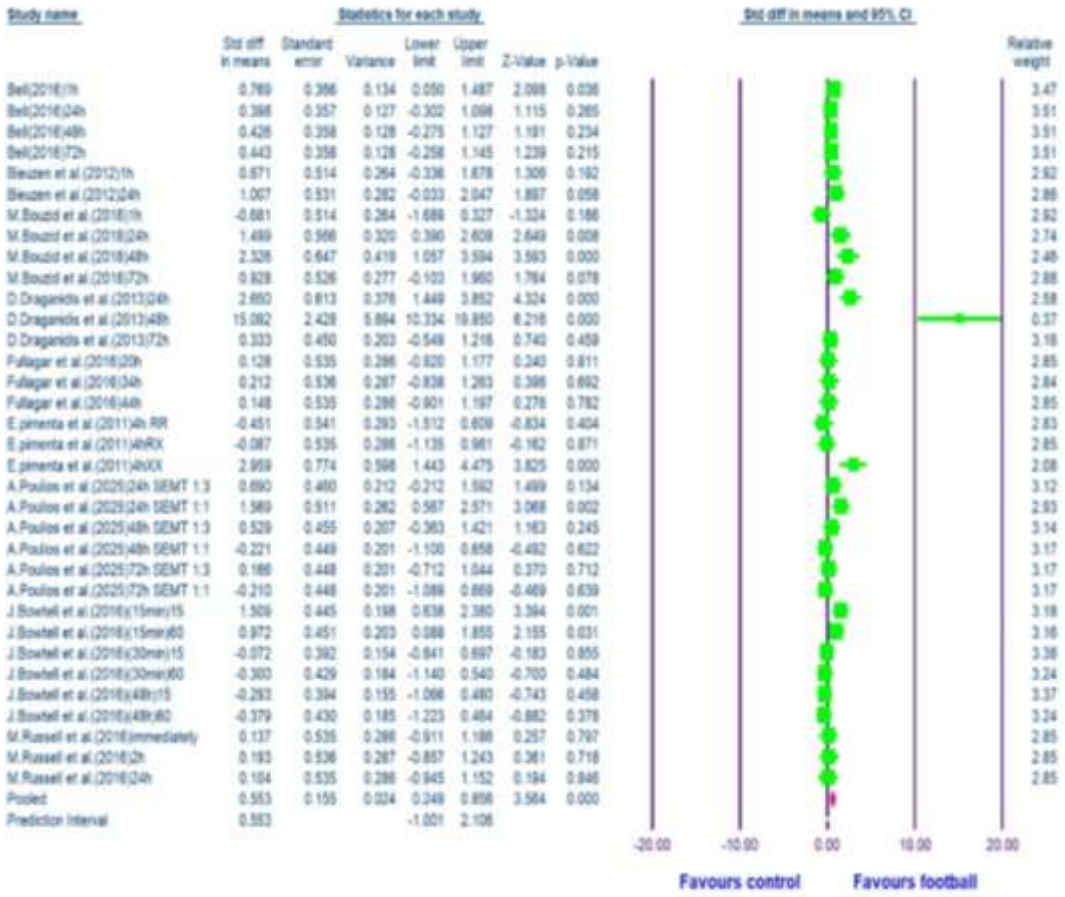

Fig. 2. Forest plot of the effect of exercise training on CK levels in soccer players. Standardized mean differences (SMD) with 95% confidence intervals (CIs) are presented for each of the 34 datasets (from 29 studies) and for the pooled estimate.

Publication Bias Assessment (Funnel Plot, Egger's Test, and Trim-and-Fill)

Publication bias was assessed through multiple complementary methods (***Fig. 3***). Both Egger's regression test (P = 0.01) and Begg and Mazumdar rank correlation test (P = 0.02) indicated significant evidence of small-study effects or funnel plot asymmetry. In addition, the classic fail-safe N calculation indicated that 374 null studies would

be required to render the observed effect non-significant, further supporting the robustness of the findings. To adjust for potential publication bias, we performed a trim-and-fill procedure, which imputed four missing studies (Fig. 4); the adjusted SMD was 0.70, compared with the observed estimate of 0.55, confirming that the correction did not alter the overall direction of the effect.

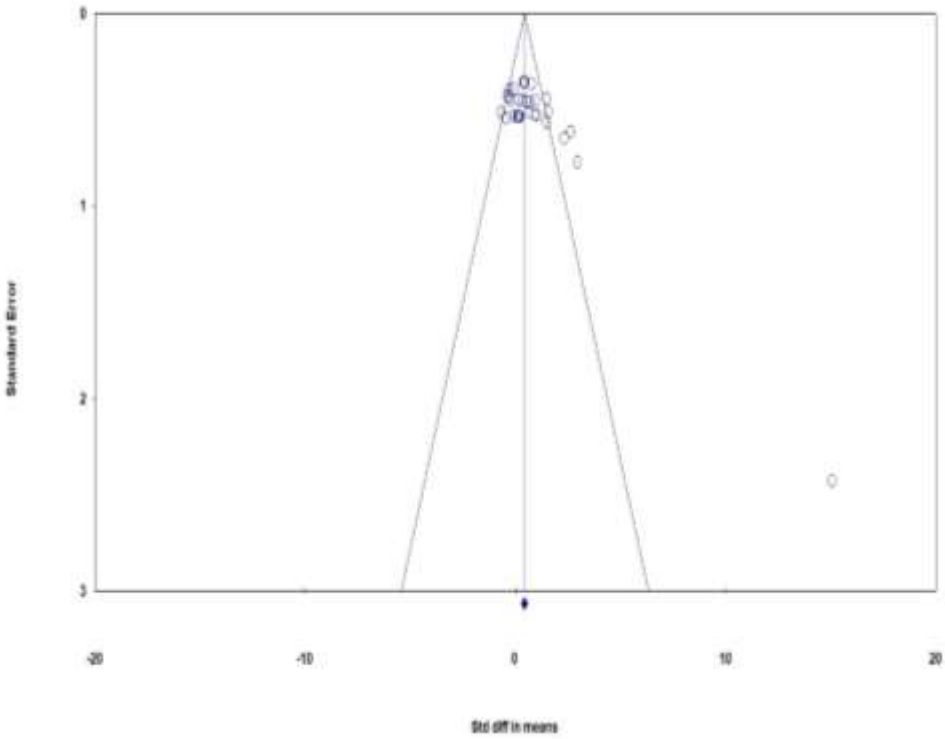

Fig 3. Funnel plot for assessment of publication bias among the 34 studies examining the effect of exercise training on CK levels in soccer players. The standard error of the standardized mean difference (SMD) is plotted against the SMD on the horizontal axis.

Sensitivity Analysis (Leave-One-Out)

A leave-one-out sensitivity analysis was conducted to evaluate the influence of individual studies on the pooled estimate (***Fig. 4***).

Systematically excluding each study produced effect sizes that consistently retained both the direction and statistical significance of the primary finding, confirming the stability and reliability of the meta-analytic conclusions. No single study disproportionately influenced the pooled effect size, indicating that no particular outlier drove the results.

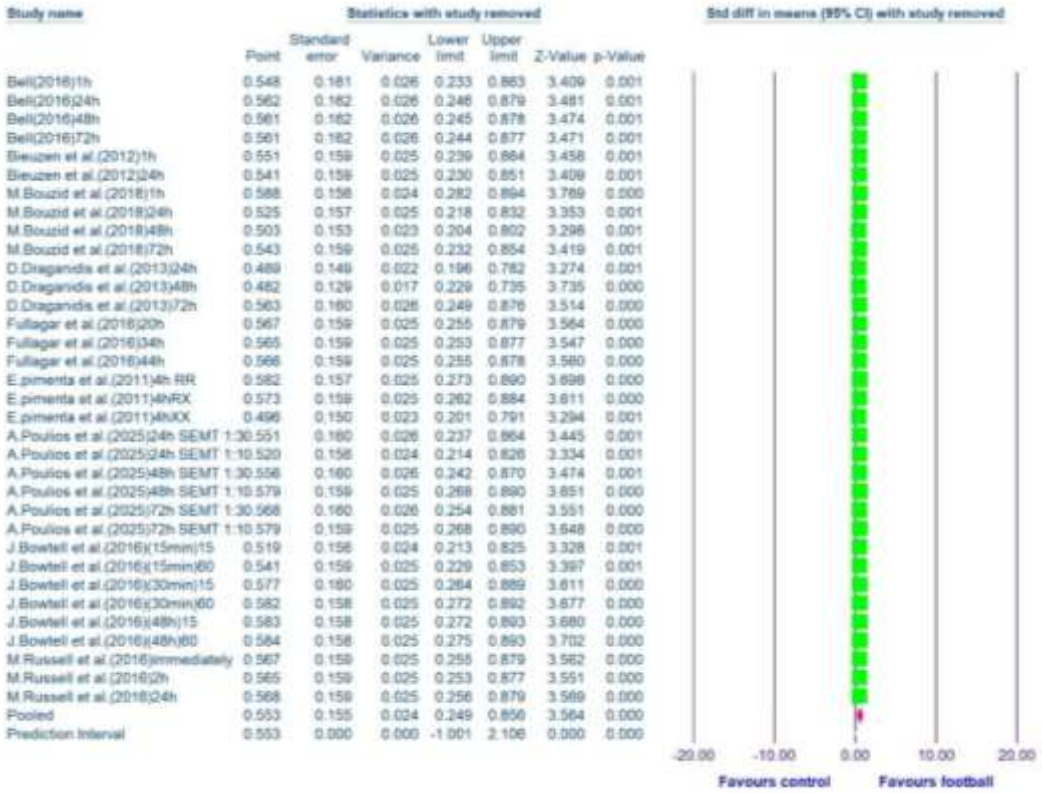

Fig. 4. Leave-one-out sensitivity analysis for the meta-analysis of exercise training on CK levels in soccer players. The plot displays the pooled standardized mean difference (SMD) and corresponding 95% confidence intervals (CIs) after systematically omitting each study.

Subgroup Analyses

To explore potential sources of the substantial between-study heterogeneity and to examine the influence of predefined moderators

on the pooled effect estimates, subgroup analyses were conducted for CK responses using mixed-effects models, as shown in **Table 1.**

Table 1. Subgroup analysis for estimated effects of exercise training on serum creatine kinase (CK) concentrations in soccer players: summary of standardized mean differences, heterogeneity statistics, and moderator analyses.

Moderator	Subgroup	k	SMD	95% CI	p-value (within group)	I^2 (%)	p-value (subgroup differences)
Time Post-Exercise (hours)	≤ 25	19	0.65	0.27, 1.04	0.001	66.6	0.614
	> 25	14	0.47	−0.06, 0.99	0.082	77.0	
Age (years)	≤ 20	10	1.26	0.28, 2.24	0.012	86.1	0.172
	> 20	21	0.42	0.13, 0.70	0.004	55.4	
VO_2max (mL/kg/min)	≤ 57	10	0.44	0.16, 0.72	0.002	15.7	0.099
	> 57	5	2.42	0.61, 4.24	0.009	90.7	

Subgroup analysis by post-exercise assessment timing

To investigate whether assessment timing moderates the response of CK levels, a subgroup analysis was performed using a mixed-effects model, dividing the studies into two groups: short-term assessment (≤ 25 hours) and long-term assessment (> 25 hours). The results, shown in the forest plot (***Fig. 5***), indicated that while both subgroups showed a trend toward increased CK levels, the effect size differed between them. For the short-term subgroup (k = 19), exercise training significantly increased CK levels (SMD = 0.65, 95% CI [0.27, 1.04]; p = 0.001), despite substantial heterogeneity (I^2 = 66.6%). In the long-term

subgroup (k = 14), the effect was not statistically significant (SMD = 0.47, 95% CI [−0.06, 0.99]; p = 0.082), with high heterogeneity (I^2 = 77.0%). However, the formal test for subgroup differences revealed no statistically significant variation between the two timing groups (Q = 0.98, p = 0.614), suggesting that the time of measurement (within or after 25 hours) did not significantly moderate the overall effect of exercise training on CK responses in soccer players.

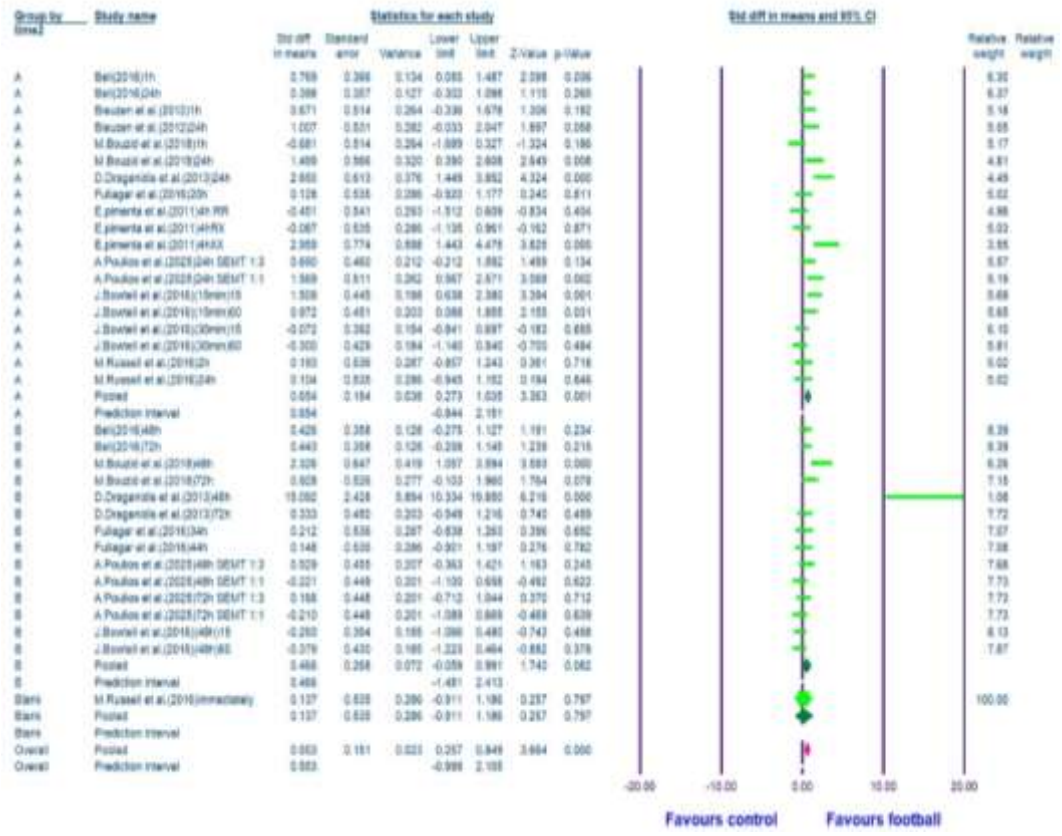

Fig 5. Subgroup forest plot of the effects of exercise training on Creatine Kinase (CK) levels categorized by post-exercise assessment timing.

Subgroup analysis by participant age

To determine whether participant age moderates CK responses, a subgroup analysis was conducted using a mixed-effects model, categorizing studies into two groups: younger players (≤ 20 years) and older players (> 20 years). As illustrated in the forest plot (***Fig. 6***), exercise training was associated with a significant increase in CK levels in both age subgroups. Specifically, for the younger subgroup (k = 10), the effect size was substantially higher (SMD = 1.26, 95% CI [0.28, 2.24]; p = 0.012), although heterogeneity was very high (I^2 = 86.1%). In the older subgroup (k = 21), a more moderate but still significant increase was reported (SMD = 0.42, 95% CI [0.13, 0.70]; p = 0.004) with moderate heterogeneity (I^2 = 55.4%). Despite the higher observed SMD in the younger group, the formal test for subgroup differences revealed no statistically significant moderation by age (Q = 3.53, p = 0.172), suggesting that while the magnitude of the CK response may vary, age did not significantly alter the direction or the overall statistical pattern of the training effect on CK levels in soccer players.

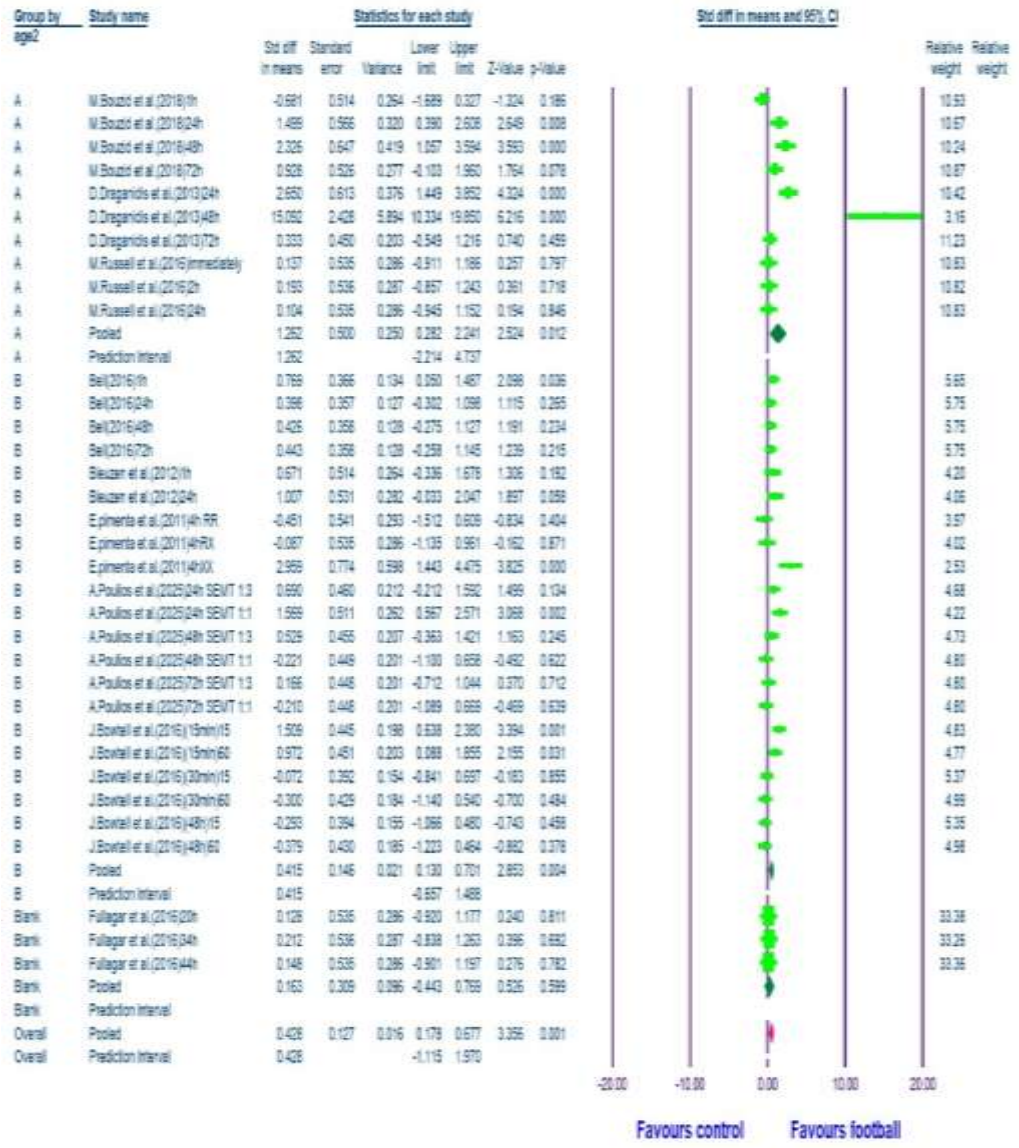

Fig. 6. Forest plot of the subgroup analysis for creatine kinase (CK) response to exercise training, stratified by participant age (<= 20 years vs. > 20 years). Effect sizes are presented as Standardized Mean Differences (SMD) with 95% Confidence Intervals (CI).

Subgroup analysis by VO_2max

To assess whether VO_2max influences the response of CK to exercise training, we performed a subgroup analysis using a mixed-effects model. Studies were divided into two groups: those with a mean VO_2max less than or equal to 57 (Subgroup A, k = 10) and those with a mean VO_2max greater than 57 (Subgroup B, k = 5). The results, as depicted in the forest plot (***Fig. 7***), indicated that exercise training led to a significant increase in CK levels in both subgroups. For Subgroup A (VO_2max ≤ 57), a moderate effect size was observed (SMD = 0.44, 95% CI [0.16, 0.72]; p = 0.002) with low heterogeneity (I^2 = 15.7%). In contrast, Subgroup B (VO_2max > 57) showed a substantially larger, significant effect size (SMD = 2.42, 95% CI [0.61, 4.24]; p = 0.009), but with very high heterogeneity (I^2 = 90.7%). The formal test for subgroup differences indicated a trend toward significance (Q = 4.63, p = 0.099), suggesting that players with higher VO_2max might show a more pronounced increase in CK levels following exercise training than those with lower VO_2max. However, this difference did not reach the conventional statistical threshold.

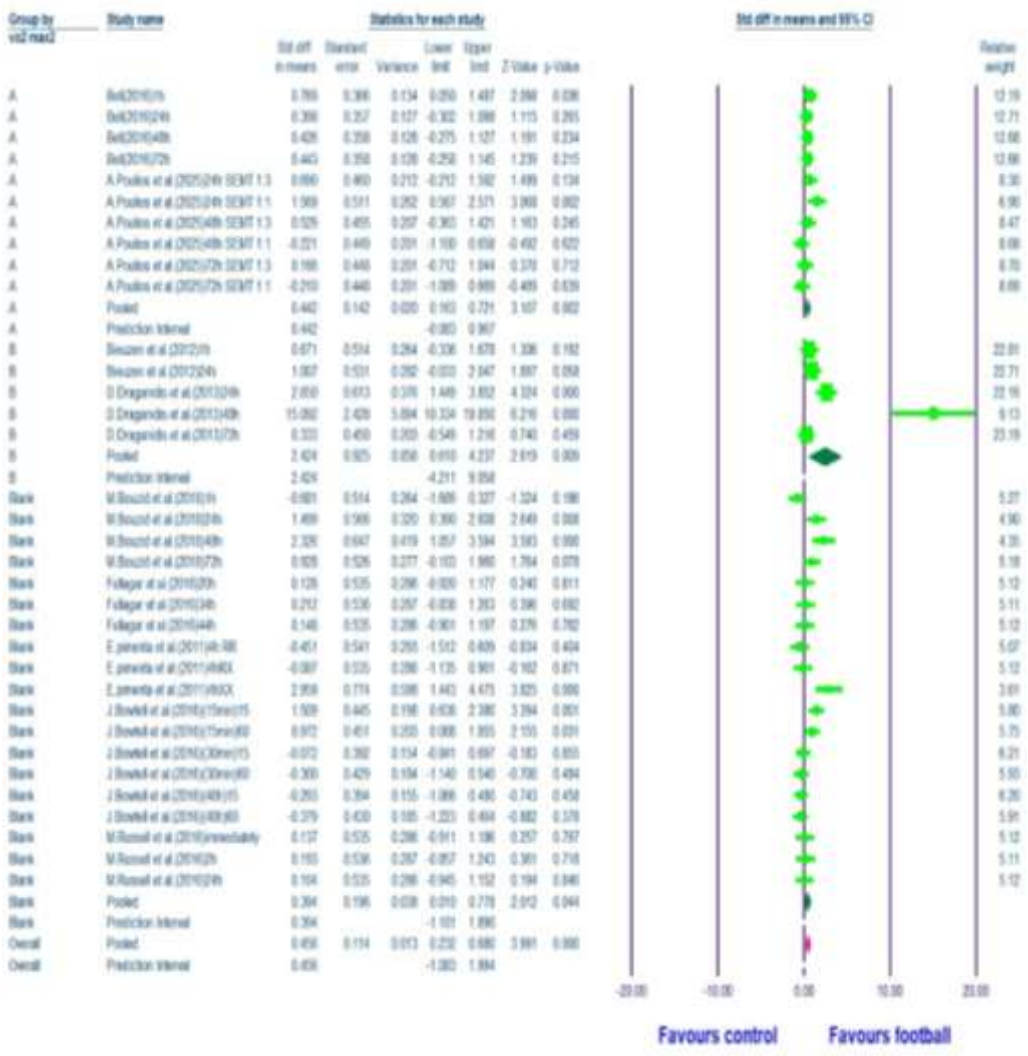

Fig. 7. Subgroup forest plot illustrating the effect of exercise training on CK levels based on VO2 max.

Discussion

Main findings

Overall effect and heterogeneity

The present meta-analysis synthesized data from 29 studies contributing 34 independent datasets demonstrated that exercise training significantly elevates serum CK concentrations in soccer players, with a pooled standardized mean difference (SMD) of 0.553 (95% CI: 0.249 to 0.856; P = 0.001). This moderate-to-large positive effect confirms our first hypothesis that soccer-specific exercise induces significant CK efflux, reflecting exercise-induced muscle membrane disruption. However, substantial between-study heterogeneity was detected ($\tau^2 = 0.558$, $I^2 = 71.069\%$), and the 95% prediction interval, ranging from −1.001 to 2.106, suggested that the true effect may vary considerably across different populations and training contexts. This level of heterogeneity, while expected given the diversity of training protocols and participant characteristics across studies, underscores the need for moderator analyses to identify sources of variation.

The substantial heterogeneity observed in the pooled analysis ($I^2 = 71.07\%$) is not merely a statistical nuisance but reflects fundamental diversity in the exercise stimuli used across studies. The included studies employed markedly different protocols, including the Loughborough Intermittent Shuttle Test, repeated-sprint protocols, small-sided games, resistance exercise, speed-endurance maintenance training, and simulated match-play activities. These protocols differ substantially in their mechanical loading patterns, eccentric component, total work volume, and metabolic demand, all of which are known to influence the magnitude and time course of CK release. For example, protocols with a high eccentric component (repeated-sprint and resistance exercise) would be expected to induce greater sarcolemma trauma than aerobic-based or small-sided game protocols. Similarly, the duration and intensity of exercise varied considerably, and some studies

used single acute bouts while others assessed responses to regular training or actual competitive matches. This methodological diversity means that the pooled SMD of 0.553 should be interpreted as an average effect across heterogeneous exercise stimuli rather than a precise estimate applicable to any single protocol. The wide 95% prediction interval (−1.001 to 2.106) further indicates that the true effect in a future study could differ substantially from the pooled estimate, depending on the specific exercise protocol employed. Consequently, the subgroup analyses by timing, age, and VO_2max should be viewed as exploratory attempts to explain part of this heterogeneity, and the residual unexplained variance highlights the need for standardized exercise protocols in future research to enable more precise comparisons.

Publication bias and sensitivity analysis

Publication bias assessment revealed significant evidence of small-study effects, with both Egger's regression test (P = 0.01) and Begg and Mazumdar rank correlation test (P = 0.02) indicating funnel plot asymmetry. Despite this, the classic fail-safe N calculation indicated that 374 null studies would be required to render the observed effect non-significant, supporting the robustness of the findings. The trim-and-fill procedure imputed four missing studies, with the adjusted SMD (0.70) confirming that the correction did not alter the overall direction or significance of the effect. Leave-one-out sensitivity analysis further confirmed the stability of the results, as excluding each study produced effect sizes that consistently retained both the direction and statistical significance of the primary finding. These complementary approaches collectively indicate that while publication bias may be present, the observed effect is unlikely to be an artefact of selective reporting.

Moderating effect of assessment timing

Subgroup analyses examined the moderating roles of three key factors: assessment timing, participant age, and VO_2max. For post-exercise assessment timing, the short-term subgroup (≤ 25 hours; k = 19) demonstrated a significant increase in CK levels (SMD = 0.65, 95% CI

[0.27, 1.04]; P = 0.001) with substantial heterogeneity (I^2 = 66.6%), whereas the long-term subgroup (> 25 hours; k = 14) showed a non-significant effect (SMD = 0.47, 95% CI [−0.06, 0.99]; P = 0.082) with high heterogeneity (I^2 = 77.0%). However, the formal test for subgroup differences revealed no statistically significant variation between the two timing groups (Q = 0.98, P = 0.614), suggesting that measurement timing did not significantly moderate the overall CK response. This finding contrasts with our hypothesis that acute measurements would capture larger CK elevations and may reflect that CK peaks between 24–48 hours post-exercise, potentially placing some "short-term" studies outside the true peak window.

Moderating effect of age

For participant age, both subgroups demonstrated significant increases in CK levels. The younger subgroup (≤ 20 years; k = 10) exhibited a substantially larger effect size (SMD = 1.26, 95% CI [0.28, 2.24]; P = 0.012), although with very high heterogeneity (I^2 = 86.1%). The older subgroup (> 20 years; k = 21) showed a more moderate but still significant effect (SMD = 0.42, 95% CI [0.13, 0.70]; P = 0.004) with moderate heterogeneity (I^2 = 55.4%). Despite the higher observed SMD in the younger group, the test for subgroup differences was not statistically significant (Q = 3.53, P = 0.172), indicating that age did not significantly alter the direction or overall statistical pattern of the training effect on CK levels. However, the magnitude of response was clinically larger in younger players. This pattern may reflect differences in training status, muscle mass, and regenerative capacity between age groups, though the high heterogeneity within the younger subgroup warrants cautious interpretation.

Moderating effect of VO_2max

For VO_2max, the subgroup with lower cardiorespiratory fitness (≤ 57 mL/kg/min; k = 10) showed a moderate effect size (SMD = 0.44, 95% CI [0.16, 0.72]; P = 0.002) with low heterogeneity (I^2 = 15.7%), while the higher VO_2max subgroup (> 57 mL/kg/min; k = 5) demonstrated a

substantially larger effect size (SMD = 2.42, 95% CI [0.61, 4.24]; P = 0.009) but with very high heterogeneity (I^2 = 90.7%). The test for subgroup differences showed a trend toward significance (Q = 4.63, P = 0.099), suggesting that players with higher VO_2max may exhibit more pronounced CK increases following exercise training than those with lower VO_2max(Nosrati Hashi et al., 2022; Piri et al., 2022). However, this difference did not reach the conventional statistical threshold. This trend aligns with the hypothesis that fitter players may sustain higher training intensities, thereby inducing greater muscle damage, but the limited number of studies in this subgroup (k = 5) and the extreme heterogeneity observed highlight the need for further research with larger samples.

Conceptual distinction: statistical association, biomarker response, physiological muscle damage, and clinical impairment

A critical interpretive consideration in this meta-analysis is the distinction between four conceptually distinct constructs: (1) statistical association, (2) biomarker response, (3) physiological muscle damage, and (4) clinically meaningful impairment. The pooled SMD of 0.553 represents a statistically significant association between soccer-specific exercise and increased serum CK concentrations. This association reflects a biomarker response—specifically, the release of CK from damaged myofibers into the circulation following sarcolemma trauma and increased membrane permeability. However, the biomarker response is not equivalent to physiological muscle damage, which encompasses structural disruption of sarcomeres, cytoskeletal disorganization, and impaired excitation-contraction coupling. Furthermore, neither the biomarker response nor physiological muscle damage necessarily translates into clinically meaningful impairment, which would manifest as persistent strength loss, restricted range of motion, impaired functional performance, or delayed return to sport.

This distinction has important implications for the interpretation of our findings. First, the significant pooled effect indicates that soccer-specific exercise reliably induces CK efflux, but it does not establish

that this efflux produces clinically relevant muscle damage in all players. Second, the substantial heterogeneity observed (I^2 = 71.07%) suggests that the magnitude of the biomarker response varies considerably across individuals and protocols, and this variability may or may not correspond to variability in clinical outcomes. Third, several studies included in this review reported a dissociation between CK levels and functional recovery markers such as countermovement jump, sprint performance, and perceived soreness, indicating that reductions in CK do not necessarily translate into improved neuromuscular recovery. Fourth, the wide prediction interval (−1.001 to 2.106) indicates that in some future study populations, the true effect could be negligible or even negative, underscoring the need for caution in generalizing the pooled estimate to clinical decision-making.

Therefore, while CK remains a useful and practical biomarker for monitoring training load and recovery in soccer, it should be interpreted alongside functional and perceptual measures rather than as a standalone indicator of clinically meaningful muscle damage. Future research should prioritize the concurrent assessment of CK, functional performance, and patient-reported outcomes to establish thresholds that are clinically meaningful, not merely statistically significant.

Compared with literature reviews

Our finding that exercise training elicits a moderate-to-large increase in serum CK concentrations (SMD = 0.553) is consistent with the systematic review by Saidi et al. (2021), which reported moderate to very large increases in CK (effect sizes ranging from 0.94 to 6.80) following 4 to 18 weeks of soccer-specific training in elite male players. However, while Saidi et al. provided a qualitative synthesis of hormonal and inflammatory responses, their review did not quantitatively pool effect sizes or systematically examine moderating factors such as age, assessment timing, or VO_2max(Saidi et al., 2021). Our meta-analysis extends this evidence by demonstrating that the pooled CK response is significant across 34 studies, but is characterized by substantial heterogeneity (I^2 = 71.07%), which is partially explained by the

moderators examined in our subgroup analyses. Regarding age, our subgroup analysis showed a larger effect size in younger players (≤ 20 years; SMD = 1.26) than in older players (> 20 years; SMD = 0.42). This pattern is partially supported by Ramos-Silva et al. (2023), who reported that CK elevation following a competitive match was more pronounced in U-13 players (skeletal age explaining 56% of CK variance) compared to U-15 players, with younger athletes requiring 24 h to restore CK levels versus 48 h in older adolescents(Ramos-Silva et al., 2023). However, our findings appear to contrast with the meta-analysis by Fernandes et al. (2023), who reported that adults exhibited substantially larger CK responses than youths (ES = −1.98). This discrepancy likely reflects differences in study populations and exercise modalities, our meta-analysis focused exclusively on soccer players undergoing sport-specific training. In contrast, Fernandes et al. included various exercise protocols across different athletic populations. Nevertheless, both studies underscore the importance of age as a moderating factor, though the direction of its effect may be context-dependent, influenced by training status, muscle mass, and the specific demands of the exercise modality(Fernandes et al., 2023). Regarding assessment timing, our subgroup analysis showed that CK elevations were significant when measured within 25 hours post-exercise (SMD = 0.65, P = 0.001) but not significant beyond 25 hours (SMD = 0.47, P = 0.082). However, the between-subgroup difference was not statistically significant (Q = 0.98, P = 0.614). This trend aligns with the findings of Ramos-Silva et al. (2023), who observed that CK peaked at 0–24 h post-match and returned toward baseline by 48–72 h, depending on age category(Ramos-Silva et al., 2023). Similarly, Schwiete et al. (2025) demonstrated that CK peaked at 96 hours following high-velocity eccentric exercise, highlighting that the optimal measurement window may vary depending on the nature of the exercise stimulus(Schwiete et al., 2025). The lack of statistical significance in our subgroup comparison may reflect the wide variation in measurement protocols across studies, reinforcing the need for standardized assessment timing in future research to capture the true

peak of muscle damage responses. Our finding that VO_2max demonstrated the strongest moderating trend (Q = 4.63, P = 0.099), with players in the higher VO_2max subgroup (> 57 mL/kg/min; k = 5) exhibiting a substantially larger effect size (SMD = 2.42) compared to the lower VO_2max subgroup (≤ 57 mL/kg/min; k = 10; SMD = 0.44), is supported by several lines of evidence. Silva (2022) reported that VO_2max values in professional soccer players typically range from 54 to 64 mL/kg/min and are associated with superior match performance and fatigue resistance(Silva, 2022). Deliceoğlu et al. (2024) further demonstrated that respiratory muscle strength, particularly maximal expiratory pressure (MEP), explains 89.9% of the variance in VO_2max, underscoring the importance of aerobic fitness as a key physiological determinant(Deliceoğlu et al., 2024). Schwiete et al. (2025) provided direct experimental evidence that higher oxygen uptake (ΔVO_2%) during eccentric exercise is associated with greater force decrements, while enhanced oxygen uptake recovery during rest intervals predicts lower CK elevations (p = 0.04). These findings collectively suggest that players with higher VO_2max may sustain greater training intensities, resulting in more pronounced muscle damage, though the high heterogeneity observed in this subgroup (I^2 = 90.7%) and the limited number of studies (k = 5) warrant cautious interpretation(Schwiete et al., 2025).

Practical applications

From a practical standpoint, the findings offer several evidence-based recommendations for practitioners. First, athletes with higher aerobic fitness may require more attentive recovery monitoring because they can sustain higher training intensities. Coaches should individualize training load prescription based on players' VO_2max profiles. Second, the age-related differences underscore the need for age-specific training and recovery protocols, particularly for younger players who may experience more pronounced acute muscle damage relative to their biological maturity. Third, the trend toward larger CK effects when measured within 25 hours post-exercise highlights the importance of

standardizing blood sampling protocols in both research and applied settings to ensure accurate and comparable assessments.

Limitations and future directions

This study has several limitations that should be acknowledged. The substantial heterogeneity (I^2 = 71.07%) indicates considerable variability in training protocols, participant characteristics, and assessment methods. The limited number of studies in the higher VO_2max subgroup (k = 5) and the very high heterogeneity within this subgroup (I^2 = 90.7%) warrant cautious interpretation of the VO_2max findings. The significant publication bias detected (Egger's test, P = 0.01) suggests that smaller studies with null or negative findings may be underrepresented. However, the trim-and-fill procedure confirmed the robustness of the overall effect (adjusted SMD = 0.70). Excluding non-English publications and focusing exclusively on soccer players may limit generalizability to other athletic populations. Future research should prioritize large-scale, well-controlled studies with standardized assessment protocols to further elucidate the moderating effects of age, measurement timing, and VO_2max on CK responses. Specifically, studies with larger samples in the higher VO_2max subgroup are needed to confirm the observed trend and investigate the mechanisms by which aerobic fitness modulates muscle damage responses. Additionally, the interplay between genetic factors (ACTN3 genotype), training history, and nutritional status in modulating CK responses warrants investigation, as these factors may explain additional sources of heterogeneity. Longitudinal studies tracking CK responses across a full competitive season would provide valuable insights into the time course of muscle damage and recovery, as well as the influence of match congestion and training periodization on these responses. Such evidence would further refine individualized monitoring strategies and enhance the practical utility of CK as a recovery biomarker in soccer populations.

Conclusion

This systematic review and meta-analysis pooled 29 studies contributing 34 independent datasets to synthesize creatine kinase (CK) responses to soccer-specific exercise and to examine age, assessment timing, and VO_2max as candidate moderators. While previous reviews have addressed hematological and inflammatory responses in soccer players (Saidi et al., 2021) and age-related differences in EIMD across athletic populations (Fernandes et al., 2023), no prior quantitative synthesis has focused specifically on soccer players while integrating these three moderators within a single framework.

Soccer-specific exercise reliably elevated serum CK (SMD = 0.553, 95% CI: 0.249–0.856; P = 0.001), confirming CK efflux as a predictable physiological response to the mechanical demands of soccer. However, CK elevation reflects a biomarker of sarcolemma disruption and increased membrane permeability, and should not be equated with clinically meaningful muscle damage or functional impairment. Statistically significant CK increases do not necessarily translate into persistent strength loss, restricted range of motion, or delayed return to sport, and several included studies reported a dissociation between CK concentrations and functional recovery markers.

Among the candidate moderators, VO_2max showed the strongest trend toward significance (Q = 4.63, P = 0.099), with higher-VO_2max players (>57 mL/kg/min; SMD = 2.42) exhibiting larger CK elevations than lower-VO_2max players (≤57 mL/kg/min; SMD = 0.44). Younger players (≤20 years; SMD = 1.26) also showed larger effects than older players (>20 years; SMD = 0.42), and CK elevations were significant within 25 hours post-exercise (SMD = 0.65) but not beyond (SMD = 0.47). None of these between-subgroup differences reached statistical significance (P = 0.099–0.614), and the VO_2max finding was based on few datasets (k = 5) with extreme heterogeneity (I^2 = 90.7%); all moderator results should therefore be regarded as exploratory and hypothesis-generating.

These findings must be interpreted in light of the substantial heterogeneity (I^2 = 71.07%) and methodological diversity of the

included evidence. The 29 studies varied widely in exercise protocols, participant characteristics, assessment timing, and co-interventions, which limits the precision of the pooled estimate and the generalizability of subgroup findings. The wide prediction interval (−1.001 to 2.106) indicates that the true effect in a future study could differ substantially from the pooled estimate. Future research should prioritize standardized protocols, uniform assessment timing, and larger samples—particularly in the higher-VO_2max subgroup—before CK thresholds can guide individualized training load prescription, recovery monitoring, and injury prevention in soccer.

Declaration

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Ethical Approval

As this study assessed previously published data, ethical approval and informed consent were not required.

Data availability

The data used to support the findings of this study are included within the article.

Conflicts of interest

The authors declare that there is no conflict of interest.

CRediT author statement

Murtadha Mohammed Radhi Al-Jazaieri: Investigation, Literature search, Data extraction, writing – Original draft preparation; **Ameneh**

PourRahim Ghouroghchi: Investigation, Methodology, Validation, Visualization, Writing – Review & editing; **Reza Farzizadeh:** Project administration, Conceptualization, Data curation, Validation, Protocol registration, Formal analysis, Original draft preparation, review & editing. All authors have read and approved the final manuscript.

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