JURNAL LOCUS: Penelitian & Pengabdian
Volume 5, Number 11, November 2026, pp 10658-10675
E-ISSN 2829-7334
DOI: 10.58344/locus.v5i11.6589

Creatine Kinase Response to Physical Exercise: A PRISMA-Based Systematic Review of Kinetics, Determinant Factors, Adaptation, and Interpretive Implications

Nur Diani Putri*, Irfannuddin, Eka Febri Zulissetiana
Universitas Sriwijaya, Indonesia
Email : Dianiputri@umrah.ac.id*

Keywords:
Creatine Kinase; Exercise-Induced Muscle Damage; Repeated Bout Effect; PRISMA; Muscle Recovery.

This is an open access article under the CC BY-SA license.

Copyright © 2026 by Author. Published by Riviera Publishing

ABSTRACT

Creatine kinase (CK) is widely used to assess muscle responses to exercise; however, elevated CK activity does not directly reflect the extent of structural muscle damage. This review synthesizes evidence on CK kinetics, exercise stimulus characteristics, interindividual variability, the repeated-bout effect (RBE), recovery, and the limitations of CK interpretation. A systematic review with narrative synthesis was conducted in accordance with the PRISMA 2020 guidelines. PubMed, ScienceDirect, and SpringerLink were searched for publications from January 2021 through 2026. Of the 1,723 records identified, 1,488 were screened after duplicate removal, 72 reports underwent full-text assessment, and 17 studies were included in the narrative synthesis. CK activity generally increases after a delay following unaccustomed or mechanically demanding exercise, with elevations commonly observed within 24–72 hours and persisting for up to 96 hours in some exercise protocols. The magnitude of the CK response depends on muscle contraction type, exercise volume and intensity, muscle length during loading, training status, individual characteristics, and the timing of sample collection. Repeated exposure to similar exercise stimuli tends to attenuate CK responses, whereas a single CK measurement has limited predictive value for muscle injury or performance recovery. Therefore, CK is most informative when interpreted longitudinally alongside neuromuscular function, delayed-onset muscle soreness, training load, clinical symptoms, and complementary biomarkers.

INTRODUCTION

Physical exercise triggers mechanical, metabolic, inflammatory, and neuromuscular responses that contribute to the adaptation process. Under intense, unaccustomed, or eccentric-dominant exercise stimuli, alterations in sarcomere structure, cytoskeletal integrity, calcium homeostasis, and sarcolemmal permeability may be accompanied by a transient decline in muscle function and an increase in circulating biomarkers. These responses are commonly discussed within the framework of exercise-induced muscle damage (EIMD), which is best assessed through a combination of muscle strength loss, delayed-onset muscle soreness (DOMS), reduced range of motion, swelling, and biochemical markers. Within this framework, creatine kinase (CK) remains relevant because it is readily measurable and sensitive to

alterations in muscle membrane integrity, although its specificity for the extent of structural muscle damage is limited (Furrer et al., 2023; Özdemir & Demir, 2026). The molecular mechanisms underlying exercise responses and training adaptations in skeletal muscle provide a broader physiological context for interpreting these biomarkers (Furrer & Handschin, 2024).

Physiologically, CK catalyzes the reversible transfer of a phosphoryl group between phosphocreatine and adenosine diphosphate (ADP), facilitating the regeneration of adenosine triphosphate (ATP) in tissues with high energy demands. The CK-MM isoenzyme predominates in skeletal muscle, whereas CK-MB is more abundant in the myocardium but is also present in skeletal muscle. Strenuous physical activity can increase circulating total CK and CK-MB activities without necessarily indicating myocardial injury. Therefore, suspected cardiac involvement should be evaluated in conjunction with clinical symptoms, electrocardiographic findings, and, particularly, cardiac troponin measurements, which provide greater specificity for myocardial injury (Costache et al., 2022; Özdemir & Demir, 2026).

A major challenge in interpreting CK measurements is their substantial biological and analytical variability. Baseline CK activity and postexercise responses are influenced by muscle mass, sex, demographic characteristics, training status, previous physical activity, genetic factors, laboratory analytical methods, and sampling time. Recent reviews examining postexercise CK variability emphasize that a single absolute CK value cannot reliably characterize the extent of muscle damage or physiological disturbance. Similarly, investigations of population-based reference intervals highlight the importance of accounting for demographic differences and laboratory-specific reference ranges. In athlete monitoring, changes relative to an individual's baseline and longitudinal CK patterns are generally more informative than isolated comparisons with reference intervals derived from the general population (Aleksovska et al., 2025; Biljak et al., 2025; Tamujo et al., 2024).

CK kinetics exhibit delayed responses and are highly dependent on exercise protocols. Following eccentric exercise, circulating CK activity may begin to increase several hours after exercise and reach peak levels during the subsequent recovery period. A meta-analysis examining lower-limb eccentric exercise demonstrated that CK activity may remain elevated for up to 96 hours, whereas sprint training produces recovery patterns influenced by resistance modality, mechanical loading, and neuromuscular demands. Consequently, interpreting CK measurements without considering the timing of blood sampling may lead to inaccurate conclusions regarding the magnitude and severity of exercise-induced physiological disturbances (Chalchat et al., 2022; Liakou et al., 2024).

Muscle contraction characteristics and exercise dose are important determinants of CK responses. Eccentric contractions impose substantial mechanical loading while active muscle fibers lengthen, whereas resistance exercise performed at longer muscle lengths may increase mechanical demands and prolong neuromuscular recovery. High-intensity interval training (HIIT), sprint exercise, multi-joint movements, and high-volume or fatiguing resistance exercise sessions may also elevate circulating CK activity, particularly when the exercise stimulus is unfamiliar. Therefore, the CK response is better understood as the result of interactions among force production, muscle length during loading, total exercise volume, intensity, proximity to muscular failure, the muscle groups involved, and previous exposure to

similar exercise stimuli (Furrer et al., 2023; Leite et al., 2023; McMahon & Onambele-Pearson, 2024).

Repeated exposure to a similar exercise stimulus produces the repeated-bout effect (RBE), characterized by an attenuation of EIMD-related symptoms and functional impairments during subsequent exercise bouts. A meta-analysis of multi-joint exercise demonstrated reductions in CK activity and DOMS following a second exercise bout, while mechanistic investigations suggest that adaptations associated with the RBE involve alterations in membrane properties, structural organization, proteostasis, and skeletal muscle cellular memory. Accordingly, a reduced CK response during repeated exercise sessions does not necessarily indicate an insufficient training stimulus; rather, it may reflect enhanced muscular resilience and adaptation to previously encountered mechanical loads (Calvo-Rubio et al., 2024; Doma et al., 2023; Sidky et al., 2022).

Recent literature also indicates that CK responses may be modified by recovery interventions and nutritional strategies; however, changes in circulating CK activity do not consistently correspond to improvements in physical performance or reductions in muscle soreness. Meta-analyses investigating cold-water immersion, protein supplementation, branched-chain amino acids (BCAAs), creatine supplementation, and other nutritional interventions have reported effects at specific recovery time points or within particular subgroups, although substantial heterogeneity remains across studies. Therefore, research examining CK responses should integrate biochemical measurements with functional assessments, perceived recovery, and training load characteristics to ensure that interpretations extend beyond reductions in isolated laboratory values (Moore et al., 2023; Pearson et al., 2023; Salem et al., 2024; Talebi, Mohammadi, et al., 2024).

Accordingly, this review aims to systematically synthesize evidence regarding CK responses to physical exercise in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. Specifically, the review addresses five key aspects: the temporal patterns of CK kinetics following exercise; the characteristics of exercise stimuli most consistently associated with elevated CK activity; the biological and methodological factors contributing to interindividual variability in CK responses; adaptations in CK responses following repeated exercise exposure through the RBE; and the principles guiding CK interpretation in scientific research, athlete monitoring, recovery assessment, and clinical practice. By integrating these dimensions, this review seeks to establish an updated, context-sensitive, and practically applicable framework for researchers, coaches, sports scientists, and sports medicine practitioners.

METHOD

This study was conducted as a systematic review with narrative synthesis and was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. Literature searches were conducted in PubMed, ScienceDirect, and SpringerLink for publications from January 2021 through 2026. The search strategy combined terms related to creatine kinase (CK), exercise modalities, exercise-induced muscle damage, recovery, and the repeated-bout effect using Boolean operators (AND and OR), with search strings adapted to each database.

Eligibility criteria were established using the PICO framework for intervention studies and the PEO framework for observational studies. Eligible populations included healthy adults, physically active individuals, athletes, and nonathletes. Exercise interventions or exposures included eccentric exercise, resistance training, high-intensity interval training (HIIT), sprinting, aerobic exercise, and endurance exercise performed in single or repeated sessions. Comparisons included baseline measurements, control conditions, exercise modalities or intensities, and repeated exercise bouts. Studies without comparator groups were also eligible if they reported relevant CK outcomes.

The primary outcomes included circulating CK activity or concentration, changes from baseline, sampling time, time to peak CK response, and recovery patterns. Secondary outcomes included delayed-onset muscle soreness (DOMS), neuromuscular function, and indicators of exercise-induced muscle damage (EIMD). Experimental, quasi-experimental, controlled trial, cohort, and observational studies involving human participants were eligible if they reported relevant CK measurements. Systematic reviews, meta-analyses, and umbrella reviews were considered secondary evidence and were analyzed separately from primary studies. Animal and in vitro studies, studies unrelated to physical exercise, and studies reporting insufficient or irrelevant CK outcomes were excluded.

Study selection involved record identification, duplicate removal, title and abstract screening, and full-text eligibility assessment (Figure 1). Of the 1,723 records identified from PubMed (n = 186), ScienceDirect (n = 750), and SpringerLink (n = 787), 235 duplicates were removed, leaving 1,488 records for screening. Following the exclusion of 1,400 records, 88 reports were sought for retrieval, of which 16 were unavailable. The remaining 72 reports underwent full-text eligibility assessment, and 55 were excluded because they did not meet the inclusion criteria (n = 27), lacked relevant CK outcomes (n = 19), or were unrelated to physical exercise (n = 9). Ultimately, 17 reports were included in the narrative synthesis.

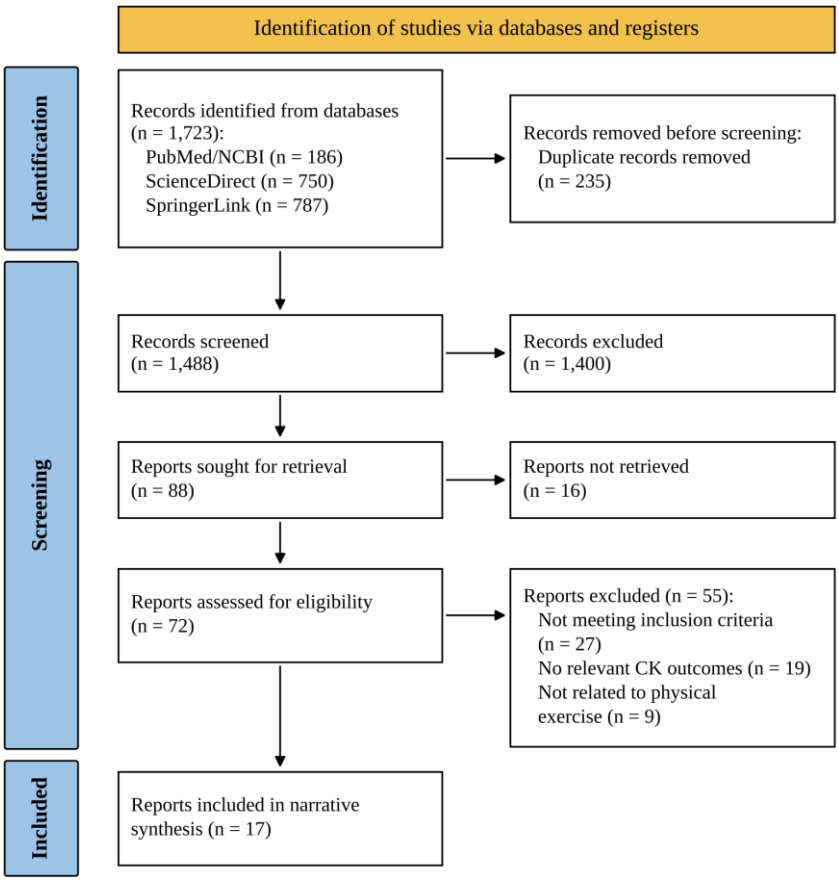

Figure 1. PRISMA 2020 flow diagram of literature selection

Extracted data included authorship, publication year, study design, participant characteristics, exercise protocols, comparator groups, CK assay methods, sampling times, CK responses, and indicators of exercise-induced muscle damage (EIMD) and recovery, where available. The findings were synthesized narratively and categorized according to CK kinetics, exercise characteristics, interindividual variability, adaptations to repeated exercise, and muscle recovery. Narrative synthesis was selected because of substantial heterogeneity in participant characteristics, exercise protocols, assay methods, CK measurement units, and sampling times. A meta-analysis was not conducted because the available data were insufficiently homogeneous to support reliable pooled estimates. Primary studies reporting direct CK measurements formed the basis of the synthesis, while secondary publications provided supporting evidence.

Literature searches, duplicate removal, screening, eligibility assessment, and data extraction were conducted solely by the first author. The second and third authors contributed methodological guidance, scientific judgment, and critical evaluation of the findings and manuscript. Independent screening and assessment by multiple reviewers were not performed, representing a methodological limitation that was considered when interpreting the findings.

RESULTS AND DISCUSSION

Literature Selection and Characteristics of the Evidence

The selection process yielded articles for narrative synthesis that were not all primary studies: the synthesis covers experimental and observational studies, systematic reviews/meta-analyses, and several references supporting mechanistic or clinical interpretation. Findings from studies that measured CK directly were therefore distinguished from secondary evidence and contextual references. The diversity of designs, populations, exercise stimuli, laboratory methods, and blood sampling times limits direct comparison across publications. Table 1 and Table 2 summarize the primary studies and secondary reviews used in the synthesis. Articles that did not measure CK directly were not used as primary evidence on the magnitude or direction of CK change.

Table 1. Characteristics of the synthesized primary studies and their relevance to the CK response

Study	Design/population	Stimulus	CK measurement	Main findings
Liakou et al. (2024)	Experimental; sprint participants. Sample size, age, and training status not detailed.	Resisted versus unresisted sprints.	Pre-exercise to recovery phase. Assay method and CK units not detailed.	Response/recovery kinetics differed according to sprint characteristics and stimulus context.
Devantier-Thomas et al. (2024b)	Experimental; resistance training participants. Sample size, age, and training status not detailed.	Two bouts of traditional resistance training.	Baseline, 24 h, and 48 h. Assay method and CK units not detailed.	EIMD symptoms were reduced in the second bout; CK did not always change in parallel with performance.
Tamujo et al. (2024)	Cohort/observational; professional football players (four-season cohort).	Football match exposure.	Second post-match day. Assay method and CK units not detailed.	Second-day CK was not sufficiently associated with the risk of subsequent muscle injury.
Kusmierczyk et al. (2024)	Experimental with intervention and control groups; 27 young women aged 19–25 years (14 WBC, 13 control).	Downhill/eccentric treadmill running; whole-body cryotherapy (WBC) before the second session.	Serum CK by spectrophotometry (RANDOX CK110) before, 5 min, 1 h, and 24 h after both sessions.	CK increased after eccentric exercise but was lower in the WBC group than in controls after the second session ($p = 0.038$).
McMahon and Onambele-Pearson (2024)	Experimental; isometric exercise participants. Sample size, age, and training status not detailed.	Isometric contractions at different muscle lengths.	Baseline, immediately after, 24 h, and 48 h. Assay method and CK units not detailed.	CK increased, and functional recovery was influenced by muscle length during loading.

Study	Design/population	Stimulus	CK measurement	Main findings
Hsu et al. (2025)	Experimental; multidirectional sprint participants. Sample size, age, and training status not detailed.	Lower-extremity resistance pre-conditioning followed by multidirectional repeated sprints.	24, 48, and 72 h. Assay method and CK units not detailed.	Pre-conditioning reduced CK at certain time points and improved recovery of several functional indicators.
Sahin et al. (2022)	Experimental/recovery protocol; 10 men. Age and training status not detailed.	Resistance exercise (squat and deadlift) followed by active/passive recovery with or without compression garments.	Before, after, 24, 48, and 72 h. Assay method and CK units not detailed.	CK increased after exercise; several recovery protocols reduced CK during the recovery phase.

Source: Authors' synthesis

Table 2. Characteristics of the synthesized secondary reviews and their relevance to the CK response

Study	Design	Stimulus/topic	CK measurement	Main findings
Chalchat et al. (2022)	Systematic review/meta-analysis	Lower-limb eccentric exercise in various human populations.	Variable assays and units; sampling immediately to 96 h.	CK rises with a delay and may remain elevated up to 96 h; sampling time affects interpretation.
Doma et al. (2023)	Systematic review/meta-analysis	Repeated multiarticular exercise; first versus second bout.	Variable assays and units; sampling 24–48 h.	Lower CK and DOMS in the second bout, consistent with RBE.
Leite et al. (2023)	Systematic review	HIIT/HIIE of various modes and doses.	Variable assays and units; sampling immediately to several days.	CK often increases after HIIT/HIIE; magnitude depends on mode and dose.
Biljak et al. (2025)	Literature review	Various forms of exercise and populations.	Variable assays, units, and sampling times.	CK responses are highly heterogeneous; a single value cannot represent structural damage or recovery.
Boyd et al. (2023)	Systematic review/meta-analysis	Pre-conditioning strategies before EIMD-inducing exercise.	Variable assays, units, and time points.	Pre-conditioning may reduce some EIMD indicators; effects depend on protocol and indicator.

Study	Design	Stimulus/topic	CK measurement	Main findings
Fernandes et al. (2025)	Systematic review/meta-analysis	EIMD studies across age groups with various protocols.	Variable assays, units, and time points.	CK was higher in young adults than in older groups at 24 h and at peak change (SMD = −0.32); older age was not associated with greater EIMD.
Doma, Ramachandran, et al. (2022)	Systematic review/meta-analysis	Creatine monohydrate supplementation in exercise and muscle damage.	Variable assays, units, and sampling times.	Effects of creatine on muscle damage markers are not straightforward; CK changes depend on measurement time and indicator.
Pearson et al. (2023)	Systematic review/meta-analysis	Protein supplementation after EIMD-inducing resistance exercise.	Variable assays, units, and sampling times.	Protein may affect some recovery indicators; CK is not the sole basis for assessing recovery.
Salem et al. (2024)	Systematic review/meta-analysis	BCAA supplementation after EIMD.	Variable assays, units, and time points.	BCAA may reduce CK and soreness under certain conditions; effects depend on protocol.
Talebi, Mohammadi, et al. (2024)	Umbrella review	Nutritional interventions for EIMD.	Variable across the summarized reviews/studies.	Quality and consistency of evidence differ; CK reduction should be interpreted together with symptoms and muscle function.

Source: Authors' synthesis

The findings in Table 1 and Table 2 show that context remains the main determinant of the interpretive value of CK. The response can increase after eccentric exercise, HIIT, sprints, and resistance exercise, but the magnitude of the increase does not automatically reflect the extent of structural damage. In team sports, CK is better used as part of load and recovery monitoring than as a single injury predictor, whereas a reduced response after repeated exercise may reflect RBE (Biljak et al., 2025; Doma et al., 2023; Tamujo et al., 2024).

Temporal Kinetics and Exercise Characteristics

The synthesis indicates that CK has a delayed temporal response. After eccentric exercise, CK changes may continue to develop during recovery and remain elevated up to 96 hours in some protocols. Sprint and resistance exercise can produce increases at 24–72 hours, while prolonged activity or extreme loads can yield much higher values. However, CK changes are not always aligned with performance decrements, so sampling time and functional indicators must be analysed together (Chalchat et al., 2022; Devantier-Thomas et al., 2024a; Liakou et al., 2024).

Figure 2 presents a conceptual model of CK kinetics that distinguishes novel eccentric-dominant exposure from repeated, adapted exposure. The curves are conceptual and do not represent meta-analysed absolute values. The model emphasizes that interpretation depends on the measurement window and exposure history, and that RBE can lower the CK response in

subsequent sessions without eliminating the adaptive training stimulus (Calvo-Rubio et al., 2024; Doma et al., 2023).

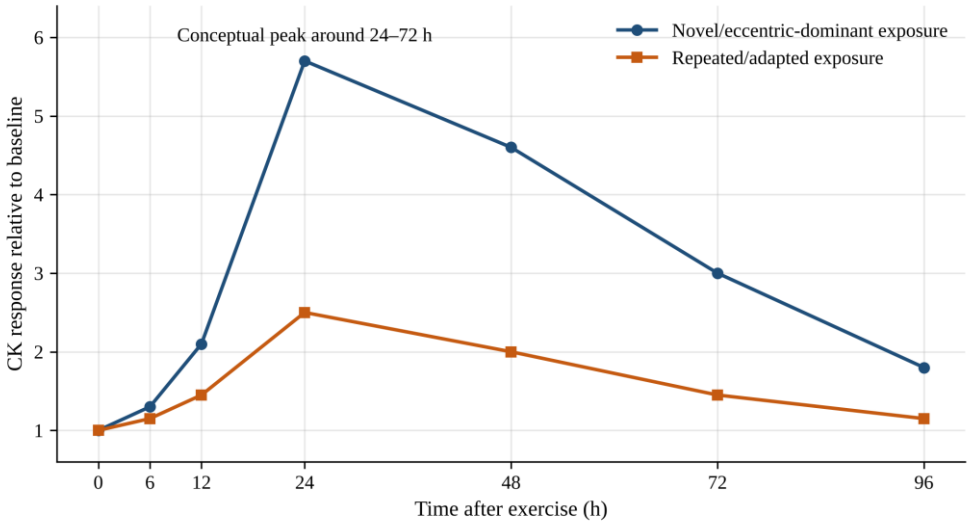

Figure 2. Conceptual model of CK kinetics after exercise
Source: Authors' conceptual synthesis of evidence on CK kinetics and the repeated bout effect

The model highlights two methodological consequences. First, blood sampling only immediately after exercise may miss the peak response because CK often rises during the subsequent recovery period. Second, comparisons between sessions should use consistent time points so that differences do not merely reflect shifts in kinetics. For protocols expected to induce EIMD, baseline plus 24, 48, and 72 hours provide stronger information, and measurement up to 96 hours may be considered for heavy eccentric stimuli or responses that are still rising.

Table 3 groups CK patterns by stimulus characteristics. The grouping shows that labels such as aerobic, anaerobic, or resistance are insufficient to predict the response. Muscle length during loading, force magnitude, total volume, proximity to failure, stimulus novelty, and the combination of acceleration and deceleration also determine the magnitude of the response and the duration of recovery (Furrer et al., 2023; Liakou et al., 2024; McMahon & Onambele-Pearson, 2024).

Table 3. CK response patterns by exercise stimulus characteristics

Stimulus characteristics	Typical CK pattern	Dominant time window	Interpretation
Unfamiliar eccentric	Large but highly variable increase	24–96 h	Mechanical load, muscle length, and stimulus novelty are the main determinants.
Resistance exercise to failure	May increase, especially with high volume or proximity to failure	24–48 h	Exercise dose and fatigue affect recovery; the relationship with function is not always linear.
HIIT/sprint	Mild to large, depending on mode, intensity, and volume	Immediately–72 h	Interaction of high force, acceleration/deceleration, and metabolic stress.
Team sport matches	Repeated increases with high individual variation	24–48 h	More informative when compared with the individual's seasonal values.
Ultra-endurance	May be very high	Immediately–48 h or longer	Extreme values require the context of function, hydration, symptoms, and total load.
Repeated/familiar bouts	Smaller response	24–96 h	RBE may suppress the CK response without eliminating the adaptive stimulus.

Source: Authors' synthesis

Table 3 shows that unfamiliar eccentric stimuli remain the most consistent drivers of CK elevation, but HIIT, sprints, resistance exercise, and team sport matches can also elicit meaningful responses. Systematic evidence on HIIT indicates that the timing and magnitude of change depend strongly on exercise mode and dose. Protocols, training status, and sampling times must therefore be reported in sufficient detail to allow valid comparisons across studies (Biljak et al., 2025; Leite et al., 2023).

Interindividual Variability and the Repeated Bout Effect

Interindividual heterogeneity is a key feature of the CK response. Absolute values are influenced by muscle mass, training status, sex, demographic characteristics, biological variation, and baseline values. Recent evidence does not support the assumption that a single demographic characteristic can explain the response; for example, a meta-analysis on age showed that older groups do not consistently experience greater EIMD than younger groups. Demographic factors should therefore be treated as moderators rather than deterministic thresholds (Aleksovska et al., 2025; Biljak et al., 2025; Fernandes et al., 2025). Table 4 summarizes the biological and methodological determinants that most often explain CK variation. These factors interact: individuals with large muscle mass may have higher absolute values, yet athletes adapted to a given stimulus may show smaller additional increases, whereas individuals unaccustomed to eccentric or high-volume loads may show large surges despite relatively low initial values.

Table 4. Main determinants of CK response variability

Factor	Direction of effect on CK	Basis of interpretation	Implications
Training status	Adapted athletes tend to show more controlled responses to familiar stimuli	Neural, structural, and membrane adaptation	Use individual baseline and training history.
Sex/demographics	Absolute values and distributions may differ, but relative responses are not uniform	Muscle mass, population characteristics, hormonal and biological factors	Use individual baselines and relevant population references.
Muscle mass/body composition	Greater muscle mass may increase the CK pool released	Amount of enzyme source tissue	Absolute values must be interpreted in context.
Contraction type	Eccentric usually larger than purely concentric	High force at increasing muscle length	Record mode and muscle length during loading.
Intensity and volume	Greater total load tends to increase the response	Cumulative mechanical and metabolic stress	Compare CK with total load and proximity to failure.
Sampling time	May substantially change conclusions	Delayed CK kinetics	Use standard time points, at minimum baseline and 24–72 h.
Biological/genetic and pre-analytical variation	May produce high and low responders and variation between samplings	Membrane permeability, clearance, hydration, and sampling conditions	Standardized serial values matter more than a single test.

Source: Authors' synthesis

The implication of Table 4 is the need to shift from single-value interpretation to interpretation based on serial patterns. In athletes, post-exercise or post-match changes are more meaningful when compared with the personal baseline, the recent load, and changes in function. Population reference intervals remain useful in clinical contexts, but the CK distribution is strongly influenced by demographic characteristics and cannot replace individual longitudinal monitoring (Aleksovska et al., 2025; Biljak et al., 2025; Tamujo et al., 2024).

RBE provides the main physiological explanation for the changing response after repeated exercise. Initial exposure can trigger neural adaptation, changes in membrane and cytoskeletal organization, improved tension distribution, and molecular remodelling that make the tissue more tolerant of subsequent stimuli. Experimental evidence on membrane proteins and cellular memory reinforces that RBE is not merely a subjective phenomenon but is linked to biological changes that can lower CK, DOMS, and functional impairment upon subsequent exposure (Bersiner et al., 2023; Calvo-Rubio et al., 2024; Jeon et al., 2022; Sidky et al., 2022). Meta-analytic evidence also shows that pre-conditioning can reduce EIMD indicators upon subsequent exposure, including CK at certain time points, and a recent study showed that preliminary resistance exercise can accelerate recovery after multidirectional sprinting.

Exposure history must therefore be recorded as part of study design and interpretation (Boyd et al., 2023; Hsu et al., 2025).

Interpretation of CK, Isoenzymes, and Recovery Implications

Total CK is useful as an indicator of muscle response, but its specificity is limited. CK-MM mainly reflects a skeletal muscle source, whereas CK-MB is not entirely specific to the myocardium because it can also rise with strenuous exercise. When cardiac injury is suspected, interpretation should prioritize cardiac troponin, clinical findings, and electrocardiography rather than CK-MB alone, reducing the risk of misinterpreting a physiological exercise response as myocardial injury (Costache et al., 2022). Table 5 integrates the use of CK across several contexts, from training monitoring to clinical risk assessment, with the aim of shifting CK from a stand-alone indicator to one component of a decision system that combines load, performance, symptom, and other biomarker data.

Table 5. Framework for interpreting CK in research and practice

Context of use	Useful CK information	Companion indicators	Interpretive caveats
Training monitoring	Change from baseline and weekly pattern	RPE, external load, CMJ/strength, DOMS	Do not use population thresholds as the sole decision criterion.
EIMD evaluation	Kinetics 24–96 h after the stimulus	Strength, ROM, soreness, myoglobin/LDH	CK is an indirect marker; its correlation with damage is not always linear.
RBE/adaptation	Reduced response in subsequent bouts	Faster functional recovery and milder DOMS	Low CK may reflect adaptation rather than an ineffective stimulus.
Suspected cardiac involvement	CK-MB only as supplementary information	Cardiac troponin, ECG, clinical symptoms	CK-MB may rise from skeletal muscle; troponin and clinical context are more specific.
Rhabdomyolysis risk	Very high CK in the context of symptoms and extreme load	Myoglobin, creatinine, electrolytes, renal function, urine, clinical status	CK alone does not determine severity or need for therapy.
Recovery strategies	CK change as a secondary outcome	Function, soreness, readiness, performance	A fall in CK does not always mean faster performance recovery.

Source: Authors' synthesis

The framework in Table 5 emphasizes that a decrease in CK after a recovery intervention is not necessarily equivalent to recovered performance. A meta-analysis of cold-water immersion showed benefits on some recovery outcomes, but effects on CK and performance were not always parallel. Similarly, in EIMD affecting cycling performance, CK elevation may coincide with changes in some functional indicators, yet not all performance measures deteriorate in the same pattern; the effects of percussive therapy dosages on recovery have also been examined. Recovery evaluation should therefore integrate CK with strength, power, soreness, readiness, and sport-specific performance (Devantier-Thomas et al., 2024a; Moore et al., 2023; Zhu et al., 2026).

Nutritional interventions show similarly heterogeneous patterns. Recent meta-analyses report that creatine, protein, BCAA, quercetin, selected root plants, coenzyme Q10, and other

nutritional interventions can reduce CK at certain time points or under certain conditions, but the effects are not consistent across all EIMD indicators. An umbrella review confirms that the quality and certainty of evidence differ between interventions, so a reduction in CK should not be interpreted as sole evidence that functional recovery has been achieved (Doma, Devantier-Thomas, et al., 2022; Doma, Ramachandran, et al., 2022; Mahmoudi Shirkoohi et al., 2025; Pearson et al., 2023; Rojano-Ortega et al., 2023; Salem et al., 2024; Talebi, Mohammadi, et al., 2024; Talebi, Shahi, et al., 2024).

Recent developments point toward broader biomarker panels. CK and myoglobin mainly reflect membrane leakage and relatively non-specific biochemical responses, whereas structural and molecular markers such as cytoskeletal protein fragments, muscle troponins, titin, or specific molecular signals may provide information closer to the location and mechanism of the disturbance. These new markers, however, require standardization and longitudinal validation before routine use, so CK remains relevant as a classic marker whose added value increases when combined with functional indicators and other markers (Özdemir & Demir, 2026). Very high CK values warrant clinical attention when accompanied by severe pain, weakness, swelling, dark urine, dehydration, electrolyte disturbances, or reduced renal function; in that context the focus shifts to evaluating possible exertional rhabdomyolysis, in which CK must be interpreted together with symptoms, myoglobinuria, creatinine, hydration status, and renal function (Bäcker et al., 2023).

Practical Implications and Research Agenda in the Indonesian Context

These findings have practical implications for sports development in Indonesia, particularly for training load monitoring, evaluation of physiological responses, and athlete recovery management. CK can be used as one component of muscle condition monitoring, but not as the sole basis for determining an athlete's readiness to train or compete. Monitoring may be considered after increases in training intensity, eccentric exercise, high training volume, or demanding matches, with results integrated with training load, *rating of perceived exertion* (RPE), DOMS, and performance changes such as strength and *countermovement jump* (CMJ). Athletes should consistently report muscle soreness, weakness, fatigue, and performance decline, while sports medicine staff and physiotherapists should consider individual baseline values, sampling time, training history, hydration status, and clinical symptoms, and refer athletes with severe pain, marked weakness, swelling, or dark urine for clinical evaluation of possible exertional rhabdomyolysis (Bäcker et al., 2023; Biljak et al., 2025; Doma et al., 2023).

In Indonesia, CK monitoring should be adapted to the availability of laboratory facilities, sports health personnel, and athlete development conditions at regional and national levels. Centres with limited facilities can use more accessible indicators such as RPE, DOMS, and physical function tests periodically, prioritizing CK testing according to monitoring needs. Future research should include longitudinal studies describing baseline values and CK change patterns across sports, age groups, and sexes; integration of CK with functional indicators; multicentre studies across regions; and intervention studies with standardized exercise protocols and sampling times to examine responses to repeated exercise and RBE (Biljak et al., 2025; Tamujo et al., 2024).

Limitations

This review has several limitations. First, the synthesis was narrative without new pooled effect estimates because of heterogeneity in protocols, populations, analytical methods, and measurement times. Second, although three databases were searched, source coverage, indexing variation, and full-text availability may have caused relevant publications to be missed. Third, the synthesized articles include diverse designs and levels of evidence, including secondary reviews; published meta-analyses should therefore not be treated as independent primary data, and the risk of study overlap must be considered. Fourth, evidence on recovery and nutritional interventions is heterogeneous, so CK changes need to be read together with functional indicators. Fifth, participant representation by sex, age, and demographic background remains uneven.

CONCLUSION

The creatine kinase (CK) response to physical exercise is a dynamic physiological phenomenon reflecting interactions among mechanical loading, alterations in muscle membrane permeability, exercise stimulus characteristics, and individual adaptive capacity. Current evidence indicates that CK activity commonly increases following unaccustomed, eccentric, high-intensity, or high-volume exercise, including high-intensity interval training (HIIT), sprinting, and prolonged endurance activities. These elevations frequently exhibit delayed kinetics, emphasizing the importance of sampling time in interpreting CK responses. The magnitude of CK elevation is influenced by training status, muscle mass, demographic characteristics, muscle length during loading, and interindividual biological variability. Repeated exposure to similar exercise stimuli generally attenuates CK responses through the repeated-bout effect (RBE), suggesting that lower CK activity during subsequent sessions may reflect protective muscular adaptations rather than an insufficient training stimulus. Conversely, elevated CK activity does not necessarily indicate severe structural muscle damage, increased injury risk, or incomplete recovery, while CK-MB lacks sufficient cardiac specificity to independently establish myocardial injury following strenuous exercise. Therefore, CK should be interpreted as a longitudinal biomarker alongside individual baseline values, exercise characteristics, sampling intervals, delayed-onset muscle soreness (DOMS), muscle strength, neuromuscular performance, and complementary biomarkers when clinically appropriate. Coaches and sports medicine practitioners should prioritize individual CK response patterns over isolated measurements or general population reference thresholds. Future research should emphasize reproducible search strategies, standardized baseline assessments and blood sampling intervals, comprehensive reporting of preanalytical conditions, greater demographic diversity, and the integration of CK measurements with functional assessments and complementary biomarkers to improve the reliability and clinical relevance of exercise-related muscle damage and recovery monitoring.

FUNDING

This research did not receive any specific funding from government, private, or other organizations.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in the conduct of the research, writing, or publication of this article.

AUTHOR CONTRIBUTIONS

All authors contributed to the preparation of this article. The first author (Nur Diani Putri) was responsible for research conceptualization, data collection and analysis, interpretation of results, and drafting of the manuscript, while the other authors contributed to reviewing, editing, and final approval of the manuscript.

GENERATIVE AI STATEMENT

The authors declare that generative artificial intelligence was not used in the preparation of this article.

REFERENCES

Aleksovska, K., Kyriakides, T., Angelini, C., Argov, Z., Claeys, K. G., de Visser, M., Filosto, M., Jovanovic, I., Kostera-Pruszczyk, A., Molnar, M. J., Sacconi, S., Schaefer, J., Siciliano, G., Vilchez, J. J., Toscano, A., & Schoser, B. (2025). What are the normal serum creatine kinase values for skeletal muscle? A worldwide systematic review. *European Journal of Neurology*, *32*(6), e70240. https://doi.org/10.1111/ene.70240

Bäcker, H. C., Richards, J. T., Kienzle, A., Cunningham, J., & Braun, K. F. (2023). Exertional rhabdomyolysis in athletes: Systematic review and current perspectives. *Clinical Journal of Sport Medicine*, *33*(2), 187–194. https://doi.org/10.1097/JSM.0000000000001082

Bersiner, K., Park, S. Y., Schaaf, K., Yang, W. H., Theis, C., Jacko, D., & Gehlert, S. (2023). Resistance exercise: A mighty tool that adapts, destroys, rebuilds and modulates the molecular and structural environment of skeletal muscle. *Physical Activity and Nutrition*, *27*(2), 78–95. https://doi.org/10.20463/pan.2023.0021

Biljak, V. R., Lazić, A., Nikler, A., Pekas, D., Saračević, A., & Trajković, N. (2025). Post-exercise creatine kinase variability: A literature review. *Biochemia Medica*, *35*(2), 020502. https://doi.org/10.11613/BM.2025.020502

Boyd, L., Deakin, G. B., Devantier-Thomas, B., Singh, U., & Doma, K. (2023). The effects of pre-conditioning on exercise-induced muscle damage: A systematic review and meta-analysis. *Sports Medicine*, *53*(8), 1537–1557. https://doi.org/10.1007/s40279-023-01839-8

Calvo-Rubio, M., Garcia-Domiguez, E., Tamayo-Torres, E., Soto-Rodríguez, S., Olaso-Gonzalez, G., Ferrucci, L., de Cabo, R., & Gómez-Cabrera, M. C. (2024). The repeated bout effect evokes the training-induced skeletal muscle cellular memory. *Free Radical Biology and Medicine*, *225*, 247–254. https://doi.org/10.1016/j.freeradbiomed.2024.09.047

Chalchat, E., Gaston, A. F., Charlot, K., Peñailillo, L., Valdés, O., Tardo-Dino, P. E., Nosaka, K., Martin, V., Garcia-Vicencio, S., & Siracusa, J. (2022). Appropriateness of indirect markers of muscle damage following lower limbs eccentric-biased exercises: A systematic review with meta-analysis. *PLOS ONE*, *17*(7), e0271233. https://doi.org/10.1371/journal.pone.0271233

Costache, A.-D., Leon-Constantin, M.-M., Roca, M., Maștaleru, A., Anghel, R.-C., Zota, I.-M., Drugescu, A., Costache, I.-I., Chetran, A., Moisă, Ș.-M., Huzum, B., Mitu, O., Cumpăt, C., Honceriu, C., & Mitu, F. (2022). Cardiac biomarkers in sports cardiology.

Journal of Cardiovascular Development and Disease, *9*(12), 453. https://doi.org/10.3390/jcdd9120453

Devantier-Thomas, B., Deakin, G. B., Crowther, F., Schumann, M., & Doma, K. (2024a). The impact of exercise-induced muscle damage on various cycling performance metrics: A systematic review and meta-analysis. *Journal of Strength and Conditioning Research*, *38*(8), 1509–1525. https://doi.org/10.1519/JSC.0000000000004629

Devantier-Thomas, B., Deakin, G. B., Crowther, F., Schumann, M., & Doma, K. (2024b). The repeated bout effect of traditional resistance training on cycling efficiency and performance. *European Journal of Applied Physiology*, *124*(7), 2005–2017. https://doi.org/10.1007/s00421-024-05422-5

Doma, K., Devantier-Thomas, B., Gahreman, D., & Connor, J. (2022). Selected root plant supplementation reduces indices of exercise-induced muscle damage: A systematic review and meta-analysis. *International Journal for Vitamin and Nutrition Research*, *92*(5–6), 448–468. https://doi.org/10.1024/0300-9831/a000689

Doma, K., Matoso, B., Protzen, G., Singh, U., & Boullosa, D. (2023). The repeated bout effect of multiarticular exercises on muscle damage markers and physical performances: A systematic review and meta-analyses. *Journal of Strength and Conditioning Research*, *37*(12), 2504–2515. https://doi.org/10.1519/JSC.0000000000004628

Doma, K., Ramachandran, A. K., Boullosa, D., & Connor, J. (2022). The paradoxical effect of creatine monohydrate on muscle damage markers: A systematic review and meta-analysis. *Sports Medicine*, *52*(7), 1623–1645. https://doi.org/10.1007/s40279-022-01640-z

Fernandes, J. F. T., Wilson, L. J., Dingley, A. F., Hearn, A. N., Johnson, K. O., Hicks, K. M., Twist, C., & Hayes, L. D. (2025). Advancing age is not associated with greater exercise-induced muscle damage: A systematic review, meta-analysis, and meta-regression. *Journal of Aging and Physical Activity*, *33*(6), 606–624. https://doi.org/10.1123/japa.2024-0165

Furrer, R., & Handschin, C. (2024). Molecular aspects of the exercise response and training adaptation in skeletal muscle. *Free Radical Biology and Medicine*, *223*, 53–68. https://doi.org/10.1016/j.freeradbiomed.2024.07.026

Furrer, R., Hawley, J. A., & Handschin, C. (2023). The molecular athlete: Exercise physiology from mechanisms to medals. *Physiological Reviews*, *103*(3), 1693–1787. https://doi.org/10.1152/physrev.00017.2022

Hsu, S.-M., Tseng, W.-C., Chiu, C.-H., Hsieh, T.-Y., Weng, M.-C., Dai, X., & Chen, C.-H. (2025). Effects of preconditioning lower-extremity resistance exercises on multidirectional repeated sprinting-induced muscle damage. *Journal of Strength and Conditioning Research*, *39*(2), e89–e95. https://doi.org/10.1519/JSC.0000000000004982

Jeon, S., Ye, X., Miller, W. M., & Song, J. S. (2022). Effect of repeated eccentric exercise on muscle damage markers and motor unit control strategies in arm and hand muscle. *Sports Medicine and Health Science*, *4*(1), 44–53. https://doi.org/10.1016/j.smhs.2021.12.002

Kusmierczyk, J., Wiecek, M., Bawelski, M., Szygula, Z., Rafa-Zablocka, K., Kantorowicz, M., & Szymura, J. (2024). Pre-exercise cryotherapy reduces myoglobin and creatine kinase levels after eccentric muscle stress in young women. *Frontiers in Physiology, 15*, Article 1413949. https://doi.org/10.3389/fphys.2024.1413949

Leite, C. D. F. C., Zovico, P. V. C., Rica, R. L., Barros, B. M., Machado, A. F., Evangelista, A. L., Leite, R. D., Barauna, V. G., Maia, A. F., & Bocalini, D. S. (2023). Exercise-induced muscle damage after a high-intensity interval exercise session: Systematic review. *International Journal of Environmental Research and Public Health*, *20*(22), 7082. https://doi.org/10.3390/ijerph20227082

Liakou, C. A., Fatouros, I. G., Poulios, A., Tsatalas, T., Karampina, E., Karanika, P., Kaloudi, D., Rosvoglou, A., Tsimeas, P., Kamperi, A., Syrou, N., Gatsas, A., Papanikolaou, K., Draganidis, D., Tsaklis, P., Giakas, G., Jamurtas, A. Z., & Deli, C. K. (2024). Recovery kinetics following sprint training: Resisted versus unresisted sprints. *European Journal of Applied Physiology*, *124*(3), 881–896. https://doi.org/10.1007/s00421-023-05317-x

Mahmoudi Shirkoohi, N., Mohammadi, H., Gallaly, D. Q., & Djafarian, K. (2025). The effects of probiotic supplementation on body composition, recovery following exercise-induced muscle damage, and exercise performance: A systematic review and meta-analysis of clinical trials. *Physiological Reports*, *13*(8), e70288. https://doi.org/10.14814/phy2.70288

McMahon, G., & Onambele-Pearson, G. (2024). Joint angle-specific neuromuscular time course of recovery after isometric resistance exercise at shorter and longer muscle lengths. *Journal of Applied Physiology*, *136*(4), 889–900. https://doi.org/10.1152/japplphysiol.00820.2023

Moore, E., Fuller, J. T., Bellenger, C. R., Saunders, S., Halson, S. L., Broatch, J. R., & Buckley, J. D. (2023). Effects of cold-water immersion compared with other recovery modalities on athletic performance following acute strenuous exercise in physically active participants: A systematic review, meta-analysis, and meta-regression. *Sports Medicine*, *53*(3), 687–705. https://doi.org/10.1007/s40279-022-01800-1

Özdemir, K., & Demir, Y. (2026). Biochemical markers of muscle damage and recovery: Insights from exercise physiology and molecular biology. *Tissue and Cell*, *101*, 103406. https://doi.org/10.1016/j.tice.2026.103406

Pearson, A. G., Hind, K., & Macnaughton, L. S. (2023). The impact of dietary protein supplementation on recovery from resistance exercise-induced muscle damage: A systematic review with meta-analysis. *European Journal of Clinical Nutrition*, *77*(8), 767–783. https://doi.org/10.1038/s41430-022-01250-y

Rojano-Ortega, D., Peña-Amaro, J., Berral-Aguilar, A. J., & Berral-de la Rosa, F. J. (2023). Quercetin supplementation promotes recovery after exercise-induced muscle damage: A systematic review and meta-analysis of randomized controlled trials. *Biology of Sport*, *40*(3), 813–825. https://doi.org/10.5114/biolsport.2023.121320

Sahin, F. B., Sahin Kafkas, A., Kafkas, M. E., Taskapan, M. C., & Jones, A. M. (2022). The effect of active vs passive recovery and use of compression garments following a single bout of muscle-damaging exercise. *Isokinetics and Exercise Science, 30*(2), 117–126. https://doi.org/10.3233/IES-210155

Salem, A., Ben Maaoui, K., Jahrami, H., AlMarzooqi, M. A., Boukhris, O., Messai, B., Clark, C. C. T., Glenn, J. M., Ghazzaoui, H. A., Bragazzi, N. L., Ammar, A., Trabelsi, K., & Chtourou, H. (2024). Attenuating muscle damage biomarkers and muscle soreness after an exercise-induced muscle damage with branched-chain amino acid (BCAA) supplementation: A systematic review and meta-analysis with meta-regression. *Sports Medicine - Open*, *10*(1), 42. https://doi.org/10.1186/s40798-024-00686-9

Sidky, S. R., Ingalls, C. P., Lowe, D. A., & Baumann, C. W. (2022). Membrane proteins increase with the repeated bout effect. *Medicine & Science in Sports & Exercise*, *54*(1), 57–66. https://doi.org/10.1249/MSS.0000000000002762

Talebi, S., Mohammadi, H., Zeraattalab-Motlagh, S., Arab, A., Mohammadian, M. K., Ghoreishy, S. M., Fard, M. A. T., Khosroshahi, R. A., & Djafarian, K. (2024). Nutritional interventions for exercise-induced muscle damage: An umbrella review of systematic reviews and meta-analyses of randomized trials. *Nutrition Reviews*, *82*(5), 639–653. https://doi.org/10.1093/nutrit/nuad078

Talebi, S., Shahi, M. H. P., Zeraattalab-Motlagh, S., Asoudeh, F., Ranjbar, M., Hemmati, A., Talebi, A., Wong, A., & Mohammadi, H. (2024). The effects of coenzyme Q10

supplementation on biomarkers of exercise-induced muscle damage, physical performance, and oxidative stress: A GRADE-assessed systematic review and dose-response meta-analysis of randomized controlled trials. *Clinical Nutrition ESPEN*, *60*, 122–134. https://doi.org/10.1016/j.clnesp.2024.01.015

Tamujo, A. C., Flores, H. N., Cetolin, T., Ribeiro-Alvares, J. B., Haupenthal, A., & Baroni, B. M. (2024). Creatine kinase concentration on the second post-match day is not associated with risk of subsequent muscle injury in professional football players: A four-season cohort study. *The Physician and Sportsmedicine*, *52*(3), 271–276. https://doi.org/10.1080/00913847.2023.2246175

Zhu, Y., Yang, L., Liu, T., Yao, F., Wang, Q., & Yi, Z. (2026). Effects of percussive therapy dosages on recovery from acute exercise-induced muscle damage: A systematic review and meta-analysis. *Chiropractic & Manual Therapies*, *34*, 34. https://doi.org/10.1186/s12998-026-00657-9