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Post-Exercise Elevations in Organ Injury-Associated Biomarkers: Kinetics, Confounders, and Clinical Red Flags - A Narrative Review

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Abstract

Background: Strenuous exercise can simultaneously alter muscle-, cardiac-, kidney-, liver-associated, inflammatory and haematological biomarkers. Values above population reference intervals may reflect exercise-related kinetics, concentration changes or pathology.

Aim: To synthesise post-exercise biomarker kinetics, major modifiers, preanalytical confounders and features distinguishing a transient response from findings requiring further evaluation.

Material and methods: This narrative review searched PubMed and Scopus for English-language publications from January 2008 to June 2026; Google Scholar and reference lists

provided supplementary coverage. Evidence was appraised qualitatively and synthesised narratively without meta-analysis.

Results: CK, myoglobin, cardiac troponin, creatinine, urinary kidney biomarkers, AST, ALT, LDH and haemolysis-associated measures followed marker- and protocol-specific trajectories. Interpretation depended on exercise modality, dose and novelty, sampling time, hydration and plasma-volume shifts, baseline values, assay characteristics and serial direction. No isolated result reliably localised structural injury or provided a universal threshold or normalisation time. Symptoms, associated findings, persistence, worsening or patterns discordant with the exposure support urgent or targeted evaluation.

Conclusions: Exact sampling time and serial trajectory are more informative than isolated reference-interval crossing. Clinical and multibiomarker context is essential; short-term normalisation may support an exercise-related explanation but does not prove benignity or exclude transient structural change. The proposed checklist is conceptual and unvalidated. Standardised longitudinal studies are needed.

Keywords: exercise; biomarkers; creatine kinase; cardiac troponin; acute kidney injury; aminotransferases; haemolysis; clinical interpretation

1. Introduction

Laboratory testing is increasingly embedded in sports medicine, in the care of physically active people, and in the assessment of patients who present after strenuous exercise. This expanding role makes preanalytical and clinical context especially important, because training itself can modify laboratory results and complicate comparison with values derived from the general population [1]. A single exercise exposure may be accompanied by concurrent changes in muscle, cardiac, kidney and inflammatory biomarkers, haematological measures, and liver-associated biochemical tests. For example, sampling around one marathon demonstrated a broad multibiomarker response spanning several biological domains, with interpretation affected by correction for plasma-volume change and by normalisation of urinary measurements [2]. Such profiles can be difficult to interpret when several results exceed population reference intervals, yet their concurrence does not by itself establish structural injury in every tissue represented by the measured analytes.

Exercise should therefore be treated as a potentially important preanalytical variable. The observed concentration depends on the type, intensity, duration and novelty of the activity; the

interval between exercise cessation and sample collection; hydration and fluid intake; haemoconcentration or haemodilution; and the burden of preceding training. The same external workload may also impose different internal demands according to training status and other individual characteristics [3]. Interpretation further requires a distinction between a population reference interval, a person's credible baseline and the direction and magnitude of change in serial measurements. Biological variation creates individual set points within the wider population distribution, while analytical and preanalytical variation also contribute to differences between consecutive results [4]. Consequently, a single measurement obtained without an exercise history or precise sampling time may encourage overinterpretation of an exercise-related change. Conversely, attributing an abnormal value to recent activity without considering symptoms, associated findings and its subsequent trajectory may delay recognition of clinically important disease.

These interpretive challenges recur across biomarker domains. Creatine kinase (CK) activity may increase markedly and often peaks after the immediate post-exercise window, whereas myoglobin can change earlier; both show substantial interindividual variability [5]. Resistance exercise can also raise aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH), illustrating divergent kinetics and the multisource nature of these enzymes [6]. Cardiac troponin may exceed an assay's upper reference limit after exercise; this is not automatically myocardial infarction, but neither the exposure nor a familiar trajectory establishes benignity [7]. After endurance events, creatinine can rise while non-steady-state kinetics, muscle-derived production and fluid balance limit interpretation of estimated glomerular filtration rate; newer kidney biomarkers add questions of source, timing and urine normalisation [8]. Exercise-induced haemolysis may reflect mechanical and metabolic mechanisms and must be distinguished from plasma-volume shifts, iron deficiency and anaemia [9].

The evidence base does not yet resolve these uncertainties uniformly. Many studies involve small, selected and predominantly male samples, while exercise protocols, environmental conditions, analysers, sampling schedules, operational thresholds and follow-up periods differ substantially. An apparently similar post-exercise value may therefore represent a different point on the underlying trajectory in another study or clinical setting. Short-term return towards baseline documents the course of an analyte within the observed period; it does not prove that no transient structural change occurred, that all represented tissues recovered in parallel, or that repeated exposures are without longer-term consequences. A possible link between recurrent cardiac and kidney stress signals and later cardiovascular sequelae in some extreme endurance

athletes has been hypothesised, but the proposed cardio-renal pathway remains speculative and a causal relationship between acute biomarker elevations and chronic disease has not been established [10].

This narrative review aimed to synthesise the kinetics, major moderators and interpretive limitations of commonly measured post-exercise biomarkers, and to identify clinical features that may help distinguish patterns compatible with a transient exercise-related response from findings requiring urgent or targeted evaluation. It considers preanalytical factors and biological variation; muscle biomarkers and exertional rhabdomyolysis; cardiac troponins; kidney biomarkers and acute kidney injury criteria; aminotransferases, LDH and haemolysis; and integration of multibiomarker patterns into clinical reasoning. The review also examines uncertainty surrounding repeated exposures and long-term consequences, and identifies priorities for future research. Its purpose is to support appropriately contextualised interpretation, not to establish sport-specific reference intervals or diagnostic thresholds, nor to validate a clinical decision algorithm.

2. Materials and methods

PubMed and Scopus were searched for English-language articles published from January 2008 to June 2026. Search terms covered physical activity, exercise and post-exercise alterations in skeletal muscle, cardiac, renal, hepatic and haematological biomarkers. Google Scholar provided supplementary coverage. Separate biomarker- and organ-focused strategies were tailored to the individual databases, while the reference lists of pertinent original investigations, reviews, meta-analyses, consensus statements and clinical guidelines were examined to identify additional eligible publications.

Observational and interventional studies of healthy athletes or physically active participants were considered if they assessed acute or repeated exercise exposure and described post-exercise biomarker concentrations, temporal profiles or clinically relevant response patterns. Biomarkers of interest included creatine kinase, myoglobin, cardiac troponins, creatinine, urinary markers of kidney stress or injury, aminotransferases, lactate dehydrogenase and indices related to haemolysis. Evidence from different age groups was included where relevant, with paediatric and adolescent data restricted to clearly defined contexts. Clinical series of exertional rhabdomyolysis and authoritative definitions, consensus statements or guidelines were used specifically to inform diagnostic criteria, complications and clinical red flags rather than the principal synthesis of exercise responses. Studies centred on established organ disease were excluded from the main analysis. Other exclusion criteria comprised the absence of a relevant

exercise exposure or biomarker outcome, non-English language, conference-only abstracts, incomplete reports and duplicate publications without additional data.

For each primary study, information was collected on design, participant characteristics, exercise modality and dose, timing of sample collection, analytical methods, baseline and post-exercise measurements, serial biomarker behaviour, accompanying symptoms or clinical findings, principal observations and key limitations. Exact quantitative statements were checked against the original reports. Findings were organised by biomarker domain and interpreted with regard to sampling time, hydration status, plasma-volume shifts, assay characteristics, individual baseline values, exercise exposure and clinical context. Methodological appraisal focused on participant selection, definition of the exercise stimulus, timing and adequacy of sampling, outcome assessment, confounding and reporting quality. No numerical quality rating, formal risk-of-bias instrument or GRADE framework was used. Owing to substantial clinical and methodological variability, no pooled estimate was calculated and the evidence was synthesised narratively.

3. Why a post-exercise value can mislead

3.1. Sampling time and serial kinetics

A post-exercise concentration is a time-stamped observation, not a stable property of the athlete or a direct measure of accumulated tissue injury. The interval from exercise cessation to venipuncture determines whether the sample reflects an immediate plasma-volume shift, early cellular release, continued appearance of an analyte in blood, redistribution, or clearance. In a crossover study of 40 middle-aged and older adults with knee osteoarthritis, estimated plasma volume was lowest immediately after 20-minute moderate-to-high-intensity running and cycling and returned to baseline by 30 minutes [11]. The magnitude and recovery time should not be extrapolated beyond that acute protocol.

Biomarkers differ in their intrinsic time courses. Creatine kinase (CK) activity may peak two to six days after a muscle insult, with timing influenced by exercise characteristics and individual factors [5]. An immediate result may precede the main rise, whereas a later value may reflect an earlier bout.

The sampling clock is therefore part of the result. When uncertainty remains, a serial trajectory obtained under comparable conditions is more informative than poorly timed snapshots: it can distinguish rapidly reversible concentration effects from delayed or persistent release, although it does not establish mechanism.

3.2. Haemoconcentration, haemodilution and hydration

Exercise can change a measured concentration even when the circulating amount of an analyte has not increased. Intravascular water shifts can produce haemoconcentration during exercise and haemodilution during recovery. Physical activity is therefore a preanalytical variable whose impact depends on exercise type, intensity and duration, training status and recovery time [3]. An immediate elevation may reflect concentration, biological release or both.

Plasma-volume change and hydration status are not interchangeable. In 12 elite male kayak–canoe athletes, both a short incremental test while hydrated and a maximal test after a 120-minute preload without fluid increased haemoglobin and haematocrit at peak effort; both returned to resting values by 30 minutes, whereas plasma osmolality remained elevated after dehydration [12]. These indices therefore tracked rapid concentration change but not residual dehydration.

Adjustment for estimated plasma-volume change can alter interpretation but is not universal. In the acute running and cycling study, correction changed two cartilage-biomarker responses in different directions; haemoglobin/haematocrit estimation was imperfect and hydration uncontrolled [11]. In 296 young trained participants undergoing a progressive treadmill test, immediate and approximately 17-hour samples showed that correction altered several biochemical interpretations [13]. Neither protocol represents prolonged endurance exercise.

Biomarkers should therefore be read beside sampling time and available fluid-balance indicators, including contemporaneous haemoglobin, haematocrit, osmolality, body-mass change and fluid intake. None, alone or after adjustment, proves or excludes tissue injury; these data indicate a possible concentration effect for integration with biomarker-specific kinetics and the clinical picture.

3.3. Biological variation, individual baselines and reference intervals

Population reference intervals describe a defined reference group; they do not define an individual athlete's usual value or serve as stand-alone disease thresholds. Biological variation includes between-person differences and within-person fluctuation around a homeostatic set point, while analytical and preanalytical variation add uncertainty. A result can therefore remain within a population interval despite a meaningful personal change, or cross a population limit without indicating organ injury [4].

Athlete data illustrate why the reference population matters. In a retrospective study of 14,010 samples from 3,588 adult elite athletes across 32 sports, samples were obtained after overnight rest and fasting rather than immediately after exercise. Basal distributions for several

biochemical and haematological analytes differed from general-population comparators, although sports and training periods were pooled and the proposed ranges were described as "pseudo" reference intervals [14]. These observations support caution but do not establish universal athlete-specific limits.

A resting baseline collected under reproducible conditions can contextualise a later result. Comparison is strongest when posture, fasting, recent exercise, hydration, sampling interval, specimen and method are similar. Biological variation and analytical imprecision inform serial interpretation [4] but do not provide sport-specific reference change values or diagnostic thresholds. Any deviation should be assessed with symptoms, examination, exposure, trajectory and complementary tests rather than labelled automatically physiological or pathological.

4. Skeletal muscle biomarkers and exertional rhabdomyolysis

4.1. Creatine kinase, myoglobin and lactate dehydrogenase: sources and kinetics

Creatine kinase (CK), myoglobin and lactate dehydrogenase (LDH) reflect related but non-identical processes and are not interchangeable measures of muscle injury. CK is a cytosolic enzyme involved in energy buffering. After exercise, circulating activity is usually dominated by the skeletal-muscle CK-MM isoenzyme, yet the measured concentration remains an indirect product of enzyme release, distribution and clearance rather than a direct measure of fibre necrosis [15]. Myoglobin often changes earlier than CK, while CK and LDH may remain elevated later; their post-exercise trajectories are marker- and protocol-dependent [16,17].

The temporal separation between these markers is clinically important. Post-exercise CK commonly rises after a delay and may not peak until one or more days after the provoking session. Its magnitude and time course vary with contraction type, exercise dose, training status, sex, body composition, and biological, preanalytical and analytical factors. Thus, neither an early low value nor a later high value has a uniform meaning [5]. In a small study of 32 male military cadets undergoing consecutive, heterogeneous training tasks, myoglobin changed mainly in the immediate post-exercise window, while CK remained elevated later and appeared to reflect preceding activities; LDH showed a more modest response. These observations cannot define universal kinetics because the protocol was highly specific and recovery conditions were incompletely controlled [16].

A synthesis focused mainly on lower-limb, eccentric-biased exercise similarly found asynchronous group trajectories: myoglobin tended to peak early, CK later, and LDH at an intermediate or later time, with timing influenced by severity and sampling schedule [17]. A

single specimen therefore compares markers at different biological phases. Immediate sampling may capture myoglobin before the CK peak; a delayed sample may detect persistent CK after myoglobin has declined. Serial results are most informative when actual time from exercise, subsequent activity and recovery conditions are recorded instead of a generic “post-exercise” label. Discordant values may reflect expected kinetics rather than different conclusions about clinically important injury.

4.2. Exercise dose, modality and functional correlates

The biomarker response depends on exercise dose and mechanical character rather than duration alone. Greater intensity or volume, unfamiliar loading and a substantial eccentric component can increase membrane disruption and prolong release. The same external workload may also represent a different internal dose in trained and untrained individuals. Repeated sessions with insufficient recovery may create overlapping curves, so a value after the latest bout may partly reflect earlier work. In the male military cohort, CK was already elevated before the most demanding session and subsequent CK, myoglobin and LDH trajectories differed [16]. The heterogeneous military protocol supports a load-accumulation concept, not a quantitative rule for other populations.

Biochemical change and functional impairment are only partially concordant. In eccentric-biased lower-limb studies, training status, modality and task type were associated with loss of maximal voluntary contraction, but indirect biomarkers did not track function consistently. Early myoglobin related only partly to later strength loss, CK was informative at selected later time points, LDH showed no consistent correlation, and soreness aligned poorly with strength loss [17]. No single marker is therefore a reliable proxy for pain, force production or readiness to train.

After a warm-weather marathon, runners with greater late-race pace reduction had higher immediate post-race myoglobin and LDH, while the CK difference was not statistically conclusive; blood was collected within three minutes of finishing [18]. This association does not establish causation, and the sampling window cannot describe later CK kinetics. Functional assessment and biochemical testing therefore answer distinct questions.

4.3. Expected muscle response versus exertional rhabdomyolysis

Strenuous or unfamiliar exercise can produce soreness, temporary strength loss and marked biochemical changes without constituting exertional rhabdomyolysis. CK is particularly vulnerable to overinterpretation because its post-exercise distribution is broad and its serum

activity does not map reliably onto the extent of structural muscle disruption [15]. An isolated increase—even a pronounced one—therefore describes a laboratory response, not by itself a clinical syndrome, confirmed organ injury or severity category. Interpretation should begin with the athlete's condition and exposure, not with retrospective relabelling of the CK value.

Marked CK elevations or myoglobinuria can occur after strenuous endurance exercise or military training without the symptom complex or end-organ complications of clinically significant exertional rhabdomyolysis [19]. Conversely, concerning symptoms or evolving renal and electrolyte abnormalities require evaluation even when sampling precedes the CK peak. The distinction cannot be reduced to one threshold, particularly when baseline CK, exposure, sampling time and trend are unknown.

For this review, exertional rhabdomyolysis is a context-dependent clinical syndrome after exercise, supported by muscle symptoms and biochemical evidence and assessed for systemic complications. Severe or escalating pain, weakness or swelling, pigmenturia, systemic illness and renal or electrolyte abnormalities increase concern. A recurrent episode, one following accustomed or modest exercise, or one disproportionate to exposure may be the first presentation of an inherited or acquired myopathy [20]. Exercise-induced muscle damage and exertional rhabdomyolysis overlap biologically but are not diagnostic synonyms; context and trajectory determine whether an expected response has crossed into disease.

4.4. Clinical red flags, acute kidney injury risk and follow-up

Urgent assessment is warranted for severe or worsening pain, objective weakness, progressive swelling, dark urine, oliguria, systemic illness, rising creatinine or important electrolyte disturbance. Evaluation should integrate exposure, examination, renal function, electrolytes, urine output, urinalysis when indicated and serial muscle markers. A general consensus supports serial CK until a peak and reliable decline, monitoring for hyperkalaemia, acute kidney injury and compartment syndrome, and renal replacement therapy only for conventional AKI indications; extrapolation to athletes must remain cautious [21].

No single CK value reliably predicts acute kidney injury, determines admission or proves that follow-up can end safely. In a prospective cohort of 136 mostly young, otherwise healthy adults, five acute kidney injury events occurred and none arose among outpatients. The authors reported that outpatient management appeared feasible for selected well patients with normal admission creatinine, possible oral hydration and exercise restriction, and reliable early reassessment [22]; this observation should not be treated as a sport-specific disposition rule. Few events and a homogeneous cohort limit generalisation. Worsening symptoms, creatinine

or urine output, important electrolyte abnormalities, unreliable observation or suspected complications favour supervised care.

After the acute episode, persistent weakness or CK elevation, recurrent or disproportionate events, onset after accustomed activity, or a personal or family history of exercise intolerance, cramps, fasting- or fever-associated episodes or malignant hyperthermia supports specialist neuromuscular evaluation [20]. Follow-up should confirm clinical recovery and a favourable laboratory trend while assessing whether the exposure plausibly explains the event.

5. Cardiac troponins after exercise

5.1. Magnitude and temporal pattern of cardiac troponin release

Exercise-related increases in cardiac troponin are common after prolonged endurance exercise, but their reported frequency and magnitude depend on the assay, population, exposure and sampling schedule. A sample obtained immediately after exercise can identify an early increase but may precede the maximum concentration. In a quantitative synthesis restricted to high-sensitivity cardiac troponin T (hs-cTnT), the rise was evident within the first hour, the modelled group peak occurred at approximately three hours, and concentrations subsequently declined towards baseline; individual studies nevertheless placed the peak on either side of that estimate, and small residual changes could persist for two to three days [23].

Across a broader range of protocols, cardiac troponin concentrations often continued to increase after exercise cessation, with peaks commonly reported between two and six hours and marked differences between individuals. Many values declined over the following 24–72 hours, but heterogeneity in exercise dose, cTnT and cTnI assays, and collection points precluded a single biphasic pattern or fixed time to normalisation [7]. An immediate value, a later peak and a falling series therefore answer different questions.

Marathon-specific pooled data provide a useful indication of scale: mean post-race changes were approximately +42 ng/L for cTnT and +77 ng/L for cTnI, although most participants were men and only a minority of contributing studies used high-sensitivity assays [24]. These pooled changes should not be transferred to shorter exercise, other sports or another analytical platform. High-sensitivity cardiac troponin T (hs-cTnT) and high-sensitivity cardiac troponin I (hs-cTnI) are related but non-interchangeable measurements, and the proportion exceeding an assay's upper reference limit depends on the selected limit and sampling time. The clinically useful description is a time-stamped, assay-specific serial trajectory rather than a generic "post-exercise troponin".

5.2. Proposed mechanisms and molecular composition

Detectable troponin confirms circulating cardiac troponin material, not its route of release or reversibility. Proposed mechanisms include transient sarcolemmal permeability during mechanical and haemodynamic stress, release through membrane wounds, blebs or extracellular vesicles, and leakage from a relatively accessible cytoplasmic pool. Proteolysis may produce smaller fragments that cross a stressed membrane more readily. Accelerated protein turnover, apoptosis and microscopic necrosis have also been proposed, but their relative contributions in humans after exercise remain uncertain. [7]

Direct human evidence is limited. In 11 middle-aged male marathon runners, mean myocardial water diffusivity on diffusion-weighted cardiac magnetic resonance increased approximately four hours after the race and correlated with conventional and single-molecule cTnI, but not significantly with hs-cTnT; diffusivity returned to baseline at two weeks. The finding supports consideration of a transient change in cardiomyocyte integrity and membrane permeability, yet the small, post hoc study cannot establish a single release mechanism, exclude microscopic injury or show that every post-exercise increase is innocuous [25].

Molecular composition offers a complementary, still exploratory observation. In samples from 45 marathon or half-marathon runners and 84 patients with type 1 myocardial infarction, short cTnT fragments predominated after running, whereas intact and longer forms were more common during the early phase of infarction. The groups differed substantially, exercise samples were collected only once without a pre-race specimen, and the long-form measurement used a novel assay [26]. Fragmentation may therefore help explain why total hs-cTnT rises under different biological conditions, but fragment analysis is not an available, validated discriminator for routine clinical decisions.

5.3. Moderators, reproducibility and special populations

Exercise duration appears to be one of the more consistent moderators of hs-cTnT, while evidence for intensity, age and sex is less stable. Modality may matter: the quantitative synthesis found lower concentrations after rowing than running, but comparisons for other modes were inconclusive. Considerable residual variation remained after modelling, plausibly reflecting baseline concentration, recent and long-term training, health status, assay technique and unmeasured features of internal load. Women were under-represented, making the estimated sex effect particularly uncertain [23]. These group-level associations cannot define an individual expected range.

Partial reproducibility has been demonstrated for hs-cTnI. Fifty-nine recreational cyclists, including 13 women, were assessed after two long races and a cardiopulmonary exercise test, with samples before and at three and 24 hours. Responses correlated across exposures, and the previous cTnI response, baseline value, workload and sampling time contributed to later values; correlations were not perfect and exercise loads differed [27]. A prior high response may therefore inform context, but it neither proves a stable "responder" phenotype nor provides a personal diagnostic threshold.

Evidence in children and adolescents is even more heterogeneous. A review of 23 studies in athletes aged 6–17.9 years found inconsistent sampling schedules, sports, analysers and comparison limits; only 16.5% of participants were female, and maturational status was not consistently recorded. Reported differences by sex, age or maturity were consequently conflicting or based on small subgroups [28]. Our interpretation is that paediatric and adolescent results require age-, assay- and context-aware assessment, while current evidence is insufficient to establish subgroup-specific exercise thresholds.

5.4. Differentiating exercise-related release from myocardial injury and infarction

Terminology must remain precise. Under the Fourth Universal Definition, myocardial injury is present when at least one cardiac troponin value exceeds the assay's 99th-percentile upper reference limit, and it is considered acute when a rise and/or fall is demonstrated. Acute myocardial infarction requires acute myocardial injury plus clinical evidence of acute myocardial ischaemia, such as ischaemic symptoms, new ischaemic electrocardiographic changes, development of pathological Q waves, compatible new imaging abnormalities or, in the appropriate infarction type, a coronary thrombus [29]. Thus, crossing the 99th percentile is not synonymous with infarction, while a detectable post-exercise release is not synonymous with irreversible cardiomyocyte necrosis.

Recent strenuous exercise is relevant exposure information, not a rule-out diagnosis. A person who is well, has an expected exposure and shows a resolving trajectory differs clinically from a person with chest pain, syncope, dyspnoea disproportionate to exertion, haemodynamic instability, a significant arrhythmia, ischaemic ECG changes or a persistent or worsening troponin trend. When acute coronary syndrome or another cardiac disorder remains a concern, evaluation should follow the usual clinical pathway, integrating history, examination, a 12-lead ECG, serial assay-specific troponin measurements and non-invasive or invasive imaging or risk assessment when indicated [7]. This is a contextual framework rather than a validated sports algorithm, and no single value or delta establishes safe discharge.

Marathon studies provide population-level context only. Pooled cardiac magnetic resonance findings showed no consistent adverse change in most conventional structural metrics and a small increase in left ventricular ejection fraction, but only six studies contributed imaging data and advanced tissue characterisation was sparse [24]. These cohort findings cannot establish that an individual rise is benign or override symptoms, ECG changes or deterioration. Conversely, exceeding the upper reference limit alone does not establish infarction; interpretation requires concordance among exposure, serial kinetics, clinical findings, ECG and selectively applied imaging.

6. Kidney biomarkers and exercise-associated acute kidney injury

6.1. Creatinine, estimated glomerular filtration rate and post-exercise AKI criteria

Serum creatinine is convenient but particularly difficult to interpret immediately after strenuous exercise. Its concentration may rise because creatinine production increases with skeletal-muscle work and breakdown, because renal handling changes, or because plasma water is redistributed or lost. The measured value therefore integrates production, distribution and excretion rather than glomerular filtration alone. Hydration status, the pre-exercise concentration and the interval from exercise to sampling further influence the apparent change. During this non-steady state, a creatinine-based estimated glomerular filtration rate (eGFR) should not be read as a direct measurement of filtration; an apparently large fall may partly be a mathematical consequence of the transient creatinine rise. Reviews of endurance events accordingly report frequent post-race creatinine increases but emphasise both heterogeneous protocols and the contribution of muscle-derived creatinine [8].

The 2012 KDIGO framework defines AKI by any of three findings: an increase in serum creatinine of at least 0.3 mg/dL (26.5 μmol/L) within 48 hours; an increase to at least 1.5 times baseline known or presumed to have occurred within the preceding seven days; or urine output below 0.5 mL/kg/h for six hours. These are general clinical criteria, not exercise-specific thresholds. KDIGO also notes that creatinine-derived eGFR is less accurate in AKI than in a stable state and that clinical judgement remains necessary when applying the criteria [30].

Consequently, a runner may meet a creatinine-based criterion without that observation alone proving structural tubular injury or establishing the clinical importance of the change. Conversely, an uncertain baseline or a single early sample can obscure a relevant deterioration. Interpretation should retain the operational wording “met creatinine-based AKI criteria”, specify the sampling interval and baseline used, and incorporate urine output and subsequent

measurements. Neither recalculating eGFR nor labelling the rise as exercise-related resolves the uncertainty; serial assessment determines whether the trajectory is recovering, stable or worsening.

6.2. Tubular stress and injury biomarkers and urine normalisation

Creatinine and cystatin C primarily describe filtration-related function, whereas urinary neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1) and other investigational analytes are intended to reflect aspects of tubular stress, injury or repair. Cystatin C is less directly affected by muscle-derived creatinine production, but remains a functional marker and does not independently localise structural injury. NGAL has renal and extra-renal sources and may increase with inflammation or hypoxia; KIM-1 is more closely linked to proximal tubular responses, yet neither is sufficiently specific after exercise to support a diagnosis in isolation. Small samples, different assays, dissimilar exercise protocols and inconsistent sampling and follow-up preclude universal cut-offs or a single expected trajectory [31].

In a small marathon cohort, serum creatinine, albuminuria, urine microscopy scores and several biomarkers assigned to injury or repair pathways peaked in the immediate post-race period, with differing patterns at 24 hours. Most participants met the study's creatinine-based AKI definition, and renal tubular epithelial cells or granular casts contributed to positive sediment scores. These concordant findings support a potential tubular stress or injury signal, but the study was hypothesis-generating, involved one race and short follow-up, and did not establish persistent structural damage [32].

Urinary concentration is itself altered by fluid balance, making the denominator part of the result. In a controlled cycling study, conclusions for urinary NGAL, urinary KIM-1 and albumin differed according to whether values were uncorrected or normalised to urinary creatinine, cystatin C or osmolality; the candidate denominators also changed during exercise [33]. A separate 2024 Boston Marathon cohort measured tissue inhibitor of metalloproteinases-2 × insulin-like growth factor-binding protein 7 (TIMP-2 × IGFBP7), NGAL and KIM-1 and normalised them to a reference urine specific gravity, with increases persisting after correction [2]. This cohort did not overlap with the 2019 Boston Marathon sample discussed below. These methods address urine concentration differently and cannot be assumed interchangeable. A concurrent marker rise may indicate a physiological response or potential kidney stress, but is not equivalent to proven tubular necrosis.

6.3. Exercise modality, hydration and repeated exposure

The post-exercise profile depends on the exposure being studied. In healthy young men cycling at a similar relative intensity, longer exercise produced larger changes in several filtration-related and urinary indices than an early, shorter sampling point. However, the prolonged bout also involved greater hypohydration, and the study could not isolate duration, fluid deficit, heat or inflammation as the causal component. Moreover, correction to creatinine, cystatin C or osmolality modified several urinary results [33].

After the 2019 Boston Marathon, urine specific gravity and uNGAL remained above pre-race values at 24 hours, whereas serum creatinine declined between the immediate and 24-hour samples. Pre-race blood could not be collected, preventing formal baseline creatinine comparisons; course, environmental and hydration factors were not separable, and reported sex differences were exploratory [34]. Modality also matters: after a single four-minute high-intensity interval resistance session in 58 healthy young adults, several creatinine-normalised urinary markers rose at two hours and were near baseline at 24 hours, while serum creatinine changed only modestly and chiefly in men. These findings are limited to that squat protocol and its sampling schedule [35].

Repeated exposure should be described equally narrowly. Sixty adults who walked 30–50 km on three consecutive days showed post-exercise uNGAL responses on days 1 and 3, whereas the apparent uKIM-1 response depended on normalisation. Because urinary cystatin C, creatinine and osmolality were all evaluated as correction factors, the appropriate conclusion is a lack of accumulation of the biomarker signal in the studied protocol—not proof that repeated exercise cannot cause cumulative kidney injury [36].

6.4. Clinical interpretation and indications for escalation

Clinical interpretation should combine exercise dose and modality, heat exposure, sampling time, baseline kidney function, urine output, serial creatinine, electrolytes, urinalysis, symptoms and comorbidity. Recent exercise can explain part of an abnormal profile but cannot make it presumptively benign. In endurance reports, severe AKI was uncommon but often presented late and usually involved additional factors such as intercurrent illness or vomiting, non-steroidal anti-inflammatory drug exposure, rhabdomyolysis or substantial volume stress [8].

Urgent or directed assessment is supported by oliguria or anuria, a rising creatinine trajectory, clinically important electrolyte disturbance, haemodynamic instability, persistent vomiting or inability to maintain oral hydration, heat illness, suspected rhabdomyolysis or severe systemic

symptoms. Persistence beyond a course plausibly compatible with the documented exposure and sampling schedule warrants further assessment. Urinalysis adds mechanistic context: haematuria, proteinuria or active sediment—particularly renal tubular epithelial cells or granular casts—should not be dismissed as concentration effects, although no single finding identifies the cause [32].

Additional caution is warranted when the pre-exercise value is unavailable, in people with known kidney disease or concurrent acute illness, and after exposure to potentially nephrotoxic medicines or substances. KDIGO supports prompt evaluation for cause and reversible contributors, with monitoring based on serial serum creatinine and urine output rather than a single measurement [30]. Electrolytes, volume status and the clinical course should determine the intensity and duration of observation. These principles support escalation when abnormalities worsen or fail to resolve, but they do not create exercise-specific admission, discharge or follow-up thresholds.

7. Aminotransferases, lactate dehydrogenase and exercise-induced haemolysis

7.1. AST, ALT and LDH after resistance and endurance exercise

Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH) are multisource analytes rather than direct measures of liver function. AST is abundant in skeletal muscle, ALT is more liver-enriched but is not tissue-exclusive, and LDH is distributed across muscle, erythrocytes, liver and other tissues [6,9]. An isolated post-exercise elevation therefore cannot localise its tissue source or establish hepatocellular injury. The same numerical result may consequently have different implications before exercise, immediately afterwards and during recovery.

The temporal pattern depends strongly on the exposure and sampling schedule. After a single, approximately one-hour weightlifting programme in healthy men not accustomed to resistance training, AST, ALT and LDH increased alongside CK and myoglobin and remained elevated in many participants for at least seven days, whereas gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP) and bilirubin were largely unchanged [6]. In 14 experienced male runners sampled before, every 25 km during, immediately after and 24 hours after a 100-km run, haemoconcentration-corrected AST, ALT, LDH and CK generally increased as distance accumulated; several values were highest during recovery [37].

In a field study conducted during a high-altitude 161-km ultramarathon, paired samples from 36 volunteers showed increases in AST, ALT and bilirubin without a corresponding change in

ALP. Post-race AST, ALT and LDH were positively correlated with CK, supporting a muscular contribution, although GGT was not measured and the association could not exclude concurrent hepatic effects [38]. Thus, concomitant CK elevation and relatively stable GGT or ALP may help frame the differential diagnosis, but neither this pattern nor the AST-to-ALT ratio is sufficiently specific to assign one tissue source.

7.2. Inflammatory and enzyme kinetics during prolonged exercise

Serial observations during prolonged running illustrate that inflammatory and enzyme responses do not evolve synchronously. In the 100-km study, AST, ALT, LDH and CK rose across successive 25-km intervals, while C-reactive protein (CRP) increased more clearly later and was highest at 24 hours [37]. These trajectories describe the studied race and should not be converted into a universal sequence or compared numerically with other protocols.

In a 12-hour track ultramarathon, interleukin-6 (IL-6) and LDH had increased by the six-hour mid-race sample and did not rise significantly further, whereas CRP increased only after race completion. CK, AST and ALT increased by mid-race and rose further immediately after the race [39]. This pattern is consistent with earlier cytokine signalling and a delayed acute-phase response, but inflammatory markers provide systemic context rather than evidence of injury to a particular organ. One normal marker cannot negate an abnormal trajectory in another. Findings from the 12 men with complete measurements and exploratory associations with distance do not establish causal or prognostic relationships.

7.3. Exercise-induced haemolysis

Exercise-induced haemolysis refers to intravascular erythrocyte destruction occurring in association with exercise. Repetitive foot impact is an important mechanical pathway in distance running, but it is not the only proposed mechanism. Erythrocyte compression during muscle contraction, shear stress, hyperthermia, dehydration, hypoxia, acidosis and oxidative or membrane stress may also increase erythrocyte fragility. Laboratory support may include increased circulating free haemoglobin, reduced haptoglobin and, less specifically, changes in unconjugated bilirubin, LDH, AST or reticulocytes [9]. No single component, particularly an isolated fall in haptoglobin, establishes clinically important haemolysis or anaemia.

A recent scoping review of nine studies comprising 267 marathon and ultramarathon runners found descriptive changes consistent with a transient haemolytic signal: weighted post-race haptoglobin was lower and reticulocyte count higher, while mean haemoglobin, haematocrit and erythrocyte count remained within accepted limits [40]. These pooled descriptive means

were not a meta-analysis, the underlying protocols and sampling times were heterogeneous, and 88% of participants were men. Plasma-volume contraction immediately after exercise may mask a fall in haemoglobin or haematocrit, whereas later expansion may produce dilution. Haemolysis should also be distinguished from iron deficiency, gastrointestinal or urinary blood loss and training-related haemodilution; these processes may coexist rather than represent interchangeable explanations. A short-lived biomarker change may be compatible with recovery after exercise, but persistence, anaemia or systemic symptoms require a broader clinical explanation.

7.4. Differential interpretation of multisource biomarkers

Interpretation is safer when laboratory findings are treated as a pattern rather than assigned prematurely to an organ. A parallel rise in CK, AST, ALT and LDH after a muscle-dominant exposure supports a muscular contribution, while GGT, ALP and bilirubin add hepatobiliary context [6,38]. However, neither resistance-exercise findings nor correlations after an altitude ultramarathon can independently rule out liver disease or prove a muscle source. Marked systemic illness or clinical features suggesting acute hepatic or biliary disease warrant urgent assessment, whereas persistent or worsening aminotransferases, discordance with the exercise exposure or muscle markers, concurrent bilirubin, GGT or ALP abnormalities, or relevant medicines, supplements and comorbidity support targeted evaluation.

When haemolysis is plausible, haptoglobin, free haemoglobin, bilirubin, a full blood count and reticulocytes should be interpreted together with plasma-volume change, urinalysis and symptoms. Dark urine may contain haemoglobin or myoglobin, and its appearance alone cannot distinguish intravascular haemolysis from muscle-derived pigment. The relevant context includes exercise modality and dose, baseline results, sampling time, serial trajectory, medicines, comorbidity and clinical examination. Symptomatic or progressive anaemia, a substantial or persistent haemoglobin fall, or haemoglobinuria warrants prompt assessment; persistent or recurrent haemolysis-associated abnormalities, discordance with the full blood count, or suspected iron deficiency supports targeted evaluation. Haemoconcentration, haemodilution and in-sample haemolysis may alter apparent values, and serial change informs context rather than tissue specificity. This synthesis does not define exercise-specific cut-offs, admission criteria or a validated diagnostic algorithm [9,40].

8. Integrating post-exercise biomarker changes into clinical interpretation

8.1. Multibiomarker patterns, exercise dose and recovery

Post-exercise laboratory change is best viewed as a multibiomarker response shaped by exercise modality, intensity, duration and novelty, as well as sampling and recovery intervals. A progressive treadmill test to exhaustion produced acute changes across routine haematological and biochemical measures, some of which differed again after 17 hours [13]. A four-minute high-intensity interval resistance session generated a different combination of early muscle- and kidney-associated signals, with marker-specific trajectories at two and 24 hours [35]. Results after short maximal or resistance exercise therefore cannot be transferred directly to prolonged endurance events.

The same principle applies across endurance exposures. In repeated moderate-intensity walking, there was no biomarker accumulation within the studied protocol, and urinary interpretation depended partly on the normalisation method [36]. Selected male finishers of three long-distance races showed different immediate post-race profiles, but event and sampling differences preclude a universal dose-response hierarchy [41]. During a 12-hour track event, inflammatory, muscle, cardiac and liver-associated markers were already altered at mid-race and followed different trajectories to the finish [39]. A Boston Marathon cohort likewise showed concurrent muscle-, intestinal- and kidney-associated signals; this pattern does not by itself establish simultaneous structural injury of all represented tissues [2].

Recovery is analyte- and protocol-specific. In one 78-km race, several biomarker domains returned to baseline within 48 hours [42]; Section 9 explains why this short follow-up cannot establish long-term safety. After an Ironman-distance triathlon, multiple markers were reassessed one week later, but the small, non-random sample and exploratory sex comparisons limit generalisation [43]. No universal normalisation time should be assumed.

8.2. A practical post-exercise laboratory checklist

We propose a non-scored checklist to structure, rather than replace, clinical reasoning. This conceptual synthesis has not undergone diagnostic or prospective validation. First, what exercise was performed: its modality, intensity, duration, novelty and degree of eccentric or repetitive loading? Second, what were the environmental conditions, hydration status and fluid intake? Third, when exactly did exercise end and specimen collection occur? A small athlete study illustrates that haemoconcentration and subsequent haemodilution depend on protocol and timing [12].

Fourth, is a credible pre-exercise value available? A population reference interval, individual baseline and serial change answer different questions. Biological and analytical variation affect consecutive results, and a value within a population interval may still differ meaningfully from an individual's usual setpoint; this framework provides no sport-specific reference-change values [4]. Fifth, what is the direction and rate of change? Sampling time is integral: pooled hs-cTnT data demonstrate a delayed, heterogeneous trajectory influenced by exercise duration and modality, but modelled limits are not clinical cut-offs for athletes [23]. Prior response may be informative but not deterministic; hs-cTnI responses showed marked interindividual variation and partial reproducibility across exposures and sampling times [27].

Finally, is the result concordant with other markers, and are non-target-tissue sources plausible? Interpretation should integrate symptoms, examination, urine output and indicated ECG, urinalysis or imaging findings, together with comorbidities, medicines, supplements and other relevant exposures. A temporally compatible result, absence of symptoms and a favourable serial trend may support a post-exercise explanation, but do not establish benignity. Conversely, no baseline, atypical kinetics or discordance between exposure and result increases uncertainty without independently diagnosing disease. The checklist assigns no points, mandatory sampling intervals, risk categories, deltas or decision thresholds.

8.3. Red flags requiring urgent or targeted evaluation

Urgent evaluation should be prompted by chest pain, syncope, disproportionate dyspnoea, haemodynamic instability, significant arrhythmia or ischaemic ECG changes; recent exercise does not supersede usual assessment, including serial troponin testing [7]. A troponin value above the 99th percentile may meet the definition of myocardial injury, but myocardial infarction additionally requires evidence of myocardial ischaemia [29].

Other urgent signals include progressive muscle pain, weakness or swelling; dark urine; oliguria or anuria; worsening creatinine; important electrolyte abnormalities; concerning active urine sediment accompanied by renal deterioration or systemic illness; persistent vomiting or inability to maintain oral hydration; suspected heat illness; and marked systemic symptoms. Exertional-rhabdomyolysis data show that CK alone is an inadequate severity measure and complications require clinical and serial laboratory context [22]. General rhabdomyolysis consensus guidance identifies AKI, dangerous electrolyte disturbance, arrhythmia and compartment syndrome as complications requiring active monitoring, but it is not sport-specific [21].

Concerning symptoms or an abnormal examination determine urgency. Targeted follow-up is distinct from emergency assessment. It should be considered when abnormalities persist beyond a course compatible with the exposure, an episode is disproportionate to the work performed, or events recur and suggest underlying disease. A falling biomarker may support interpretation, but cannot alone exclude acute pathology or define safe discharge, cessation of observation or return to training.

9. Uncertain long-term consequences and evidence gaps

9.1. Repeated transient elevations and uncertain long-term consequences

Short-term biomarker normalisation describes the measured trajectory of an analyte; it is not, by itself, evidence that every represented tissue remained structurally intact or fully recovered. In ten male Tarahumara runners completing a 78-km race at moderate altitude, serial cardiac-, kidney-, muscle- and haemolysis-associated markers generally returned to pre-race values within the 48-hour observation period. This finding is appropriately described as normalisation within the studied follow-up, given the small sample, absence of a control group and lack of direct hydration measurements; it cannot establish the safety of other ultramarathons, repeated participation or an ethnic adaptation [42].

Whether recurrent intense exercise and repeated episodes of cardiac- or kidney-associated biomarker release have consequences in susceptible individuals remains uncertain. A proposed cardio-renal model links incomplete recovery, comorbidity, environmental stress and repeated extreme endurance exposure to possible later fibrosis, arrhythmia or renal dysfunction, but the authors explicitly identify the pathway as speculative and note that a causal association between acute markers and chronic disease has not been established [10]. Repeated exposure must therefore not be equated with repeated structural injury, while biomarker normalisation must not be interpreted as proof of complete tissue recovery. Prospective evidence is needed before late outcomes can be attributed to transient post-exercise elevations.

9.2. Evidence gaps and research priorities

Future studies require reproducible descriptions of exercise modality, novelty, intensity, duration, internal and external load, environmental conditions, hydration and fluid intake. Pre-exercise sampling should document the interval since the last training session, and every subsequent specimen should be time-stamped with the biological material, analyser, assay and decision limit reported. These preanalytical and analytical variables are central to sports

laboratory interpretation, while athlete-specific biological-variation data remain limited [1]. Reliable baselines and serial sampling must span early release, delayed peaks and later recovery; one immediate post-event sample cannot define kinetics. Cardiac studies particularly need standardised sampling, training reporting, imaging and longitudinal follow-up [24].

Research populations should include more women, young people, older adults, different training levels and participants with comorbidity. In young-athlete troponin studies, women were sparsely represented, maturation was inconsistently characterised, and assays and cut-offs varied [28]. Exploratory sex patterns in a small, non-random Ironman-distance cohort do not establish biological moderation [43]; similarly, a marathon field study lacked pre-race blood measurements and could not isolate hydration or sex effects [34]. Muscle research should pair standardised sampling with symptoms, strength and performance because indirect markers show timing-dependent and incomplete agreement with functional loss [17].

Kidney studies should report raw and normalised urinary values and relate them to creatinine, cystatin C, urine output, urinalysis and clinical outcomes; protocols, follow-up and normalisation methods remain markedly heterogeneous [31]. Molecular troponin composition is promising but exploratory, not a validated clinical test [26]. Haemolysis research needs consistent definitions, sampling and marker panels, with better representation of women; an isolated haptoglobin decrease does not establish clinically important haemolysis or anaemia [40]. Longitudinal cohorts should examine repeated exposure, recovery, imaging, function and clinical events without presupposing cumulative injury [10].

10. Conclusions

Post-exercise biomarker elevations should be interpreted as time-dependent observations rather than isolated labels. Relevant context includes the type, novelty and dose of exercise; the exact sampling time; hydration and plasma-volume shifts; a credible baseline; serial kinetics; symptoms and examination findings; and concordance with other laboratory, electrocardiographic, imaging or functional information. Exceeding a population reference interval does not automatically establish clinically important organ injury, and concurrent changes across several biomarker domains do not prove simultaneous structural injury in multiple tissues. Conversely, a pattern that appears compatible with a recognised post-exercise trajectory cannot, by itself, exclude acute pathology.

Urgent evaluation should be guided by the standard clinical significance of red flags, including cardiopulmonary symptoms, haemodynamic instability, marked muscle symptoms, reduced urine output, significant electrolyte disturbance, systemic illness, or a worsening trend.

Targeted follow-up should be considered when abnormalities persist beyond the period plausibly explained by the documented exposure, recur, or are disproportionate to the exercise performed. No single biomarker, threshold, delta or normalisation time is applicable across all exercise modalities, populations and analysers. The interpretive checklist proposed in Section 8 is a conceptual synthesis intended to structure clinical questions; it has not undergone diagnostic or prospective validation. Larger and more representative studies are needed, with credible pre-exercise measurements, multiple early and late sampling points, explicit analytical methods, clinically meaningful outcomes and longitudinal follow-up. Such work should link biomarker trajectories to symptoms, function and imaging without assuming either cumulative injury or long-term safety in advance.

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