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RESEARCH ARTICLE

Change in neutrophil-to-lymphocyte ratio after acute and chronic exercise: a systematic review and meta-analysis

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Abstract

Chronic inflammation contributes to many common diseases, and exercise is a widely accessible tool to modulate it. This meta-analysis evaluates the neutrophil-to-lymphocyte ratio (NLR), a simple inflammatory marker, to better understand and optimize the anti-inflammatory effects of exercise. The present meta-analysis aims to systematically evaluate existing evidence on NLR changes induced by acute and chronic exercise. This study was registered in PROSPERO (CRD420251042422). Studies were selected based on PICO criteria: Population (P)—human participants regardless of age or health; Intervention (I)—acute or chronic exercise; Comparison (C)—NLR levels before exercise; Outcome (O)—within-subject change in NLR measured before and after exercise. We searched PubMed, EMBASE, Scopus, Web of Science, and the Cochrane Library extensively. Pooled results were expressed as mean difference (MD) with 95% confidence intervals (CIs) using STATA version 19.0. Twenty-six studies with a total of 1,203 participants were included. NLR levels showed no significant change immediately after acute exercise (MD = 0.03; 95% CI: −0.24 to 0.30; $P = 0.82$; $k = 12$, $I^2 = 93.6\%$) but increased significantly 1–3 h postexercise (MD = 1.23; 95% CI: 0.46–1.99; $P = 0.002$; $k = 5$, $I^2 = 93.3\%$). Chronic exercise was associated with a significant overall decrease in NLR (MD = −0.30; 95% CI: −0.56 to −0.04; $P = 0.02$; $k = 15$, $I^2 = 98.4\%$). Studies with older participants reported greater reductions in NLR following chronic exercise. Sensitivity analysis confirmed that no single study had a disproportionate influence on the pooled estimates, and publication bias tests did not suggest bias. Acute exercise induces a transient increase in NLR between 1 and 3 h postexercise, whereas chronic exercise leads to sustained reductions, reinforcing the value of exercise as a nonpharmacologic strategy to reduce systemic inflammation, as reflected by this inflammatory marker.

NEW & NOTEWORTHY Neutrophil-to-lymphocyte ratio (NLR) was unchanged immediately after acute exercise but increased significantly by 1–3 h later, reflecting a transient inflammatory response. Chronic exercise leads to a significant reduction in NLR, indicating long-term anti-inflammatory benefits. Studies with older participants reported greater reductions in NLR following chronic exercise.

exercise; inflammation; meta-analysis; neutrophil-to-lymphocyte ratio

INTRODUCTION

Exercise has a major impact on the immune system, with effects that differ depending on intensity, duration, and frequency (1). Certain forms of acute exercise can elicit a transient inflammatory response, depending on the exercise modality, intensity, and individual characteristics. For example, a recent meta-analysis found that exercise performed under both hypoxic and normoxic conditions led to an increase in interleukin 6 (IL-6) levels, whereas tumor necrosis factor-alpha (TNF-α) elevation was observed only during hypoxic exercise (2). However, chronic training has been shown to provide anti-inflammatory advantages through many pathways, thereby holding considerable promise for the prevention and treatment of conditions associated with chronic inflammation (3–7). For example, a recent meta-analysis reported that, regardless of the type of training, exercise reduced circulating levels of several inflammatory and metabolic markers—including adiponectin, C-reactive protein (CRP), interleukins (IL-6, IL-18, IL-20), leptin, and tumor necrosis factor-alpha (TNF-α)—in individuals who were overweight or with obesity (4). Another meta-analysis suggested that in patients with type 2 diabetes, exercise reduces the level of inflammatory cytokines, including CRP, TNF-α, and IL-6 (5). In addition, Sheldon et al. (7) examined exercise-induced inflammatory and metabolic adaptations in older adults and found that aerobic training produced the greatest anti-inflammatory benefits, followed by resistance training.

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These divergent responses between acute and chronic exercise highlight a complex pattern of immune modulation that may be effectively captured using integrated indicators such as neutrophil-to-lymphocyte ratio (NLR)(8). Neutrophils, as part of the innate immune response, are among the first responders to exercise-induced stress or muscle damage, releasing enzymes and reactive species that promote inflammation (9). Lymphocytes, in contrast, mediate adaptive immunity and contribute to immune surveillance and recovery (10). The dynamic and often opposing behavior of these two cell types during and after exercise underpins the utility of the NLR, measured within the blood circulation, as a simple and integrative marker reflecting the balance between proinflammatory activation and immune regulation.

NLR is a widely accessible, simple, and sensitive biomarker of inflammation (11) and has been used and studied in a variety of disorders, including cancer, urinary tract infection, COVID-19 infection, stroke, and myocardial infarction (12–17). In contrast to commonly studied cytokines that require specialized laboratory techniques, NLR is easily calculated from standard hematological parameters, offering a cost-effective and widely accessible measure of systemic inflammatory status that may enhance translational applicability. Despite the presence of numerous original studies examining NLR modulation following acute or long-term exercise, no meta-analysis or systematic review has been conducted on this subject to date.

To address this gap, the present meta-analysis aims to systematically evaluate the existing evidence on the variations in NLR levels induced by acute and chronic exercise. By consolidating these findings, this study seeks to elucidate the role of NLR in exercise, offering insights into its potential as a predictive marker for recovery and advancing our understanding of the interplay between exercise, inflammation, and recovery processes. By elucidating the inflammatory profile associated with exercise, this work may provide a foundation for optimizing exercise prescriptions for people needing anti-inflammatory interventions.

METHOD

The protocol of the study was registered in PROSPERO (ID: CRD420251042422), and the completed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist is provided in Supplemental Tables S1 and S2.

Search Strategy

We systematically searched PubMed, Embase, Web of Science, Cochrane, and Scopus for articles published before September 2, 2025. The search strategy was as follows: (“exercise”[MeSH Terms] OR “exercise”[Title/Abstract] OR “Sport”[Title/Abstract] OR ((“Physical”[All Fields] OR “high-intensity interval”[Title/Abstract] OR “weightlifting”[Title/Abstract] OR “Moderate-Intensity continuous”[Title/Abstract] OR “strength”[Title/Abstract] OR “aerobic”[Title/Abstract] OR “resistance”[Title/Abstract]) AND (“training”[Title/Abstract] OR “Program”[Title/Abstract]))) AND (“Neutrophil to lymphocyte ratio”[All Fields] OR “NLR”[All Fields]). No limitations regarding date or language were imposed. Reference lists of eligible studies were also screened. Supplemental Table S3 contains the complete search strategies for each database.

Study Selection

Every article found through systematic searches of electronic databases was converted to the EndNote bibliographic and reference manager software. All duplicates were omitted. Two authors then independently reviewed the abstracts and titles, and potential studies were assessed for eligibility using predetermined criteria. Any disagreements were settled via discussion by the third author.

Eligibility Criteria

The PICO framework was used to define the following inclusion criteria:

1) Population (P): human participants of any age or health status, regardless of baseline physical activity level;
2) Intervention (I): acute or chronic exercise programs, with NLR assessed in peripheral human blood samples;
3) Comparison (C): NLR levels of peripheral human blood measured before exercise compared with levels after exercise; and
4) Outcome (O): within-subject change in NLR measured before and after exercise.

Exclusion criteria were as follows:

1) nonpeer-reviewed studies (e.g., conference abstracts), patents, or noncomparative studies (e.g., case series, case reports);
2) nonquantitative studies (e.g., book chapters, commentaries, reviews, editorials);
3) animal model studies; and
4) studies focusing on specific tissues (e.g., cerebrospinal fluid) rather than peripheral blood.

Data Extraction

For each included study, we extracted the first author, year, country, sample size, mean age, sex (% male), body mass index (BMI), exercise type and duration (acute or chronic), health status (healthy vs. patient), exercise intensity, and pre- and postexercise NLR data.

Risk of Bias Assessment

We assessed methodological quality using the National Institutes of Health (NIH) Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group, which includes 12 items on design, outcome reliability, adherence, and statistics (18). Each item was rated “Yes,” “No,” “Cannot determine,” or “Not reported.” Two reviewers independently evaluated all studies and reconciled inconsistencies through discussion.

Statistical Analysis

The statistical analysis was carried out using STATA version 19.0 (Stata Corporation, College Station, TX). In studies where only graphical findings were presented rather than numerical data, we digitized the graphs and retrieved the data using WebPlotDigitizer Software. The reliability of WebPlotDigitizer has been previously validated (19). We imputed $r = 0.7$. The correlation coefficient (r) accounts for the within-subject relationship between pre- and post-intervention values (20–22). Overall mean difference (MD) in NLR values, along with the corresponding 95% confidence intervals (CIs), was reported. When the median and interquartile range were reported, we converted them to mean ± standard deviation (SD) using the method by Wan et al. (23). In addition, standard error (SE) was converted to SD using $SD = SE \times \sqrt{n}$.

To further assess statistical heterogeneity among the studies, the Cochrane Q test ($\chi 2$) and the I^2 test were used (24). A random-effect model was then used, with subgroup analysis based on participants' health status, exercise intensity, and quality of evidence, and meta-regression based on age, percentage of males, sample size, BMI, and exercise duration used to determine the source of heterogeneity. To categorize exercise severity for subgroup analysis, we used the authors' own classification of exercise intensity. When studies did not report exercise intensity, we used the following definitions to determine exercise intensity (25):

1) High-intensity or severe exercise was defined as ≥77% of maximum heart rate (HRmax), ≥64% of $\dot{V}O_{2max}$, rating of perceived exertion (RPE) ≥14, or ≥70% of one-repetition maximum (1RM) for resistance training.
2) Moderate-intensity exercise was defined as 64%–76% of HRmax, 46%–63% of $\dot{V}O_{2max}$, or 50%–69% of 1RM, or an RPE between 11 and 13.

Sensitivity analysis was conducted by a leave-one-out meta-analysis to illustrate the impact of each individual study on the overall estimate by sequentially excluding one study from the meta-analysis. In addition, the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method was used to assess the certainty of evidence (26). The funnel plot, Egger's test, and Begg's test were all used to investigate publication bias. A two-tailed $P < 0.05$ indicated statistical significance.

RESULT

Study Selection and Characteristics

The PRISMA flow diagram in Fig. 1 shows the selection process for studies included in this meta-analysis. Initially, 1,885 records were identified. After removing duplicates, studies were screened in two steps: first by title/abstract, then by full-text review. Through this process, our meta-analysis includes 26 studies with 1,203 participants in total. Among these, 12 studies assessed NLR changes immediately after acute exercise (27–38), with five of those also evaluating NLR changes 1–3 h postexercise (29, 30, 34–36). Fifteen studies focused on NLR changes after chronic exercise (29, 39–52). Among the acute exercise studies, 10 involved healthy participants (28, 30–38), and eight were rated as having high methodological quality (27, 29–34, 38). In the chronic exercise group, 10 studies included participants with chronic disorders (29, 40, 42–44, 47–49, 51, 52), and 11 demonstrated high methodological quality (29, 39–45, 48, 51, 52). Additional details on the acute and chronic exercise studies are provided in Tables 1 and 2, respectively. In addition, Supplemental Table S4 shows the quality assessment results of each included study using the NIH tool.

Meta-Analysis of the Differences in NLR Level Before and Immediately After Acute Exercise

Immediately after acute exercise, there was no significant change in NLR levels (MD = 0.03; 95% CI: −0.24 to 0.30; P = 0.82; Fig. 2). Based on the GRADE method, the certainty of evidence was downgraded to very low (Supplemental Table S5). Substantial heterogeneity was present across studies (I^2 = 93.6%; P for heterogeneity < 0.001), and a random-effects model was used.

For exercise intensity, studies assessing moderate exercise reported no effect on NLR (MD = 0.10; 95% CI: −0.26 to 0.45; P = 0.59), whereas those evaluating vigorous exercise also showed no significant change (MD = −0.02; 95% CI: −0.35 to 0.32; P = 0.92). The between-group difference was not statistically significant (P = 0.65; Supplemental Fig. S1).

For participant health status, studies involving healthy individuals or athletes showed no effect (MD = 0.02; 95% CI: −0.26 to 0.29; P = 0.91), and those including patients with chronic disorders also reported no significant change (MD = 0.10; 95% CI: −0.34 to 0.55; P = 0.65). The between-group difference was not significant (P = 0.75; Supplemental Fig. S2).

For NIH quality assessment, studies rated as good (MD = −0.00; 95% CI: −0.38 to 0.38; P = 0.99) and those rated as fair (MD = 0.10; 95% CI: −0.24 to 0.45; P = 0.56) both showed null effects. The between-group difference was not statistically significant (P = 0.69; Supplemental Fig. S3). Overall, these factors did not explain the observed heterogeneity.

Meta-regression analyses revealed that none of the examined covariates—sample size (coefficient = 0.0023; P = 0.71), age (coefficient = −0.0041; P = 0.75), BMI (coefficient = −0.072; P = 0.43), or male percentage (coefficient = −0.0054; P = 0.38)—were significantly associated with the effect size. All models showed substantial residual heterogeneity (I^2 ranging from 79.7% to 94.1%), indicating that these variables did not explain the between-study variability. The adjusted R^2 values were near 0 (ranging from −11.8% to 2.8%), suggesting no meaningful reduction in heterogeneity. These findings indicate that sample size, age, BMI, and sex distribution are unlikely to be major sources of heterogeneity in the effect of acute exercise on NLR.

Meta-Analysis of the Differences in NLR Level Before and 1–3 h After Acute Exercise

The meta-analysis of five studies assessing NLR levels 1–3 h after acute exercise demonstrated a statistically significant increase in NLR (MD = 1.23; 95% CI: 0.46–1.99; P = 0.002; Fig. 3). Based on the GRADE method, the certainty of evidence was downgraded to very low (Supplemental Table S5). Substantial heterogeneity was present across studies (I^2 = 93.3%; P for heterogeneity < 0.001), and a random-effects model was applied.

For exercise intensity, moderate exercise was associated with a significant increase in NLR (MD = 1.10; 95% CI: 0.14–2.05; P = 0.02), whereas vigorous exercise showed a nonsignificant trend toward an increase in NLR (MD =

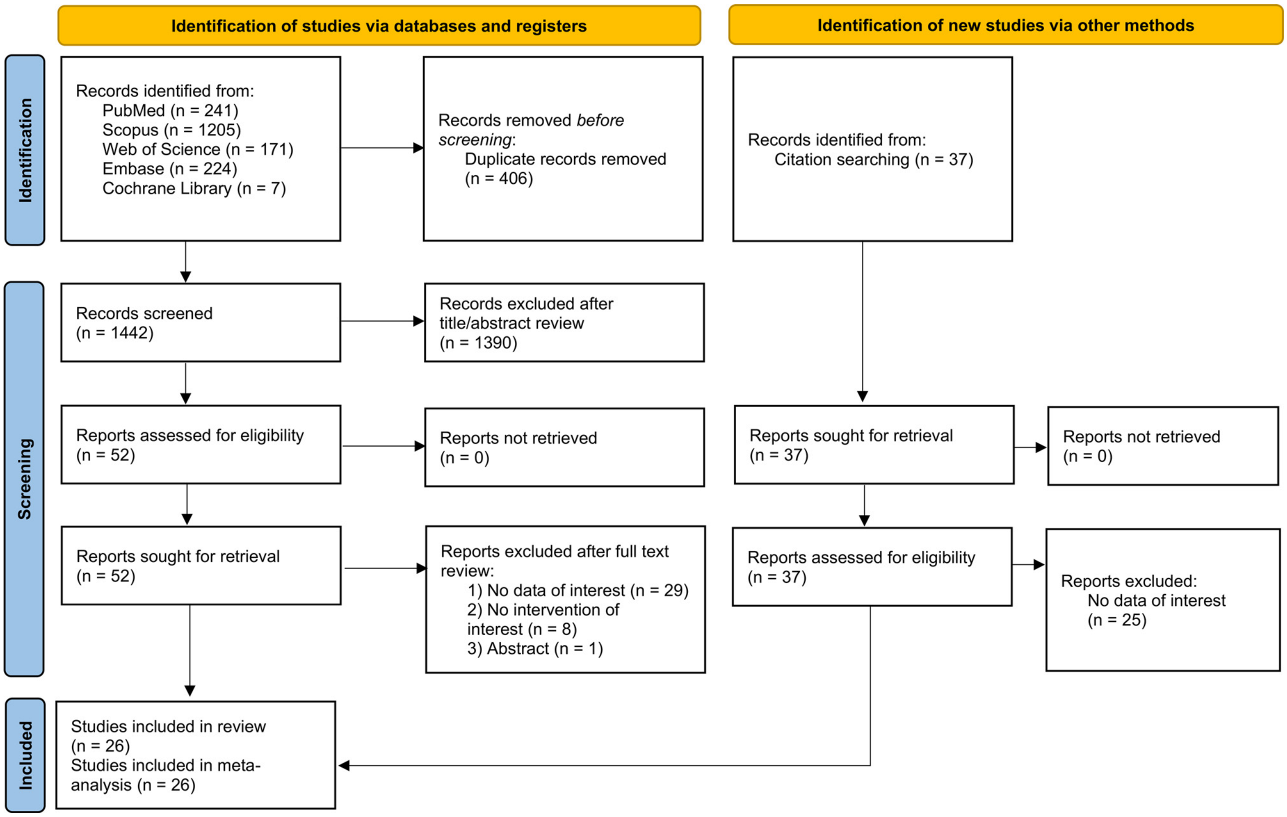

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the selection process of the studies.

1.45; 95% CI: −0.11 to 3.01; $P = 0.06$). The between-group difference was not statistically significant ($P = 0.71$; Supplemental Fig. S4).

For participant health status, studies involving healthy individuals or athletes demonstrated a significant increase in NLR (MD = 1.18; 95% CI: 0.22–2.15; $P = 0.01$), whereas those including patients with chronic disorders did not (MD = 1.43; 95% CI: −0.38 to 3.24; $P = 0.12$). The between-group difference was not significant ($P = 0.81$; Supplemental Fig. S5).

For NIH quality assessment, studies rated as good showed a significant increase in NLR (MD = 1.29; 95% CI: 0.40–2.17; $P = 0.005$), whereas studies rated as fair did not (MD = 1.13; 95% CI: −0.85 to 3.11; $P = 0.26$). The between-group difference was not statistically significant ($P = 0.89$; Supplemental Fig. S6).

Meta-regression analyses revealed that none of the examined covariates—sample size (coefficient = 0.009; $P = 0.87$), age (coefficient = 0.026; $P = 0.54$), BMI (coefficient = −0.419; $P = 0.35$), or male percentage (coefficient = −0.015; $P = 0.35$)—were significantly associated with the effect size. All models showed substantial residual heterogeneity (I^2 ranging from 89.5% to 94.6%), indicating that these variables did not explain the between-study variability. The adjusted R^2 values were close to 0 (ranging from −28.6% to 14.5%), suggesting no meaningful reduction in heterogeneity. These findings indicate that sample size, age, BMI, and sex distribution are unlikely to be major sources of heterogeneity in the effect of acute exercise on NLR.

Meta-Analysis of Changes in NLR Following Chronic Exercise

The meta-analysis of 15 studies evaluating changes in NLR levels before and after chronic exercise showed a significant overall reduction in NLR (MD = −0.30; 95% CI: −0.56 to −0.04; $P = 0.02$; Fig. 4). Based on the GRADE method, the certainty of evidence was downgraded to low (Supplemental Table S5). Substantial heterogeneity was observed across studies ($I^2 = 98.4\%$; P for heterogeneity < 0.001), and a random-effects model was used.

When stratified by exercise intensity, moderate exercise was associated with a nonsignificant reduction in NLR (MD = −0.32; 95% CI: −0.73 to 0.09; $P = 0.12$), and severe exercise also showed a nonsignificant reduction (MD = −0.28; 95% CI: −0.62 to 0.06; $P = 0.10$). The between-group difference was not significant ($P = 0.87$; Supplemental Fig. S7).

For participants' health status, healthy individuals showed no significant change in NLR (MD = −0.03; 95% CI: −0.34 to 0.28; $P = 0.83$), whereas people with comorbidities demonstrated a significant reduction (MD = −0.47; 95% CI: −0.80 to −0.13; $P = 0.006$). The between-group difference was not statistically significant ($P = 0.06$; Supplemental Fig. S8).

In terms of NIH quality assessment, studies rated as good showed a significant reduction in NLR (MD = −0.44; 95% CI: −0.75 to −0.12; $P = 0.007$), whereas those rated as fair did not (MD = 0.01; 95% CI: −0.16 to 0.17; $P = 0.93$). The difference between subgroups was statistically significant ($P =$

Table 1. *General characteristics of the included studies in acute exercise analysis*

Author	Year	Region	Participants	Mean Age	BMI	Exercise Type	Gender (Male %)	Sample Size	NLR Level: Preexercise	NLR Level: Immediately After Exercise	NLR Level: 1–3 h After Exercise	Exercise Protocol	Exercise Intensity	NIH
Korkmaz (27)	2018	Turkey	Patients with stable coronary symptoms	57		Treadmill exercise testing	78	113	2.04 ± 0.63	2.41 ± 0.78		Bruce protocol	Moderate	Good
Kaniganti (28)	2019	India	National-level trained weightlifters	19		Weightlifting training sessions (snatch, clean and jerk, and back squats)	38.46	13	1.46 ± 0.64	2.15 ± 0.69		High-intensity weightlifting training sessions (75% relative intensity)	Vigorous	Fair
Joisten (29)	2021	Switzerland	Patients with multiple sclerosis	49.7	25.4	24-min single bout of moderate-intensity continuous training on a bicycle ergometer	45.45	33	3.18 ± 2.00	3.23 ± 2.01	After 3 h: 3.83 ± 2.38	Moderate-intensity continuous training at 65% of their maximum heart rate	Moderate	Good
				50.9	25.3	5 × 1.5-min intervals, single bout of high-intensity interval training on a bicycle ergometer	31.42	35	3.80 ± 3.27	3.31 ± 2.15	After 3 h: 6.32 ± 6.54	High-intensity interval training at 95%–100% of their maximum heart rate	Vigorous	
Bankowski (30)	2025	Poland	Amateur middle-aged long-distance runners	38.33	23.85	Treadmill running test	100	30	1.73 ± 0.61	1.26 ± 0.55	After 1 h: 3.73 ± 1.68	A graded maximal treadmill running test with increasing speed/tilt until exhaustion	Vigorous	Good
Chang (31)	2020	Taiwan	Healthy male national division I track-and-field athletes	21.35	21.55	Repeated vertical jumping exercises	100	20	1.5 ± 2.16	0.95 ± 1.09		High-intensity jumping exercises at a frequency of 0.7 Hz (12 repetitions of 10 jumps; total of 120 jumps)	Vigorous	Good
Gomes (32)	2020	Brazil	Healthy recreational high-intensity functional training practitioners	31	25.7	Single high-intensity functional training session, gymnastics, also known as the "Cindy" workout	52.17	23	1.26 ± 0.43	0.80 ± 0.25		Training consisted of completing as many rounds of 5 pull-ups, 10 push-ups, and 15 air squats as feasible within a 20-min timeline	Vigorous	Good
Isik (33)	2022	Turkey	Healthy, elite Taekwondo athletes	20.5	21.12	90 min of unit training tailored to Taekwondo, which includes a 50-min high-intensity interval training component	50	24	2.15 ± 1.11	3.50 ± 2.0		The range of training intensity was 80%–90%	Vigorous	Good

Continued

Table 1.— *Continued*

Author	Year	Region	Participants	Mean Age	BMI	Exercise Type	Gender (Male %)	Sample Size	NLR Level: Preexercise	NLR Level: Immediately After Exercise	NLR Level: 1–3 h After Exercise	Exercise Protocol	Exercise Intensity	NIH
Lee (34)	2021	Taiwan	Untrained and healthy males	25.1	23.66	30 min of treadmill-based fixed-intensity trial	100	16	2.06 ± 0.78	1.76 ± 0.86	After 1.5 h: 2.60 ± 1.08	60% $\dot{V}O_{2max}$ exercise challenge	Moderate	Good
Adammek (35)	2024	Germany	Young healthy adults	25.5	22.9	40-min aerobic exercise on a bicycle ergometer	50	12	1.64 + 0.60	1.54 + 0.63	After 1 h: 3.80 + 1.44	A moderate intensity of 60% $\dot{V}O_{2max}$ was chosen	Moderate	Fair
Schlagheck (36)	2020	Germany	Healthy males	24.6	25.4	Acute resistance exercise for 50 min	100	24	1.99 ± 0.76	1.82 ± 0.71	After 1 h:2.13 ± 0.85	Exercise machine at 70% one-repetition maximum	Vigorous	Fair
Zacher (37)	2022	Germany	Healthy National Olympic squad athletes	16.1	20.3	Hallman-Venrath protocol on a standardized bicycle ergometer	44	25	1.42 ± 0.56	1.43 ± 0.70		Maximal exercise test	Vigorous	Fair
Dumic (38)	2022	Croatia	Recreational healthy divers	39.25	26.13	Recreational SCUBA dive at 20–30 m depth, lasting 30 min each, in cold seawater conditions	100	14	1.87 ± 0.70	2.70 ± 2.19		A dive was conducted to a maximum depth of 20 m for a duration of 30 min, involving a steady descent to the maximum depth and a gradual rise to the surface without a decompression stop	Moderate	Good

Values are means ± SD. BMI, body mass index; NIH, National Institutes of Health; NLR, neutrophil-to-lymphocyte ratio.

Table 2. *General characteristics of the included studies in chronic exercise analysis*

Author	Year	Region	Participants	Sample Size	Mean Age (Years)	BMI	Gender (Male%)	Exercise Intervention/ Evaluation	NLR Preexercise	NLR Postexercise	Exercise Protocol	Exercise Intensity	NIH Score
Makras (39)	2005	Greece	Healthy young males at a basic military training camp	48	21.3	23.2	100	4-wk, five times per week, moderate intermittent mixed endurance exercise and resistance exercise	3.3 ± 1.25	2.3 ± 0.69	Gymnastics, walking, running, and climbing, with or without backpacks	Moderate	Good
Joisten (29)	2021	Switzerland	Patients with multiple sclerosis	33	49.7	25.4	45.45	Moderate-intensity continuous training on a bicycle ergometer, three times per week for 3 wk	3.18 ± 2.00	3.00 ± 1.72	Moderate-intensity continuous training at 65% of the maximum heart rate	Moderate	Good
				35	50.9	25.3	31.42	Training with high-intensity intervals on a bicycle ergometer, three times weekly for 3 wk	3.80 ± 3.27	2.91 ± 2.27	High-intensity interval training at 95%–100% of their maximum heart rate	Vigorous	
Rias (40)	2020	Indonesia	Participants with type 2 diabetes mellitus	20	54.70		35	Regular walking for a duration of at least 30 min, five times per week for 8 wk	2.55 ± 0.18	1.36 ± 0.18	Walk around the house, park, or roads for a total of 150 min/wk	Moderate	Good
Hadjicharalambous (41)	2024	Cyprus	Well-trained adolescent soccer players	36	16.4	22.3	100	8-wk soccer-specific training 6 days/wk, 8 friendly matches, and 48 training sessions. The sessions lasted between 60 and 90 min	1.15 ± 0.35	1.70 ± 0.80	Soccer-specific, high-intensity training	Vigorous	Good
Kaya (42)	2019	Turkey	Outpatient patients of the cardiac rehabilitation unit	211	56.28		46	30 sessions of the tailored cardiac rehabilitation program in 10 wk Cycle ergometer training, strengthening exercises (after 2 wk), and tailored adjustments every 10 sessions (based on Borg scale and progress)	1.70 ± 0.67	1.53 ± 0.60	Aerobic exercise + the program is structured to engage the major muscle groups of the upper and lower extremities using 60%–80% of the maximal load for 10 repetitions per muscle group	Moderate	Good

Continued

Table 2.— *Continued*

Author	Year	Region	Participants	Sample Size	Mean Age (Years)	BMI	Gender (Male%)	Exercise Intervention/ Evaluation	NLR Preexercise	NLR Postexercise	Exercise Protocol	Exercise Intensity	NIH Score
Mahmoud (43)	2022	Iran	Sedentary, overweight, nonmenopausal women	19	Between 28 and 43	29.69	0	Linear or nonlinear periodized resistance training, three weekly training sessions for 12 wk	2.21 ± 0.27	1.91 ± 0.25	Resistance training programs at 60%–90% of one-repetition maximum	Vigorous	Good
Malczynska-Sims (44)	2022	Poland	People who have been diagnosed with Parkinson's disease	15	64.24	26.55	60	12 wk of high-intensity interval training using a stationary cycloergometer. Three 1-h training sessions were completed three times per week, for a total of 36 training sessions lasting 60 min	2.58 ± 1.16	1.8 ± 0.5	High-intensity interval training 60%–80% of their individualized maximum heart rate	Vigorous	Good
Mohamed (45)	2021	Egypt	Young and healthy adults with a past history of COVID-19	30	Between 18 and 35	Less than 35		40-min aerobic program using cycle ergometer protocols, 6 wk, three sessions per week	1.78 ± 0.6	1.68 ± 0.3	Aerobic program three times per week (on different days) at a moderate intensity of 65%–75% peak heart rate	Moderate	Good
				30				Resistance training for the lower body using free weights (e.g., weightlifting, sandbags), 6 wk, three sessions per week	1.7 ± 0.78	1.73 ± 0.54	The resistance training group initiated progressive training sessions, which consisted of one set of exercises for a maximum of three sets and 10–15 repetitions at 70% of one-repetition maximum	Vigorous	

Continued

Table 2.— *Continued*

Author	Year	Region	Participants	Sample Size	Mean Age (Years)	BMI	Gender (Male%)	Exercise Intervention/ Evaluation	NLR Preexercise	NLR Postexercise	Exercise Protocol	Exercise Intensity	NIH Score
Nobari (46)	2021	Iran	Professional youth soccer players	15	15.5	21.7	100	Players participated in four training sessions and one match per week for 14 wk	1.5 ± 0.6	1.9 ± 1.1	All participants underwent standardized training, and based on the introduction, the average heart rate during youth soccer has been reported as 82%–87% of maximum heart rate	Vigorous	Fair
Pagola (47)	2020	Spain	Short-term breast cancer survivors who had previously reported cancer-related fatigue at baseline	10	51	27.3	0	Unsupervised aerobic training, instructed to complete ≥150 min/wk moderate-vigorous physical activity, and less supervised resistance exercises for 16 wk	2.3 ± 0.6	2.2 ± 1.3	Moderate exercise aerobic training: ≥150 min/wk of moderate-vigorous physical activity + resistance training	Moderate	Fair
				9	47	25.8		Supervised high-intensity aerobic (treadmill running, aerobic games, cycle-ergometer pedaling, or elliptical ergometer exercise) and resistance exercises for 16 wk	2.0 ± 0.8	1.6 ± 0.6	High-intensity aerobic exercise at very hard intensity level + resistance training	Vigorous	
Poyraz (48)	2021	Turkey	Nondipper hypertensive patients	58	56	26.30	44.8	16-wk supervised cardiac rehabilitation program (aerobic exercise on a cycle ergometer). Each session is 60 min, twice a week for the first 4 wk, then three times a week for the next 12 wk	2.21 ± 0.69	2.07 ± 0.66	Moderate-intensity aerobic exercise program. Patients maintained a perceived exertion rating of 11–13 on the 6–20 Borg scale	Moderate	Good

Continued

Table 2.— *Continued*

Author	Year	Region	Participants	Sample Size	Mean Age (Years)	BMI	Gender (Male%)	Exercise Intervention/ Evaluation	NLR Preexercise	NLR Postexercise	Exercise Protocol	Exercise Intensity	NIH Score
Qian (49)	2024	China	Patients with type 2 diabetic mellitus	22		24.76		2 wk of preadaptation training followed by 8 wk of slow-velocity eccentric-only resistance training, conducted three times per week every other day for a duration of 10 wk	1.38 ± 0.28	1.51 ± 0.25	Borg RPE scale (6–20) was between 11 and 13	Moderate	Fair
Widasari (50)	2023	Indonesia	Healthy health-care workers with a previous history of mild and moderate COVID-19 infection	19	40.11	27.58	21.9	Moderate intensity: continuous aerobic exercise lasting 30 min every day, prescribed as treadmill walking for 6 wk	1.93 ± 0.47	1.83 ± 0.38	Three miles per hour (mph) as the starting pace, with a goal of 55%–69% of maximum heart rate	Moderate	Fair
				11	33.09	25.26	81.8	30 min a day of interval high-intensity aerobic exercise, prescribed as running or jogging on a treadmill for 6 wk	1.74 ± 0.54	1.77 ± 0.41	Initiate with a velocity of 4.5 mph to attain 70%–89% of maximum heart rate	Vigorous	
Zengin (51)	2019	Turkey	Patients with STEMI diagnosis, who underwent primary PCI	68	58.23		79.4	8 wk of cycling ergometry at least 1 mo after primary PCI, for an average of four sessions weekly, each lasting 30 min	3.11 ± 1.95	2.39 ± 1.03	70%–85% of maximum heart rate	Vigorous	Good
Kara (52)	2023	Turkey	Stable coronary artery disease undergoing exercise-based cardiac rehabilitation	200	56.2	28.3	78	Aerobic exercise on a cycle ergometer + muscle training before sessions for 5 days each week, totaling 6 wk. Each session lasted 30 min	2.64 ± 1.04	1.70 ± 0.55	Progressively increased to 70%–85% of maximal heart rate reserve after starting at 40%–50%. The RPE for the patients' activity was 13–15	Vigorous	Good

Values are means ± SD. BMI, body mass index; MET, metabolic equivalent of task; NIH, National Institutes of Health; NLR, neutrophil-to-lymphocyte ratio; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

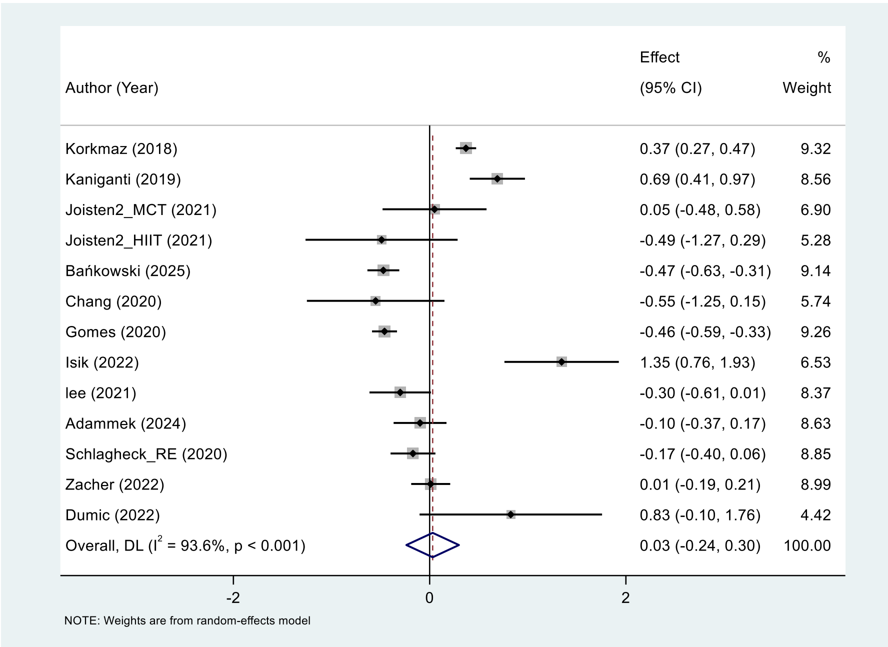

Figure 2. Meta-analysis of the differences in NLR level before and immediately after acute exercise. CI, confidence interval; DL, DerSimonian Laird test for heterogeneity; NLR, neutrophil-to-lymphocyte ratio.

0.01; Supplemental Fig. S9). These findings suggest that chronic exercise is generally associated with reductions in NLR, with stronger evidence observed in studies rated as higher quality.

Meta-regression analyses were conducted to explore potential sources of heterogeneity in the change in NLR following chronic exercise. Age was significantly associated with the effect size (coefficient = −0.017; 95% CI: −0.034 to −0.0004; P = 0.04), suggesting that studies with older participants tended to report greater reductions in NLR. In contrast, sample size (coefficient = −0.001; 95% CI: −0.005 to 0.002; P = 0.35), BMI (coefficient = −0.087; 95% CI: −0.209 to 0.035; P = 0.14), male percentage (coefficient = 0.0015; 95% CI: −0.006 to 0.009; P = 0.68), and exercise duration (coefficient = 0.027; 95% CI: −0.031 to 0.086; P = 0.33) were not significantly associated with effect size. Residual heterogeneity remained very high in all models (I^2 ranging from 95.17% to 98.49%), indicating that these covariates did not adequately explain the between-study variability.

Leave-One-Out Sensitivity Analysis

As shown in Fig. 5, the leave-one-out sensitivity analysis revealed that no single study had a disproportionate influence on the overall effect size for changes in NLR following both

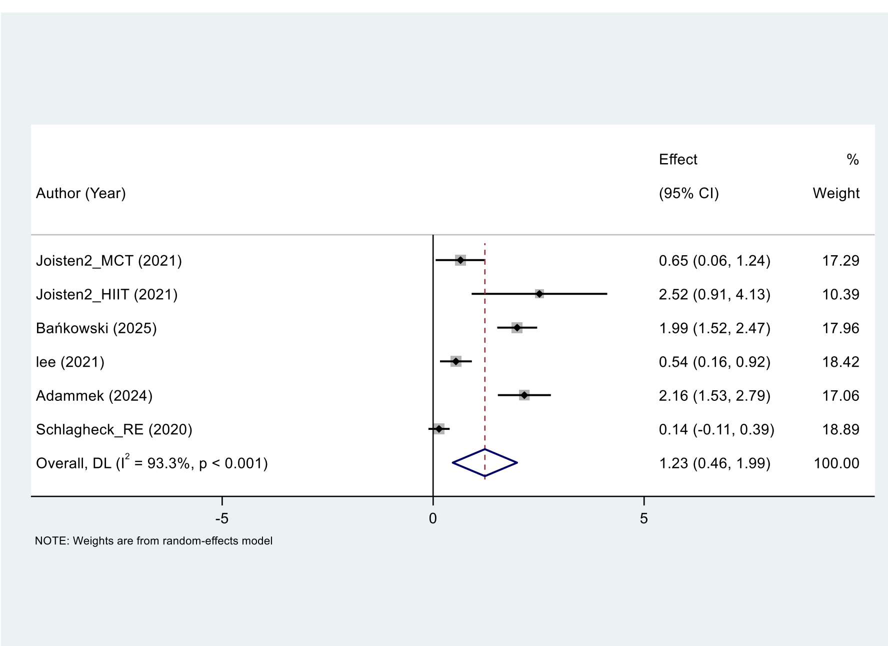

Figure 3. Meta-analysis of the differences in NLR level before and 1–3 h after acute exercise. CI, confidence interval; DL, DerSimonian Laird test for heterogeneity; NLR, neutrophil-to-lymphocyte ratio.

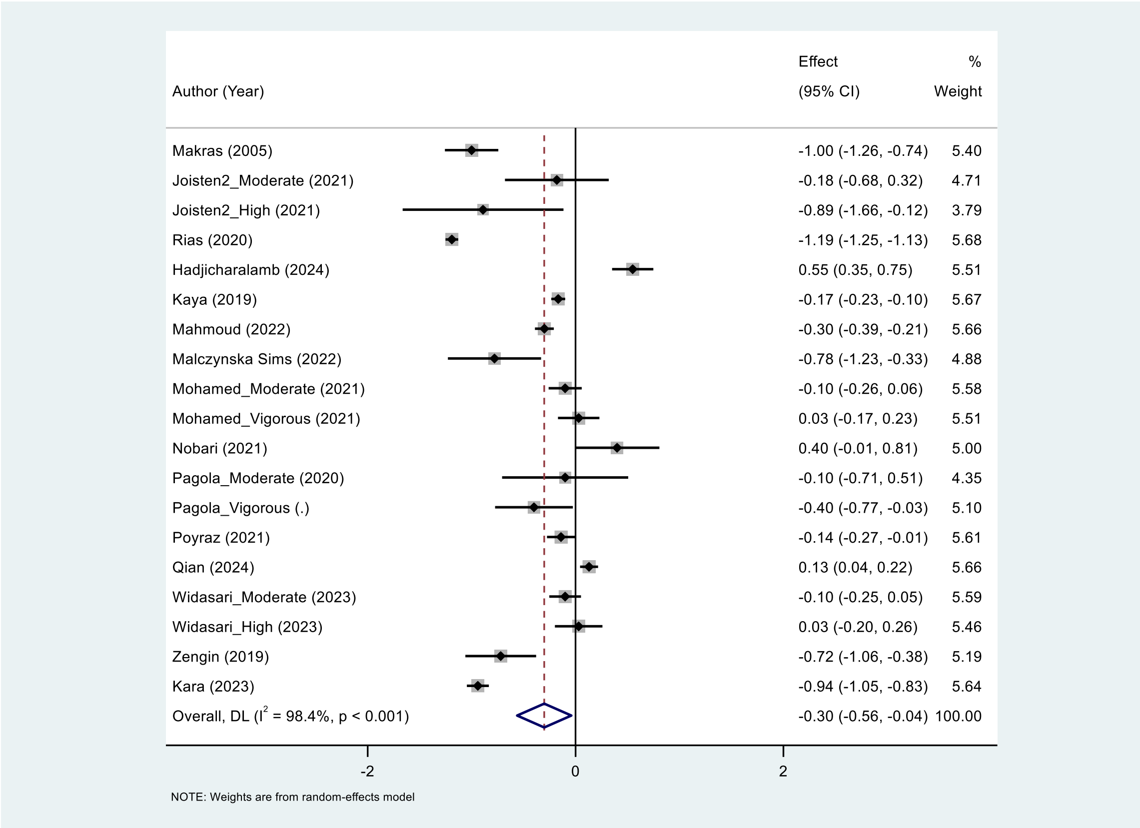

Figure 4. Meta-analysis of the differences in NLR level before and after chronic exercise. CI, confidence interval; DL, DerSimonian Laird test for heterogeneity; NLR, neutrophil-to-lymphocyte ratio.

acute and chronic exercise. These results suggest that the overall findings are stable and not driven by any single study.

Publication Bias

Figure 6 presents funnel plots assessing potential publication bias among studies evaluating changes in NLR in response to exercise. For studies examining NLR immediately after acute exercise (Fig. 6*A*), the funnel plot appeared largely symmetrical, and neither Egger's test ($P = 0.41$) nor Begg's test ($P = 0.58$) suggested evidence of publication bias. Similarly, for studies evaluating NLR 1–3 h after acute exercise (Fig. 6*B*), the funnel plot also appeared symmetrical, and neither Egger's test ($P = 0.07$) nor Begg's test ($P = 0.25$) indicated evidence of publication bias. Taken together, these results suggest that publication bias is unlikely to have substantially influenced the observed findings. Similarly, for studies evaluating changes in NLR after chronic exercise (Fig. 6*C*), the funnel plot appeared symmetrical. Neither Egger's test ($P = 0.78$) nor Begg's test ($P = 0.20$) provided evidence of publication bias. Together with the results for acute exercise, these findings suggest that the observed effects are unlikely to be driven by small-study effects or selective publication.

DISCUSSION

This meta-analysis explored the effect of exercise on NLR, a readily accessible marker of systemic inflammation and immune response. The results of our study highlight that NLR can function as a useful lens through which to understand how exercise influences inflammatory pathways, complementing evidence from cytokine studies and other immune markers. By reflecting the dynamic balance between neutrophils and lymphocytes, NLR provides a simple way to track how acute and chronic exercise modulates systemic inflammation.

NLR Change Immediately After Acute Exercise

No significant difference was observed in NLR levels immediately following acute exercise. This likely reflects the short time frame required for measurable systemic changes to occur after exercise. Although immune processes such as neutrophil mobilization and cytokine release are initiated soon after physical activity, these responses may not yet be detectable in circulating blood counts in the immediate post-exercise window. Thus, the lack of change in NLR right after exercise may be due to the delay between the onset of immune activation and its measurable expression in peripheral blood.

Heterogeneity of results immediately after acute exercise.

Considerable heterogeneity was observed in NLR responses immediately after acute exercise. We explored whether this variability could be explained by factors such as participants'

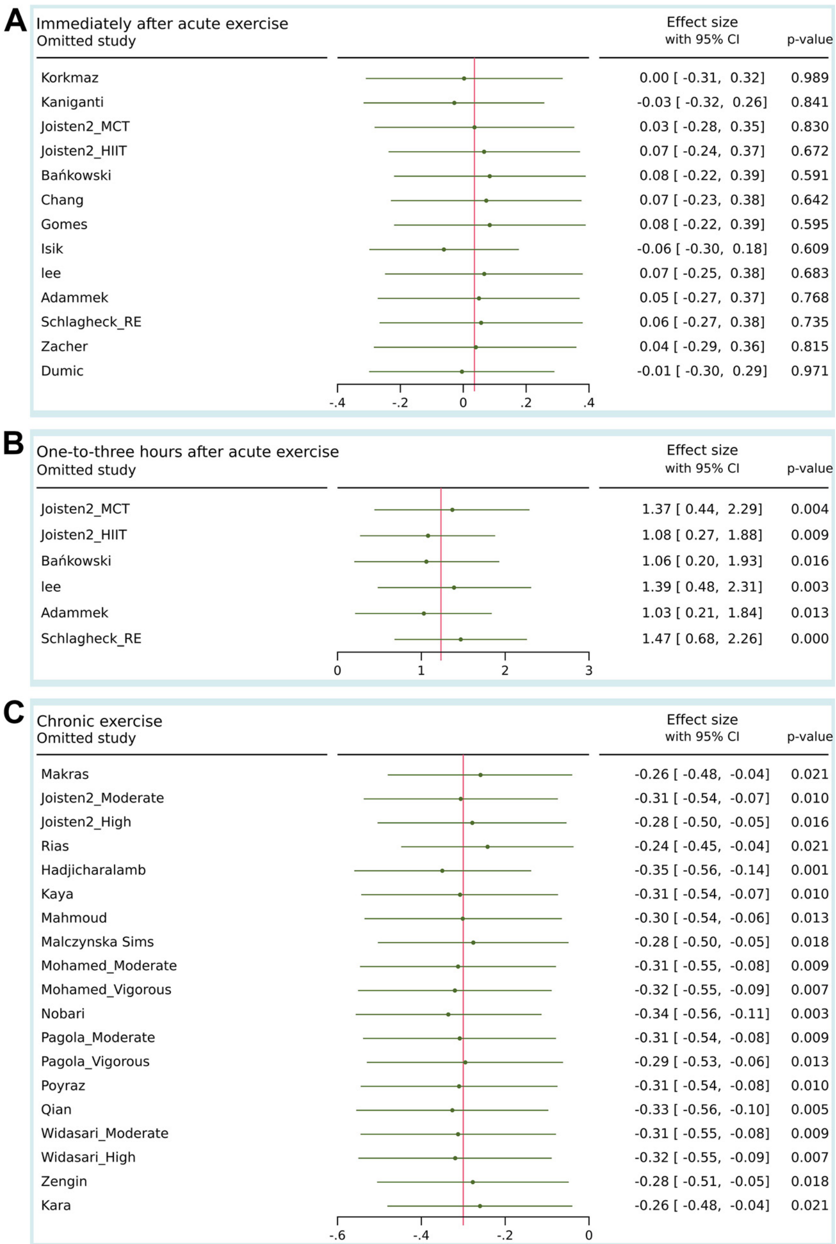

Figure 5. Results of sensitivity analysis immediately after exercise (*A*), one-to-three months after exercise (*B*), and chronic exercise (*C*). CI, confidence interval.

health status, exercise intensity, study quality, age, sex distribution, sample size, or BMI, but none of these factors consistently accounted for the differences between studies. It is possible that unmeasured influences contributed to this heterogeneity, including other individual-level factors such as sleep quality, recent diet, hydration status, exercise training experience, and starting fitness.

NLR Change 1–3 h After Acute Exercise

The second meta-analysis, including studies measuring NLR after 1–3 h following acute exercise, demonstrated a statistically significant increase. This is consistent with a transient stress-induced immune response, increased neutrophils (53, 54), and relative lymphocytic suppression (55). In fact, the increased NLR reflects a physiological response to exercise-induced muscle stress and tissue repair processes, which require the engagement of innate immune components. These results emphasize the significance of sampling time when assessing postexercise inflammatory markers. It has long been recognized that skeletal muscle inflammation is triggered by acute exercise. For example, in a study by Jiménez-Jiménez et al. (56), 11 participants, aged 66–75, performed two eccentric exercise sessions separated by 8 wk of training. In peripheral blood mononuclear cells from older individuals, they found that acute eccentric exercise increases the expression of several genes associated with inflammation and the activation of nuclear factor kappa B (NF-κB) immediately after and at 3 h after cessation of a bout of eccentric-damaging protocol (56).

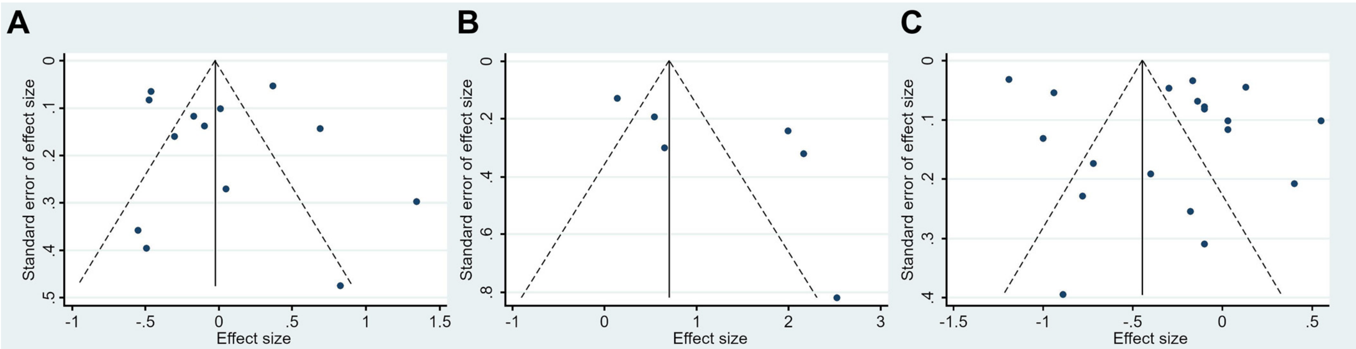

Figure 6. Funnel plots assessing the publication bias. Studies reporting neutrophil-to-lymphocyte ratio (NLR) change immediately after acute exercise (*A*); studies reporting NLR change 1–3 h after acute exercise (*B*) and; studies reporting NLR change after chronic exercise (*C*).

Heterogeneity of results 1–3 h after acute exercise. Subgroup analyses examined whether exercise intensity, participant health status, or study quality could explain the variability in the results. Although NLR increased significantly in some subgroups, such as in healthy participants, exercise with moderate intensity, or studies rated as good quality, other subgroups showed similar trends without reaching significance. However, the differences between these subgroups were not statistically meaningful, indicating that the apparent variation was not due to real group differences. In line with this, meta-regression based on age, sample size, sex distribution, and BMI also did not identify any significant sources of heterogeneity. The observed heterogeneity may stem from unaccounted individual-level factors, such as differences in the time frame of NLR measurement, sleep quality, recent dietary intake, hydration status, or baseline inflammatory condition.

Chronic Exercise

In contrast to acute exercise, there was a significant overall decrease in NLR linked to chronic exercise. This supports the well-established anti-inflammatory benefits of long-term physical activity (57). Our findings that NLR decreases after long-term exercise are consistent with mechanistic studies demonstrating that regular training attenuates inflammatory signaling. For example, Jiménez-Jiménez et al. (56) reported that although acute eccentric exercise enhanced NF-κB activation and the expression of genes associated with inflammation in elderly individuals, these effects were significantly blunted following 8 wk of eccentric training. This supports the interpretation that chronic exercise reduces baseline inflammatory activity and enhances the body's ability to regulate immune responses (56).

Heterogeneity of results after chronic exercise. The observed variability in NLR responses to chronic exercise appears to be largely explained by differences in study quality and participant age, which emerged as major sources of heterogeneity across studies.

The subgroup analysis based on NIH quality ratings revealed that methodological rigor substantially influenced the observed effect of chronic exercise on NLR. Studies rated as good demonstrated a clear reduction in NLR, whereas those rated as fair showed no change. The statistically significant difference between these subgroups indicates that higher-quality designs tend to capture the anti-inflammatory effect of long-term exercise more consistently. This may reflect more standardized protocols and better control of confounding variables in well-conducted studies. Conversely, fair-quality studies—often with smaller sample sizes or incomplete reporting—may underestimate or obscure true biological changes due to greater measurement variability.

In addition, meta-regression identified age as a significant moderator. The negative coefficient suggests that studies with older participants reported greater reductions in NLR following chronic exercise. This pattern aligns with physiological expectations: older adults typically exhibit higher baseline systemic inflammation (58) and thus may experience a more pronounced normalization of immune balance with sustained exercise. Regular physical activity likely mitigates age-related immune-senescence and chronic low-grade inflammation ("inflammaging"), leading to larger measurable decreases in NLR in this subgroup (59).

The primary limitation of our meta-analysis is the high heterogeneity observed among the included studies. Although the main sources of variability were identified in the chronic exercise analysis, particularly related to study quality and participant age, they could not fully explain the acute exercise results. To address this issue, we used a random-effects model to provide more robust and generalized estimates; however, some residual heterogeneity may still influence the pooled outcomes. In addition, the certainty of evidence was low for chronic exercise and very low for acute exercise according to the GRADE approach, primarily reflecting heterogeneity in study design, participant characteristics, and outcome assessment. These findings indicate that current evidence is limited and should be interpreted with caution.

In conclusion, our results emphasize the dynamic and time-dependent nature of immune responses to exercise. Although acute exercise induces a transient increase in inflammatory markers after a delay, chronic exercise contributes to sustained reductions, supporting exercise as a practical approach to inflammation control.

DATA AVAILABILITY

Data will be made available upon reasonable request.

SUPPLEMENTAL MATERIAL

Supplemental Tables S1–S5 and Supplemental Figs. S1–S9: https://doi.org/10.6084/m9.figshare.31079284.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

S.K., S.M., and R.K.S. conceived and designed research; S.K., S.M., F.F., and R.K.S. performed experiments; S.K., S.M., F.F., and R.K.S. analyzed data; S.K., S.M., F.F., and R.K.S. interpreted results of experiments; S.K., S.M., F.F., and R.K.S. prepared figures; S.K., S.M., F.F., and R.K.S. drafted manuscript; S.K. and R.K.S. edited and revised manuscript; S.K., S.M., F.F., and R.K.S. approved final version of manuscript.

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