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Exercise-based interventions and circulating irisin concentrations in older adults: A systematic review and meta-analysis

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Abstract

Ageing is accompanied by progressive metabolic dysfunction and alterations in skeletal-muscle endocrine activity. Irisin, a contraction-induced myokine, has been implicated in energy metabolism and metabolic homeostasis; however, the effect of exercise on circulating irisin levels in older adults remains uncertain. The aim of this systematic review and meta-analysis was to evaluate the association between exercise-based interventions and circulating irisin levels in older adults. PubMed, Scopus, and Embase were systematically searched for eligible studies published up to March 20, 2026. Prospective studies assessing post-intervention irisin levels among older adults receiving exercise-based interventions and control participants were included. Pooled mean differences (MDs) were calculated using a random-effects model. Eight prospective cohort studies comprising 299 participants, including 152 participants in intervention groups and 147 controls, were included. Exercise modalities included strength, resistance, aquarobic, periodized, and Nordic walking training, with intervention durations ranging from three to six months. Exercise-based interventions were associated with higher circulating irisin levels than control conditions (MD: 1.40; 95% confidence interval (CI): 0.17–2.62; p=0.026). Significant between-study heterogeneity was observed (p for heterogeneity <0.001), whereas Egger's test did not indicate statistically significant publication bias (p=0.160). In conclusion, exercise-based interventions may increase circulating irisin levels in older adults. Nevertheless, the substantial heterogeneity, relatively small pooled sample, and predominance of nonrandomized studies warrant cautious interpretation.

Keywords: Elderly, exercise, irisin, myokine, systematic review

Introduction

The global increase in life expectancy has brought the challenging issue of age-related physiological decline and sedentary lifestyles to the forefront of public health [1]. The high prevalence of physical inactivity among older adults contributes significantly to the rising incidence of metabolic disorders and increased cardiovascular mortality [2]. While physical exercise is widely recognized as a primary intervention for healthy aging, its systemic benefits are influenced by a complex interplay of neural, muscular, and endocrine adaptations. Among these adaptations, the secretion of muscle-derived signaling molecules—known as myokines—serves as a critical mechanism through which skeletal muscle communicates with distant organs to

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maintain metabolic homeostasis [3]. Consequently, emphasizing the role of specific myokines, such as irisin, is essential to understanding how exercise-based interventions exert their therapeutic effects in the geriatric population [4].

Irisin, a myokine generated through the proteolytic cleavage of fibronectin type III domain-containing protein 5 (FNDC5), is released into the circulation in response to skeletal muscle contraction and has emerged as an important regulator of metabolic homeostasis. Its proposed physiological effects include promoting the browning of white adipose tissue and improving glucose homeostasis, both of which are frequently impaired with advancing age [5]. Supporting data suggest that circulating irisin levels are positively correlated with better metabolic profiles and muscle quality in elderly cohorts [6-8]. However, evidence regarding the effects of different exercise modalities on circulating irisin levels remains inconsistent, particularly because age-related alterations in skeletal muscle may attenuate physiological responses to exercise [9-13]. This uncertainty highlights the need to synthesize the available evidence and quantify the overall association between exercise-based interventions and circulating irisin levels in older populations.

The aim of this systematic review and meta-analysis was to evaluate the effects of exercise-based interventions on circulating irisin levels among older adults. It was hypothesized that structured exercise interventions would be associated with higher circulating irisin levels than control conditions. The findings may clarify the endocrine response of ageing skeletal muscle to exercise and inform the development of evidence-based exercise strategies for supporting metabolic health in older adults and the elderly.

Methods

Study design and protocol

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14]. The literature search included studies published through March 20, 2026. Data from eligible studies were systematically extracted and synthesized to estimate the pooled effect of exercise-based interventions on circulating irisin levels in older adults. The review protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42023414897).

Eligibility criteria

Studies were eligible for inclusion if they: (1) employed a randomized controlled trial (RCT) or cohort design; (2) were identified through electronic database searches or manual reference screening; (3) evaluated the effects of exercise-based interventions on circulating irisin levels in older adults; and (4) reported sufficient post-intervention data, including the mean and standard deviation, to calculate the effect estimate. Reviews, commentaries, letters to the editor, gray literature, duplicate publications, and studies with insufficient outcome data were excluded.

Search strategy

A comprehensive literature search was conducted in PubMed, Scopus, and Embase to identify eligible studies published through March 20, 2026. The search was restricted to articles published in English. The PubMed search combined Medical Subject Headings (MeSH) and free-text terms as follows: (aged OR elderly OR older adults OR seniors OR geriatric OR aging) AND (exercise OR exercise therapy OR exercise OR physical activity OR exercise training OR aerobic training OR resistance training OR endurance training) AND (irisin OR FNDC5 OR fibronectin type III domain-containing protein 5 OR circulating irisin OR serum irisin). The Embase search strategy was (older adults OR elderly OR aged OR seniors) AND (exercise OR physical activity OR exercise training) AND (irisin OR FNDC5). The Scopus search strategy was (older adult* OR elderly OR aged OR senior* OR geriatric*) AND (exercise OR physical activity OR exercise training OR aerobic training OR resistance training) AND (irisin OR FNDC5 OR serum irisin OR circulating irisin). In addition, the reference lists of eligible articles and relevant reviews were manually screened to identify additional studies not retrieved through the electronic database searches.

Quality assessment

The methodological quality of the included studies was independently assessed by two reviewers (WF and CYR). Any disagreements were resolved through discussion and, when necessary, consultation with a senior reviewer (SS). Randomized controlled trials were evaluated using the modified Jadad scale, with scores ranging from 0 to 5 [15]. This scale assesses the reporting and methodological appropriateness of randomization, blinding, and participant withdrawals or dropouts. Nonrandomized and cohort studies were assessed using the Newcastle–Ottawa Scale, with scores ranging from 0 to 9 [16], covering three domains: selection of study groups, comparability of groups, and ascertainment of outcomes. Studies were classified as having low, moderate, or high methodological quality according to prespecified score thresholds for each assessment tool [15,16].

Data extraction

Data were independently extracted by two reviewers (WF and CYR) using a standardized data-extraction form. Any discrepancies were resolved through discussion and, when consensus could not be reached, consultation with a senior reviewer (SS). The extracted information included the first author's name, year of publication, country, study design, participant characteristics, sample sizes of the intervention and control groups, type of exercise intervention, duration of follow-up, and post-intervention irisin data required for the meta-analysis.

Study variables

The primary intervention of interest was structured physical exercise, encompassing different exercise modalities, including strength, resistance, aquarobic, periodized, and Nordic walking training. The comparator consisted of participants who did not receive the corresponding exercise intervention or who received the control condition specified in each included study.

The primary outcome was the post-intervention circulating irisin level, measured in serum or plasma and reported as a continuous variable. Where available, information on exercise modality, intervention duration, participant characteristics, irisin measurement methods, and units of measurement was also extracted to characterize potential sources of between-study variability.

Statistical analysis

Statistical analyses were performed using Comprehensive Meta-Analysis software, version 3.7 (Biostat, Englewood, NJ, USA). Continuous data were summarized as mean±standard deviation (SD). The pooled effect of exercise-based interventions on circulating irisin levels was expressed as the mean difference (MD) with the corresponding 95% confidence interval (CI) and calculated using the inverse-variance method. Between-study heterogeneity was assessed using Cochran's Q test and the I^2 statistic. The selection of a fixed-effect or random-effects model was based on the magnitude and statistical significance of heterogeneity. Potential publication bias was explored using funnel plot inspection and Egger's regression test. Statistical significance was defined as a two-sided $p<0.05$

Results

Article selection

The literature search identified 209 records, including 205 records retrieved from PubMed, Scopus, and Embase and four records identified through additional sources (**Figure 1**). After six duplicate records were removed, 203 records underwent title and abstract screening. Of these, 176 records were excluded because they were considered irrelevant to the review objective. The full texts of the remaining 27 reports were assessed for eligibility. Nineteen reports were subsequently excluded because they provided insufficient data for quantitative synthesis (n=7) or were review articles (n=12). Ultimately, eight studies met the eligibility criteria and were included in the systematic review and meta-analysis [6-13].

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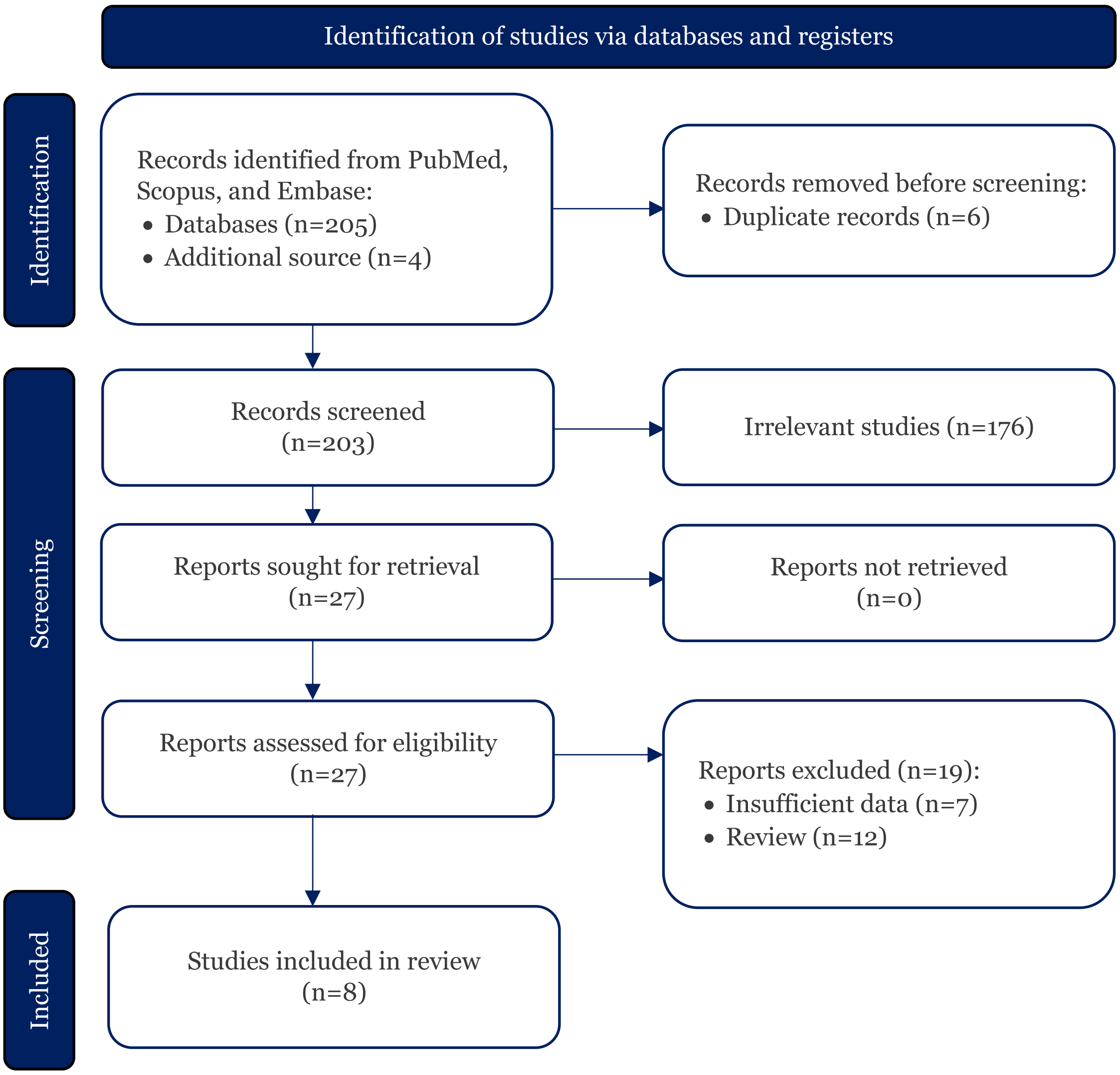

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the study identification, screening, eligibility assessment, and inclusion process.

Baseline characteristics of the included studies

The baseline characteristics of the eight included studies are presented in **Table 1**. The studies were published between 2015 and 2019 and were conducted across diverse geographical settings, including Germany [9,12], Iran [10], Korea [6], Spain [11], Brazil [7], Poland [13], and China [8]. All studies employed a prospective cohort design. The exercise interventions comprised strength training [9-12], aquarobic exercise [6], periodized training [7], Nordic walking [13], and resistance training [8], with follow-up durations ranging from 3 to 6 months. Based on the methodological quality assessment, all eight studies were classified as high quality (**Table 1**).

Table 1. Baseline characteristics of articles included in the study

Author (year)	Country	Study design	Sample size		Age (years)	Type of exercise	Follow-up (month)	Study quality
			T	C				
Boeselt *et al.*, 2016 [9]	Germany	Prospective cohort	14	17	65.73±8.3	Physical strength training	6	High
Damirchi *et al.*, 2017 [10]	Iran	Prospective cohort	11	9	68.81±3.68	Physical training	6	High
Kuster *et al.*, 2017 [12]	Germany	Prospective cohort	17	18	73.18±5.99	Physical training	4	High
Kim *et al.*, 2017 [6]	Korea	Prospective cohort	14	12	71.77 ±3.07	Aquarobic exercises	4	High
Farrugia *et al.*, 2019 [11]	Spain	Prospective cohort	14	20	66.4 ±4.6	Physical training	4	High

Author (year)	Country	Study design	Sample size		Age (years)	Type of exercise	Follow-up (month)	Study quality
			T	C				
Prestes *et al.,* 2015 [7]	Brazil	Prospective cohort	39	20	69.20±6.05	Periodization training (linear and undulating)	4	High
Walentukiewicz *et al.,* 2018 [13]	Poland	Prospective cohort	33	34	67.8±5.4	Nordic walking training	3	High
Zhao *et al.,* 2017 [8]	China	Prospective cohort	10	7	62.3±3.5	Resistance training	3	High

C: control group; T: treatment group

Effect of exercise interventions on circulating irisin levels

The meta-analysis included eight studies comprising nine effect estimates, with a total of 299 participants: 152 in the exercise-intervention groups and 147 in the control groups. Exercise-based interventions were associated with significantly higher circulating irisin levels than control conditions (pooled MD: 1.40; 95%CI: 0.17–2.62; p=0.026) (**Figure 2**). However, the magnitude and precision of the study-specific estimates varied considerably, and several CIs crossed the null value. Significant between-study heterogeneity was observed (p<0.0001), indicating substantial variability in the intervention effects across studies.

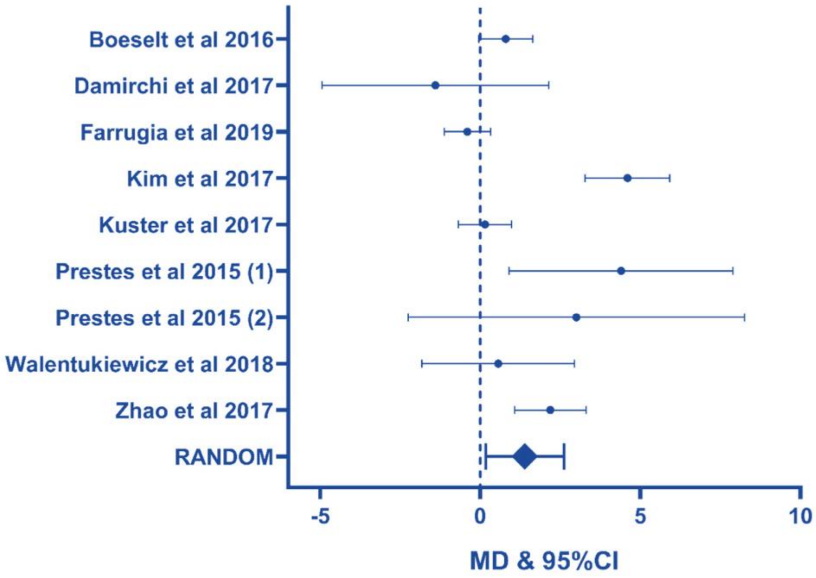

Figure 2. Forest plot of the pooled effect of exercise interventions on circulating irisin levels (mean difference 1.40; 95%CI: 0.17–2.62; p=0.026; p-value of heterogeneity <0.0001; p-value of Egger's test 0.160).

Heterogeneity and assessment of publication bias

Significant between-study heterogeneity was observed (p<0.0001); therefore, a random-effects model was applied to estimate the pooled effect while accounting for variability across studies. Egger's regression test showed no statistically significant evidence of small-study effects or publication bias (p=0.160). This finding was consistent with the approximately symmetrical distribution of studies in the funnel plot.

Discussion

This systematic review and meta-analysis found that exercise-based interventions were associated with higher circulating irisin levels in older adults. The pooled estimate indicated a significant effect, although substantial between-study heterogeneity was observed. These findings suggest that skeletal muscle retains its capacity for exercise-responsive endocrine signalling during ageing, despite age-related declines in muscle mass, function, and metabolic activity. This interpretation is consistent with previous evidence describing skeletal muscle as a metabolically active endocrine organ throughout adulthood [17]. Repeated muscle contraction during resistance, aerobic, aquatic, and walking-based exercise may directly stimulate irisin secretion, while longer-term adaptations in muscle metabolism may further contribute to changes observed after 3–6 months of intervention [18].

A potential biological mechanism underlying this association involves activation of the peroxisome proliferator-activated receptor-gamma coactivator 1-alpha (PGC-1α) pathway in skeletal muscle. Exercise-induced PGC-1α activation promotes the expression of FNDC5, which is subsequently cleaved to release irisin into the circulation [19]. Irisin has been implicated in several metabolic processes, including the browning of white adipose tissue, energy expenditure, glucose regulation, and insulin sensitivity [20]. However, the present findings demonstrate changes in circulating irisin rather than direct improvements in these downstream metabolic outcomes. Therefore, the clinical and physiological implications of exercise-induced changes in irisin among older adults require further investigation.

The included studies applied diverse exercise modalities, including strength training, resistance training, aquarobic exercise, periodised training, and Nordic walking. The overall pooled association across these interventions suggests that several forms of structured physical activity may stimulate irisin responses in older populations. Nevertheless, the magnitude of the study-specific effects varied considerably, and several confidence intervals included the null value. This variability may reflect differences in intervention type, intensity, frequency, duration, participant characteristics, baseline physical activity, and methods used to measure circulating irisin. Consequently, the findings should not be interpreted as demonstrating that all exercise protocols produce equivalent effects or that a particular exercise modality is superior.

These findings may have implications for the development of exercise programmes for older adults. Exercise is already recommended for maintaining physical function, muscle strength, mobility, and metabolic health, and changes in irisin may represent one of several biological pathways contributing to these benefits. However, the current evidence is insufficient to support the use of circulating irisin as a clinical biomarker for prescribing or monitoring exercise. Further studies should directly compare different exercise modalities and doses, standardise the timing and methods of irisin measurement, and evaluate whether changes in irisin correspond to clinically meaningful improvements in muscle function, body composition, glucose metabolism, and age-related disease outcomes [21].

Some limitations should be considered in this study. Substantial between-study heterogeneity reduced the certainty and comparability of the pooled estimate. Differences in exercise protocols, study populations, geographical settings, follow-up periods, and laboratory assays may have contributed to this variability. The relatively small total sample of 299 participants may limit the precision and generalisability of the findings. The inclusion of prospective cohort studies rather than exclusively RCTs increased the possibility of selection bias, residual confounding, and baseline differences between intervention and control groups. Potentially relevant factors, including nutritional status, medication use, comorbidities, baseline physical activity, body composition, and adherence to the intervention, were not consistently measured or adjusted for across the included studies.

Conclusion

This meta-analysis suggests that exercise-based interventions are associated with higher circulating irisin levels in older adults. However, the substantial between-study heterogeneity indicates that the magnitude of this association may vary according to the type, intensity, and duration of exercise. These findings support the potential role of structured exercise in maintaining skeletal muscle endocrine function during ageing. However, further well-designed studies are needed to determine the optimal intervention characteristics and clarify the clinical relevance of exercise-induced changes in irisin levels.

Ethics approval

Not required.

Acknowledgments

None.

Competing interests

The authors declare that there are no conflicts of interest.

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Underlying data

All data generated or analysed during this systematic review and meta-analysis are presented in the article and its supplementary materials. The complete data-extraction dataset and statistical analysis outputs are available from the corresponding author upon request.

Declaration of artificial intelligence use

Artificial intelligence tool, Gemini AI, was used for language refinement. Authors confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were made solely by the authors.

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