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RESEARCH SUBMISSION

How much aerobic exercise is needed to reduce migraine? A dose–response meta-analysis of pain intensity and frequency

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Abstract

Background: Evidence suggests that exercise has clinically relevant benefits for migraine, but an optimal prescription standard remains undefined. We aimed to assess the effectiveness of aerobic exercise on migraine intensity and frequency through a dose–response meta-analysis.

Methods: A data search was performed in PubMed, PEDro, Google Scholar, and EBSCO from inception to September 1, 2024. Randomized controlled trials and quasi-experimental studies of aerobic exercise in patients with a clinical diagnosis of migraine were included. The outcome measures were pain intensity and migraine frequency. The dose–response relationship was evaluated using a dose–response meta-analysis.

Results: Fifteen studies (253 participants) were included. Meta-analysis showed a statistically significant decrease in pain intensity between pre and post intervention (standardized mean differences [SMD], −1.1; 95% confidence interval [CI], −1.72 to −0.47). The spline model showed a U-shape statistically significant association ($\chi^2=112.03$, df $=2$, $p<0.001$) between total minutes of aerobic exercise and reduction in pain intensity. A minimum dose of 200 min was required for moderate effects, with a maximum effect at 900 min (SMD, −2.4; 95% CI, −2.85 to −1.95). Meta-analysis showed a statistically significant decrease in migraine frequency between pre and post intervention (SMD, −0.79; 95% CI, −1.1 to −0.47). The spline model showed a U-shape statistically significant association ($\chi^2=86.41$, dl $=2$, $p<0.001$) between total minutes of aerobic exercise and reduction in migraine frequency. A minimum dose of 300 total minutes of aerobic exercise program duration was required to obtain a moderate effect in reducing migraine frequency, with a maximum effect at 950 min (SMD, −1.55; 95% CI, −1.87 to −1.22).

Conclusions: This meta-analysis suggests that aerobic exercise may be effective in reducing both pain intensity and migraine frequency in people with migraine. The greatest observed effect on both variables was observed at a cumulative dose of

Abbreviations: CI, confidence interval; DALY, disability-adjusted life year; GRADE, grading of recommendations, assessment, development and evaluation; ICHD-3, International Classification of Headache Disorders, 3rd edition; LFK, Luis Furuya-Kanamori index; PRISMA, preferred reporting items for systematic reviews and meta-analyses; PROSPERO, International Prospective Register of Systematic Reviews; RCT, randomized controlled trial; RoB-2, cochrane risk of bias tool for randomized controlled trials, version 2; ROBINS-I, risk of bias in non-randomized studies of interventions; RPE, rating of perceived exertion; SD, standard deviation; SMD, standardized mean difference; VO_2peak, peak oxygen uptake; YLD, years lived with disability.

approximately 900–950 total minutes of aerobic exercise during the program, and higher doses may not present additional benefits. These findings support a preliminary recommendation of 3 weekly 30-min sessions over 10–11 weeks, to be confirmed in future high-quality trials.

Plain Language Summary: Migraine is a common condition that can be improved with exercise but the ideal amount is still unclear. We reviewed studies on aerobic exercise in people with migraine and found that patients who engaged in approximately 900 min over the course of treatment (e.g., 30 min sessions three times per week for 10–11 weeks) reported significantly reduced pain and number of migraine attacks. Higher amounts of aerobic exercise did not lead to greater benefits, suggesting an optimal range for exercise prescription.

KEYWORDS
aerobic exercise, headache, migraine, pain frequency, pain intensity

INTRODUCTION

Migraine is defined as a common disabling primary headache disorder by the International Headache Society classification (ICHD-3),[1] with a high prevalence and socioeconomic and personal impacts documented by many epidemiological studies.[2,3] In the Global Burden of Disease Study 2021, headache disorders ranked as the third leading cause of years lived with disability (YLDs) worldwide (48.0 million YLDs; 5.2% of all-cause YLDs), after low back pain and depressive disorders.[2] Migraine prevalence peaked globally in the 35–39 age group, representing a 39.52% increase since 1990.[3] The condition disproportionately affects women and individuals in their most productive years, with substantial consequences for quality of life, employment, and social functioning.[4] This growing public health burden necessitates accessible, cost-effective interventions like exercise that can be widely implemented.

Despite decades of research dedicated to developing effective treatments for migraine, the persistent and rising prevalence of this condition suggests that current therapeutic approaches may be insufficient to address the growing burden of this disorder. Consequently, it is imperative to expand research efforts to evaluate the effectiveness of nonpharmacological strategies, including exercise-based interventions,[5] that could offer a sustainable and accessible option for reducing the impact of migraine on individuals and health care systems worldwide. For instance, a recent systematic review[6] of randomized controlled trials showed that exercise may improve pain and disability and could be considered clinically relevant for primary headaches, with a moderate clinical effect. Possible pathways for exercise effectiveness include the endogenous opioid and cannabinoid systems, brain-derived neurotrophic factor, neurogenic inflammation, and possible mediation by behavioral and psychological factors.[7,8] In fact, current evidence-based clinical practice guidelines recommend aerobic exercise to promote an improvement in symptoms in people with migraine,[9] and there is common consensus that it should be moderate-intensity continuous aerobic exercise.[8] In fact, recently a network meta-analysis of clinical trials showed moderate-intensity aerobic exercise as one of the best interventions for reducing migraine frequency and intensity.[10,11] However, to date, no gold standard that can be accurately prescribed to patients with migraine has been determined. Currently, general advice for exercise in migraine management often lacks specific parameters; however, a regimen of 30- to 60-min sessions of moderate-intensity continuous aerobic exercise, performed 3 days per week, is emerging as a suitable prescription. This approach is recommended to likely decrease pain frequency, intensity, and duration and to improve quality of life.[8]

As such, specific dosing recommendations that could increase the effectiveness of exercise interventions are still needed. Previous systematic reviews have primarily focused on whether exercise is effective for migraine management, but have not addressed the critical question of "how much exercise is optimal?" A dose–response meta-analysis allows for the identification of minimum effective doses and optimal therapeutic ranges, which has not been conducted to date. Therefore, we aimed to assess the effectiveness of aerobic exercise on migraine intensity and frequency through a dose–response meta-analysis.

METHODS

Design

This systematic review and dose–response meta-analysis was conducted in accordance with PRISMA 2020 guidelines.[12] This study is a secondary and more specific analysis derived from a previously registered systematic review protocol (PROSPERO ID: CRD42020208796), which originally aimed to evaluate the overall effectiveness of exercise in patients with headaches. Following completion of that review, we identified sufficient homogeneous data on aerobic exercise interventions in patients with migraine to warrant a focused dose–response analysis that provides novel and valuable information from a scientific and clinical point of view. The PROSPERO record was accordingly updated to reflect this specific objective and scope.

Information sources and search strategy

We systematically searched PubMed/MEDLINE, PEDro, Google Scholar, and EBSCO databases to identify all studies related to this topic. The search strategy combined Medical Subject Headings (MeSH) terms with non-MeSH terms, adding Boolean operators (OR and AND) to combine them. The detailed search strategy for MEDLINE/PubMed was: *((“Migraine Disorders”[MeSH Terms] OR “Migraine without aura”[All fields] OR “Migraine with aura”[All fields]) AND ((“Exercise”[MeSH Terms] OR “Exercise Therapy”[MeSH Terms] OR “Aerobic exercise”[MeSH Terms] OR “Exercise rehabilitation”[All Fields] OR “Physical activity”[All Fields] OR “Physical exercise”[All Fields]) AND “Pain measurement”[MeSH Terms] OR “Visual analogue scale”[MeSH Terms] OR “Headache frequency”[All Fields] OR “Pain intensity”[All Fields])*. It is also provided in the Supporting Information Table S1, which was adapted for electronic searching in the other databases. No language restrictions were applied to ensure the inclusion of all relevant studies. The last search was conducted on September 1, 2024. We employed the citation management software Zotero (George Mason University, VA, USA) and manually verified all results to remove duplicates.

Eligibility criteria

Trials were included if they met the predetermined eligibility criteria summarized according to the Population, Intervention, Comparator, Outcome, Time, and Study model: (1) population: men and women aged 18 years and older with a medically reported diagnosis of migraine. Patients must have been diagnosed with migraine by specialists (e.g., neurologist) in any health care setting according to the criteria established by the International Classification of Headache Disorders (ICHD). (2) Intervention: any type of aerobic exercise applied in isolation (walking/jogging, cycling, running, treadmill, etc.), excluding those that combined it with any other type of exercise or any other therapy. There were no restrictions on intervention duration. (3) Comparison: pre-intervention (baseline) measures were used as comparators to determine the effect of the intervention. (4) Outcomes: the measures used were the Visual Analog Scale, Numeric Rating Scale or any other numerical measure of pain intensity, and/or the frequency of headache. (5) Time: no restrictions were placed on the duration of training. Results were evaluated in the week in which the treatment was completed. (6) Study design: randomized controlled trials (RCTs) or quasi-experimental studies were included. Because the main objective of this research is to determine the effective and optimal dose of aerobic exercise in patients with migraine, quasi-experimental studies containing pre-post results do not represent a significant bias. Studies were excluded if they included any other type of intervention added to exercise, or if they included patients with any other medical condition that could affect the results of the intervention.

Selection process

To select valid studies for our systematic review, the articles retrieved from the search were subjected to a two-step selection process. In the first step, the relevance of the studies to the research questions and objectives was assessed based on information in the title, abstract, and keywords of each study. Potentially eligible studies and studies that did not present sufficient information in these sections were considered for the second stage. Full-text review represents the second stage, in which studies were assessed to ensure that they met all inclusion criteria. Two independent reviewers applied the eligibility criteria for study selection. A third reviewer acted as a referee in the event of disagreement at any stage.

Data collection process

Data were extracted using a form designed to systematically extract the most relevant information from each study. The following data were extracted from each study: first author, year of publication, number of participants, pre- and post-experimental means for each outcome, pre- and post-experimental standard deviations (SD) for each outcome, mean difference for each outcome, and SD of mean difference for each outcome. When data were not in the expected format, we requested information from the respective authors. If the authors did not reply, means and SDs from the figures provided in the articles were extrapolated using the WebPlotDigitizer (version 4.6; Pacifica, CA, USA) tool.[13] To be able to include some studies in the subsequent meta-analysis, when needed, we estimated the sample means and SDs according to previously published statistical methods and treated them as the true sample values.[14–16] We also acknowledge the use of OpenAI's ChatGPT (GPT-4o model) for assistance in translating two original Persian articles[17,18] into English. This was crosschecked by human experts, and the data were contrasted with previous reviews and by asking the original authors. To determine the specific aerobic exercise dose per session, the minutes of the main training phase were extracted, disregarding the warm-up and cool-down minutes. In case the authors reported a range of session duration (e.g., 20–30 min), the mean value of the session (i.e., 25 min) was estimated.

Study risk of bias assessment

Risk of bias was assessed using the Cochrane Risk of Bias Tool for Randomized Controlled Trials 2.0,[19] which includes five domains:

randomization process, deviations from intended interventions, missing data on outcomes, measurement of the outcome, and selection of reported outcomes. Each item was rated as high risk of bias, low risk of bias, or some concern. Once the five domains have been scored, the overall study score is defined as the highest score achieved in any of the domains. Two experts independently reviewed the trials. The results were then compared, and any disagreements were resolved by a third reviewer.

The risk of bias in nonrandomized studies of interventions was assessed using the Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool.[20] ROBINS-I is a comprehensive instrument designed to evaluate the risk of bias across seven domains: confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result. Each domain is rated as low, moderate, serious, or critical risk of bias. The assessment was independently performed by two reviewers, and discrepancies were resolved through discussion or consultation with a third reviewer.

Certainty of evidence assessment

Two authors (R.N.-C. and L.S.-M.) used the GRADE approach to rate the certainty of the evidence for the outcomes of pain and frequency. GradePRO (https://gradepro.org) was used to create a summary table of the results. The level of certainty was graded as very low, low, moderate, and high. The criteria for the downgrading of the level of certainty were as follows (1) risk of bias: one level was downgraded if 25% or more of the included articles for each outcome were at high risk of bias according to Cochrane Risk of Bias Tool for Randomized Controlled Trials 2.0; (2) inconsistency: one level of downgrade was applied if there was high heterogeneity ($I^2 < 75\%$); (3) indirectness: one level of downgrade was applied if there were differences between participants, interventions, outcome measures, or indirect comparisons; (4) imprecision: a downgrade was applied if the 95% CI included the null value of the effect and/or the sample size was small ($n < 300$); and (5) other considerations such as risk of publication bias.

Synthesis methods

RStudio environment (version 2024.12.1 + 563; Posit PBC, Boston, MA, USA) along with R (version 4.4.3; R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis. The effect of aerobic exercise on pain intensity and migraine frequency was analyzed in a random-effects pre-post meta-analysis using additional packages (meta v8.0-2, metafor v4.8-0, and metasens v1.5-2). Between-study variance was estimated using restricted maximum likelihood method. Standardized mean differences (SMDs) and corresponding 95% confidence intervals (CIs) were obtained. The SMDs were interpreted as follows: trivial effect <0.2; small effect: 0.2–0.6; moderate effect: >0.6–1.2; large effect: >1.2–2.0; very large effect: >2.0–4.0; and extremely large effect: >4.0.[21] Heterogeneity was analyzed using the I^2 statistic. A heterogeneity >25% represented small heterogeneity, $I^2 > 50\%$ represented medium heterogeneity, and $I^2 > 75\%$ represented large heterogeneity. To detect publication bias, a visual inspection of the DOI plots was performed to look for any asymmetry. The Luis Furuya-Kanamori (LFK) index was also employed as a quantitative measure. An LFK index within ±1 represents no asymmetry, an LFK index above ±1 but within ±2 represents a small asymmetry, and an LFK index above ±2 represents a large asymmetry.[22]

To assess the dose–response relationship between exercise dose (total minutes) and pain intensity and frequency, a one-stage mean difference dose–response meta-analysis was performed.[23,24] Selected effect sizes and corresponding covariances (SDs) were used to estimate study-specific dose–response curves, using the SMD of within-group change from baseline to final measurement for each variable (i.e., pain intensity and headache frequency) and minutes of exercise as the dose. A restricted cubic spline model with knots set at the 10th, 50th, and 90th percentiles was used to define the dose–response relationship, using the *dosresmeta* R package (version 2.0.1).[25] Dose–response curves characterize the relative effectiveness of the dose studied compared to a "zero" dose. All hypothesis tests were two-tailed and considered significant at a p value <0.05.

RESULTS

The systematic search of electronic databases identified 568 potentially eligible records, and 149 duplicate records were eliminated. After title and abstract screening, 160 studies were excluded. After applying the eligibility criteria, 15 studies[17,18,26–38] were finally included, of which only two were not RCTs[26,27] (Figure S1). The list of articles read in full text and excluded, with reasons, is presented at Table S2. A high level of agreement was observed between the two reviewers during screening (91%; κ coefficient = 0.81; 95% CI, 0.72–0.90), indicating high inter-rater reliability.

Study characteristics

In total, 253 participants were included in the review. Total minutes of the aerobic exercise program ranged from 360 to 1620, with a session duration range between 20 and 45 minutes and 6 to 12 total weeks of exercise. Moderate exercise intensity was assessed based on $VO2_{peak}$ (set between 50% and 70%) and the rate of perceived exertion (RPE) (set between 13 and 16). The characteristics of the included studies are summarized in the Supporting Information (Table S3).

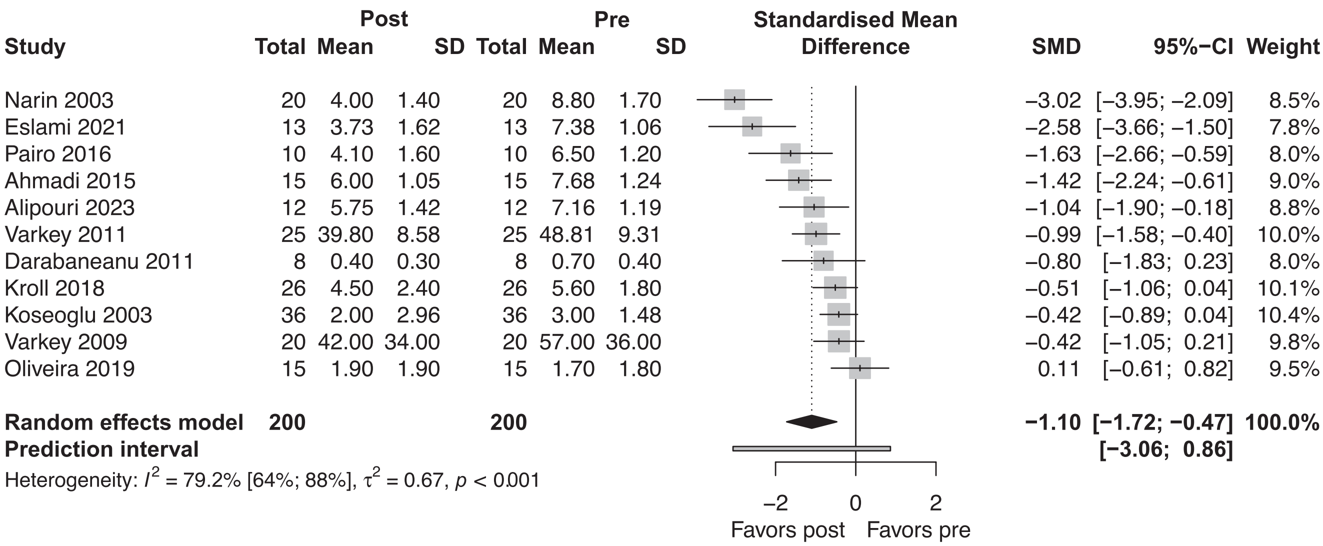

FIGURE 1 Forest plot of the effect on pain intensity. Each study included in the meta-analysis represents a point estimate with the corresponding 95% CI. The polygon at the bottom of the graph corresponds to the overall effect, and its width represents its 95% CI. Trials with larger squares contributed more to the overall effect size than other trials. CI, confidence interval.

Pain intensity

Eleven studies ($n=200$) that used Visual Analog Scale and Numeric Rating Scale to measure pain intensity were included in the quantitative synthesis. Meta-analysis showed a statistically significant decrease in pain intensity with a large effect (SMD, −1.1; 95% CI, −1.72 to −0.47) with evidence of large heterogeneity ($p<0.01$, $I^2=79.2\%$) (Figure 1) and very-low certainty evidence (Table S5). The shape of the DOI plot presented asymmetry with an LFK index of −2.72, indicating a high risk of publication bias (Figure S2).

Publication bias was assessed using a contour-enhanced funnel plot and the Trim and Fill method. Visual inspection of the funnel plot revealed marked asymmetry, with a lack of studies on the left-hand side, suggesting that smaller or nonsignificant studies might be missing (Figure S3). The Trim and Fill procedure imputed four potentially missing studies to correct for this asymmetry. After adjustment, the pooled SMD decreased from the unadjusted estimate to −0.56 (95% CI, −1.29 to 0.18), and the p value increased to 0.121, indicating that the overall effect may have been overestimated due to publication bias (Figure S4).

Dose–response relationships for pain intensity

The spline model showed a U-shape statistically significant association ($\chi^2=112.03$, df$=2$, $p<0.001$) between total minutes of exercise and reduction in pain intensity (within-group change from baseline to final measurement). The estimated coefficient for dose was −0.0033 (95% CI, −0.0039 to −0.0026, $p<0.001$), suggesting an initial decrease in effect as dose increases. However, the coefficient for the curvature of the relationship was 0.0043 (95% CI, 0.0032 to 0.0054, $p<0.001$), indicating a change in the slope, suggesting a possible inflection point at higher doses (Figure 2). The model showed a good fit, with a log-likelihood of −16.45, Akaike Information Criterion (AIC) = 36.9, and Bayesian Information Criterion (BIC) = 37.7. A minimum dose of 200 total minutes of aerobic exercise program duration was required to obtain a moderate effect in reducing pain intensity (SMD, −0.65; 95% CI, −0.77 to −0.52). A maximum effect was observed at 900 min (SMD, −2.4; 95% CI, −2.85 to −1.95) (Table S4).

Migraine frequency

Fifteen studies ($n=253$) that measured migraine frequency were included in the quantitative synthesis. Meta-analysis showed a statistically significant decrease in the migraine frequency with a moderate effect (SMD, −0.79; 95% CI, −1.1 to −0.47) with evidence of medium heterogeneity ($p<0.001$, $I^2=54.7\%$) (Figure 3), and very-low certainty evidence (Table S5). The shape of the DOI plot presented asymmetry with an LFK index of −3.32, indicating a high risk of publication bias (Figure S5).

Publication bias was assessed using a contour-enhanced funnel plot and the Trim and Fill method. Visual inspection of the funnel plot revealed marked asymmetry, with a lack of studies on the left-hand side, suggesting that smaller or nonsignificant studies might be missing (Figure S6). The Trim and Fill procedure imputed five potentially missing studies to correct for this asymmetry. After adjustment, the pooled standardized mean difference (SMD) decreased from the unadjusted estimate to −0.48 (95% CI, −0.87 to −0.1; $p<0.001$) (Figure S7).

Sensitivity analysis: Migraine type

Seven studies that measured migraine frequency performed the intervention in patients only with chronic migraine ($k=3$) or

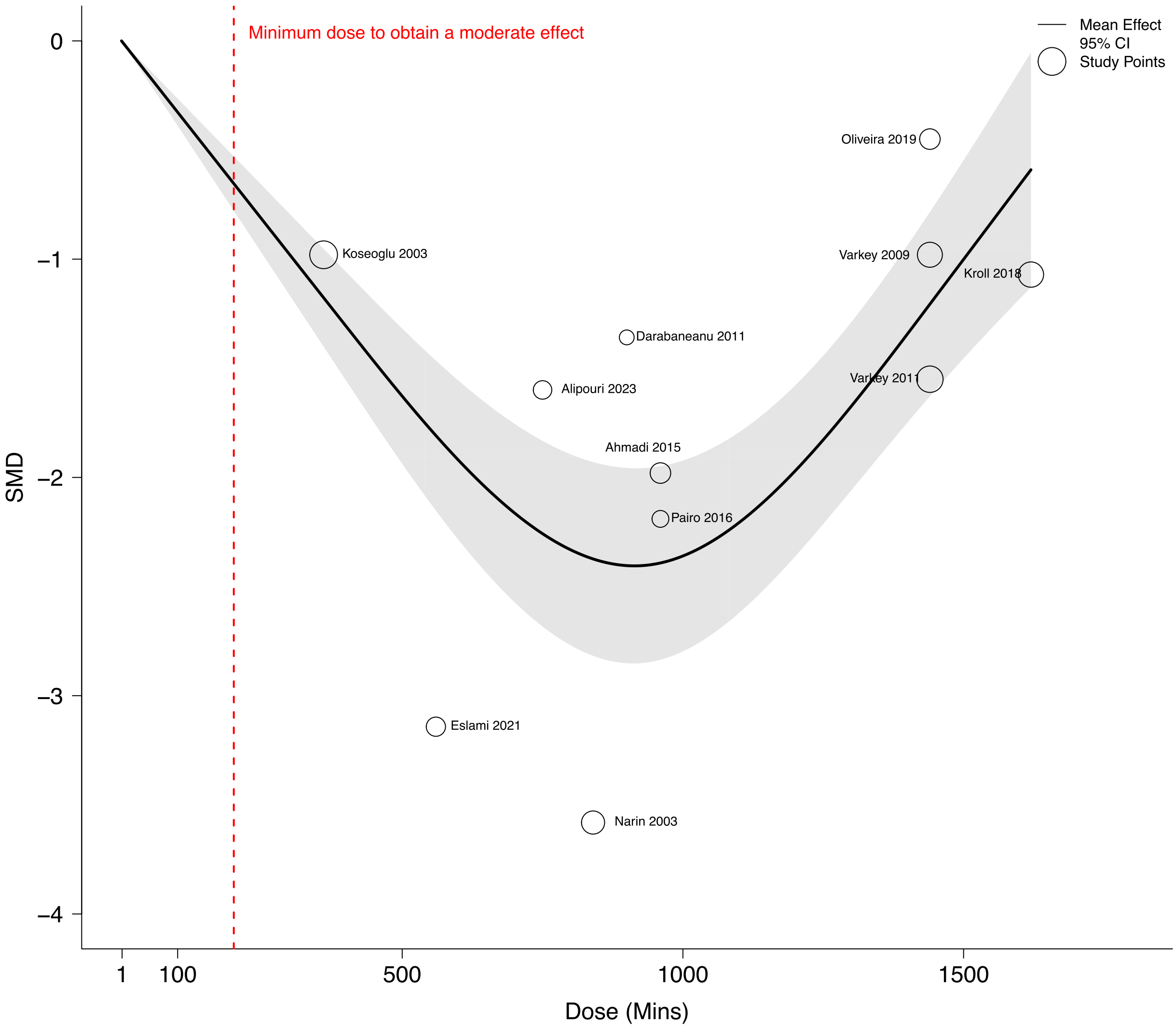

FIGURE 2 Dose–response association between total minutes of aerobic exercise and change in pain intensity (effect size). Each included study represents a point estimate. The standardized mean difference corresponds to the within-group change between baseline and final measurement. Studies with larger circles contributed more to the overall effect size than other studies. The solid line represents the estimate of the mean difference from baseline, and the dashed lines represent the 95% CI. [Color figure can be viewed at wileyonlinelibrary.com]

episodic migraine ($k=4$). Subgroup meta-analysis showed a statistically significant decrease in the migraine frequency in chronic migraine (SMD, −0.33; 95% CI, −0.39 to −0.27) without evidence of heterogeneity ($p=0.99$, $I^2=0\%$) and in episodic migraine (SMD, −0.73; 95% CI, −1.28 to −0.19) without evidence of heterogeneity ($p=0.591$, $I^2=0\%$). Test for subgroup differences showed statistically significant differences between both types of migraine ($p=0.02$) (Figure S8).

Sensitivity analysis: Sex

Five studies that measured migraine frequency performed the intervention only in female patients. Meta-analysis showed a statistically significant decrease in the migraine frequency (SMD, −1.45; 95% CI, −1.93 to −0.98) without evidence of heterogeneity ($p=0.556$, $I^2=0\%$) (Figure S9).

Sensitivity analysis: Aura

Six studies that measured migraine frequency performed the intervention in patients with migraine without aura. Meta-analysis showed a statistically significant decrease in the migraine frequency (SMD, −0.89; 95% CI, −1.5 to −0.29) with evidence of medium heterogeneity ($p=0.022$, $I^2=61.1\%$) (Figure S10).

Dose–response relationships for migraine frequency

The spline model showed a U-shape statistically significant association ($\chi^2=86.41$, dl = 2, $p<0.001$) between total minutes of exercise and reduction in migraine frequency (within-group change from baseline to final measurement). The estimated coefficient for dose was −0.002 (95% IC: −0.0025 to −0.0016, $p<0.001$) suggesting an initial decrease in effect as dose increases. However, the coefficient

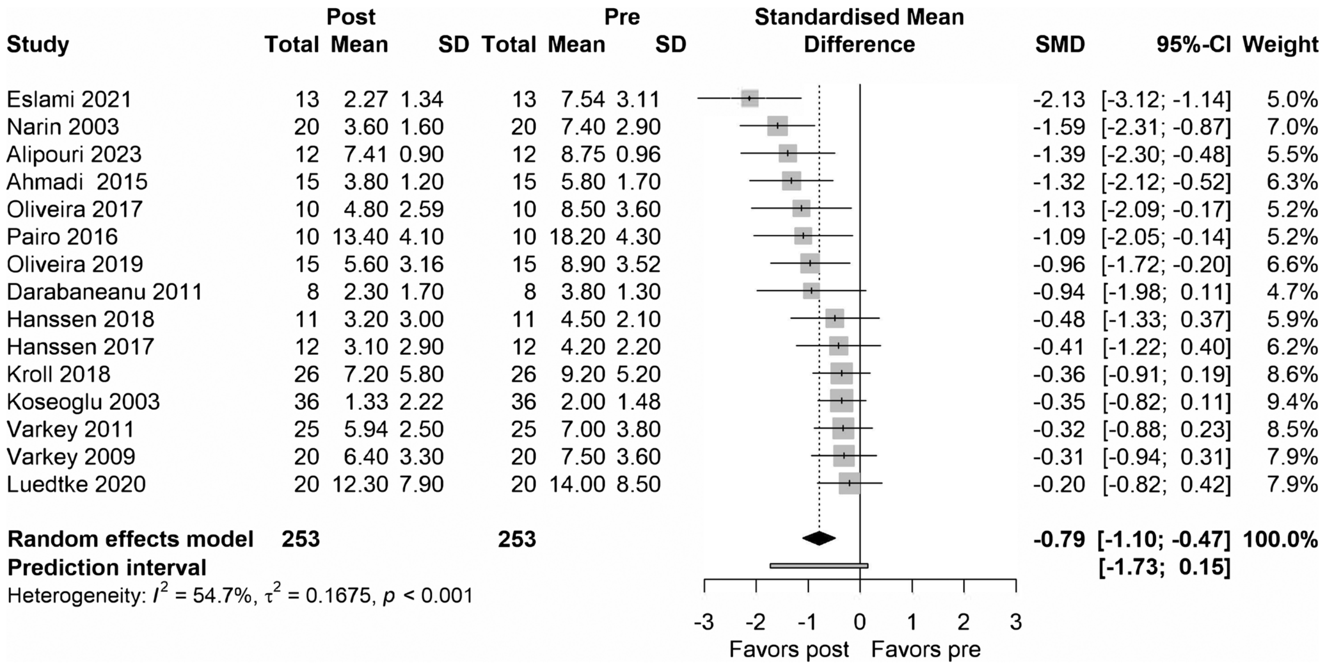

FIGURE 3 Forest plot of the effect on migraine frequency. Each study included in the meta-analysis represents a point estimate with the corresponding 95% CI. The polygon at the bottom of the graph corresponds to the overall effect, and its width represents its 95% CI. Trials with larger squares contributed more to the overall effect size than other trials. CI, confidence interval.

for the curvature of the relationship was 0.0025 (IC 95%: 0.0018 to 0.0031, $p<0.001$), indicating a change in the slope, suggesting a possible inflection point at higher doses (Figure 4). The model showed a good fit, with a log-likelihood of −17.71, AIC = 39.42, and BIC = 40.84. A minimum dose of 300 total minutes of aerobic exercise program duration was required to obtain a moderate effect in reducing migraine frequency (SMD, −0.61; 95% CI, −0.73 to −0.47). A maximum effect was observed at 950 min (SMD, −1.55; 95% CI, −1.87 to −1.22) (Table S4).

Risk of bias

The RCTs included in this review were evaluated using the Risk of Bias 2 (RoB-2) tool. In the summary of the findings, the domain that presented the highest risk of bias was D1 (selection of the reported results) and D2 (deviations from intended intervention), with more than 46% of the studies showing a high risk of bias and the other ones with some concerns in this domain. Furthermore, all the studies presented certain risks because of measurements of the outcome (D4). Missing outcome data was the domain with more articles in low risk of bias (almost 43%), and the other two domains had a combination of low, some concerns and high risk of bias. Finally, 84.7% of the studies were considered to have an elevated risk of bias in the overall assessment. The Risk of Bias 2 summary results and risk of bias graph are shown in Figures 5 and 6. The interrater reliability of the risk of bias assessment was high (89%; κ coefficient = 0.78; 95% CI, 0.462–1.00). The nonrandomized studies included in this review were evaluated with the ROBINS-I tool. Both studies present serious risk of bias in the overall assessment, showing D1 (bias due to confounding as the worst domain assessed) and D3 (classification of interventions) as the best. The ROBINS-I results are presented in Figure 7.

DISCUSSION

This study examined the dose–response relationship of aerobic exercise with migraine intensity and frequency. The meta-analysis showed a significant reduction in pain intensity, with a large effect size, indicating a clinically relevant effect of aerobic exercise. Similarly, migraine frequency was significantly reduced, with a moderate effect size. Dose–response analyses showed a nonlinear relationship, with the largest effect observed at moderate doses of aerobic exercise (900–950 min total), whereas higher or lower doses appeared to have a smaller effect on either outcome. These results highlight the optimal doses of aerobic exercise, as a nonpharmacological intervention, effective for the treatment of migraine, but with very-low certainty of evidence.

Our findings extend beyond previous research by not only confirming the benefits of aerobic exercise in migraine management but also establishing, for the first time, specific dose thresholds for clinical effectiveness and optimal therapeutic response. Varangot-Reille et al.,[39] in a previous meta-analysis, identified that aerobic exercise has a small to moderate clinical effect on pain intensity in patients with migraine, albeit with low certainty of evidence. Similarly, La Touche et al.[40] reported that aerobic exercise could reduce the intensity, frequency, and duration of migraine and improve quality of life, supported by low to moderate quality evidence. On the other hand, Lemmens et al.[41] in a meta-analysis concluded that aerobic

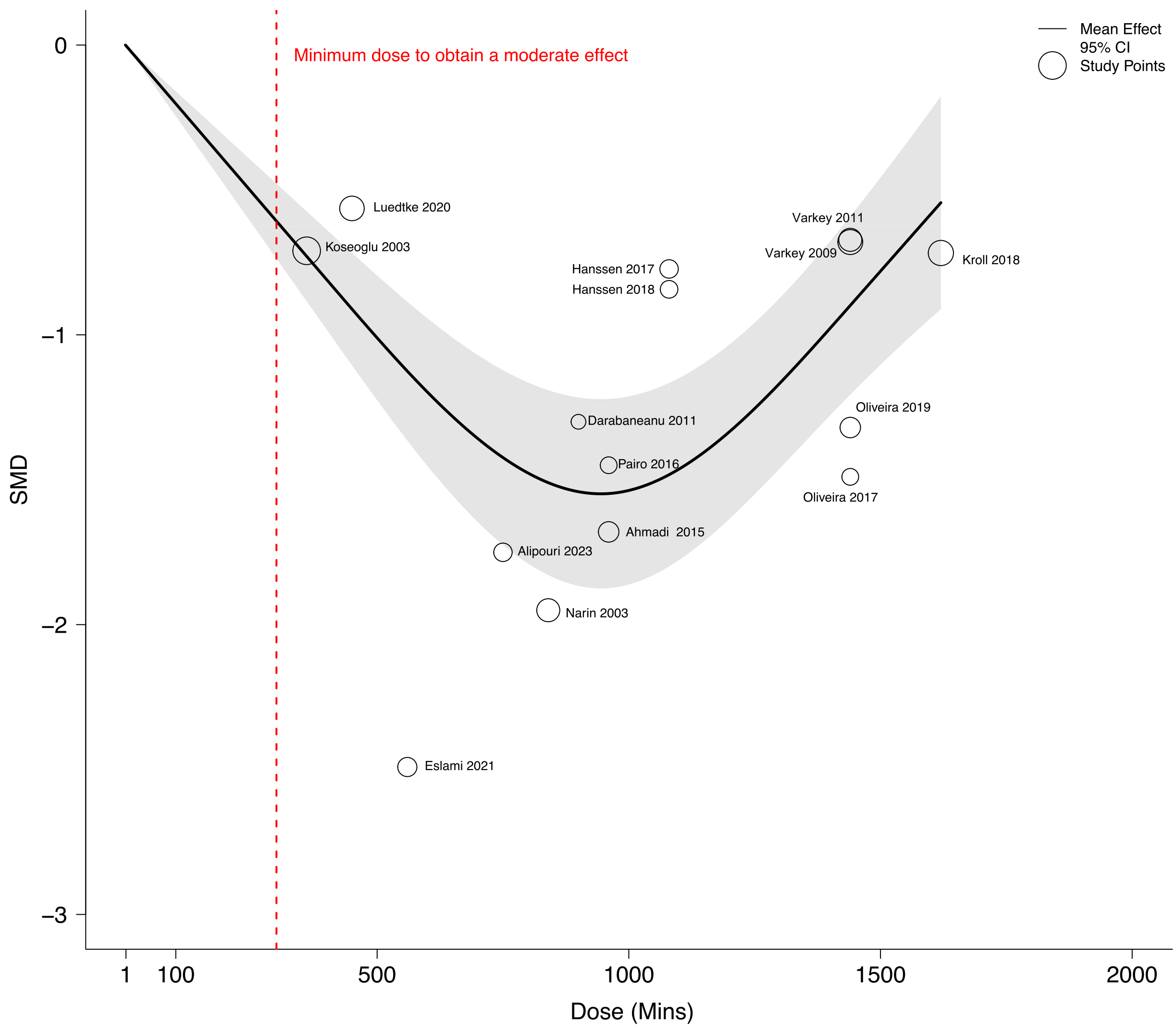

FIGURE 4 Dose–response association between total minutes of aerobic exercise and change in migraine frequency (effect size). Each included study represents a point estimate. The standardized mean difference corresponds to the within-group change between baseline and final measurement. Studies with larger circles contributed more to the overall effect size than other studies. The solid line represents the estimate of the mean difference from baseline, and the dashed lines represent the 95% CI. CI, confidence interval. [Color figure can be viewed at wileyonlinelibrary.com]

exercise might decrease the number of migraine days in patients, although there was insufficient evidence to draw conclusions about its impact on pain intensity or duration of attacks. These results are in line with the pre- versus post-meta–analysis performed in our research. Furthermore, the dose–response relationship identified in this study adds a novel perspective, because previous research has not examined how cumulative exercise duration affects outcomes.

Importantly, network meta-analysis of clinical trials has positioned high- and moderate-intensity aerobic exercise as one of the best interventions for reducing migraine frequency and intensity.[10,11] In particular, our findings highlight the importance of optimizing the dose of aerobic exercise to maximize benefits in reducing migraine intensity and frequency. The U-shaped association observed in this study suggests the existence of an optimal "therapeutic window" for exercise dosing, with benefits increasing up to approximately 900–950 min of total aerobic exercise and then diminishing at higher doses. This pattern may reflect physiological adaptations at optimal doses versus potential overtraining/accumulated fatigue or increased migraine triggers at excessive durations, providing crucial insights for personalized exercise prescription. Although the U-shaped dose–response pattern suggests an optimal aerobic exercise interval, the reduction in effects beyond 950 min should be interpreted with caution. This inflection may reflect statistical artifact, limited data at higher doses, or unmeasured factors such as exercise adherence or tolerability. Further mechanistic studies are needed to clarify whether this decline reflects physiological limits or methodological bias. Identifying this minimum and optimal dose is important not only to motivate patients to set achievable and realistic goals but also to guide health professionals in accurate exercise prescription and evidence-based physical activity promotion. Further studies are needed to clarify how these effects can be maximized, particularly beyond 1000 min of aerobic program duration, by

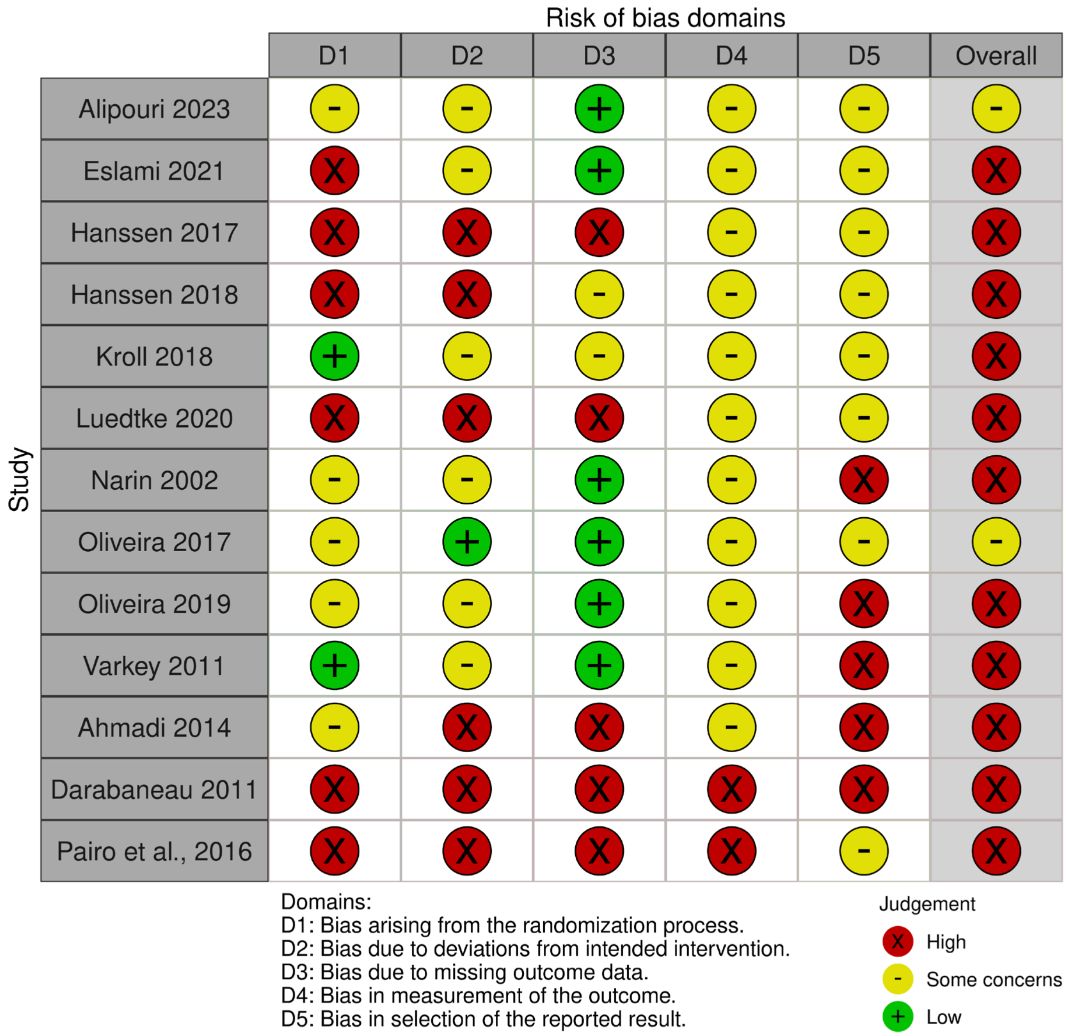

FIGURE 5 Risk of bias of the included studies (Cochrane Risk of Bias Tool for Randomized Controlled Trials 2.0). [Color figure can be viewed at wileyonlinelibrary.com]

exploring variables such as different exercise intensities, modalities, or complementary pharmacological therapies.

Previous studies have suggested that migraine share mechanisms of central sensitization,[42] a common phenomenon in several chronic pain conditions, with impaired regulation of descending inhibitory modulatory mechanisms.[43] Previous studies have also shown increased glial density at the brain level in patients with migraine, supporting the role of neuroinflammation.[44] These previous studies indicate that elevated levels of inflammatory markers such as C-reactive protein, pro-inflammatory cytokines, and changes in adipocytokines such as tumor necrosis factor-α and interleukin-6 are involved in migraine pathogenesis.[45–47] In this context, it has been proposed that the effect of exercise may be related to changes in inflammatory and neurovascular pathways, including an effect on obesity or adiposity, as well as psychological and behavioral factors.[45]

Endogenous opioids, such as endorphins, increase during exercise, activating descending inhibitory pathways and reducing pain perception.[48] The endocannabinoid system is also stimulated by moderate-intensity exercise, promoting analgesia through the regulation of neurotransmitters and anti-inflammatory responses.[49] In addition, exercise increases levels of neurotrophic factors, such as brain-derived neurotrophic factors, which enhance neuronal plasticity and reduce central sensitization associated with migraine.[49] Other mechanisms related to aerobic exercise are the modulatory effects it exerts on affective and cognitive aspects. For example, changes in self-efficacy and reduction of antidepressant symptoms after aerobic exercise may be related to improvements in migraine.[45] Thus, exercise-induced changes in migraine could be explained by several parallel mechanisms.

Notably, the literature has discussed that exercise can act both as a trigger for migraine and as a prophylactic strategy. For example, attacks may be induced by the acute release of neuropeptides, such as calcitonin gene-related peptide, or by alterations in hypocretin and lactate metabolism, whereas its preventive effect may be related to the increase of beta-endorphins, endocannabinoids and brain-derived neurotrophic factors in plasma after physical activity.[50] These findings underline the importance of identifying optimal exercise doses.

From a clinical perspective, these results establish aerobic exercise as an evidence-based, cost-effective nonpharmacological

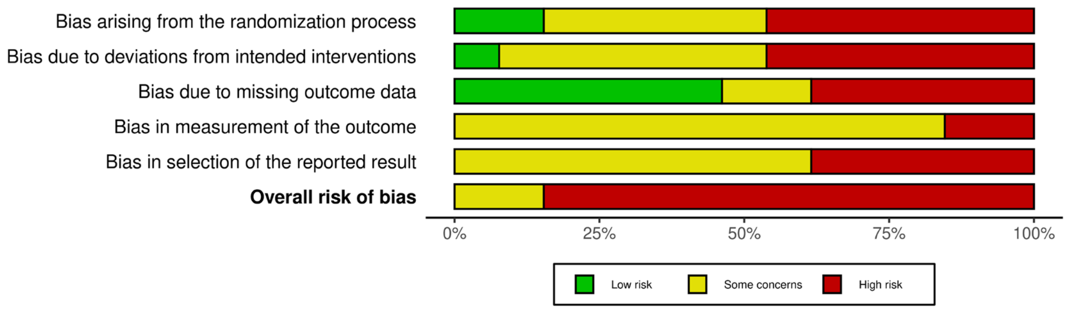

FIGURE 6 Summary of the risk of bias assessment (Cochrane Risk of Bias Tool for Randomized Controlled Trials 2.0).

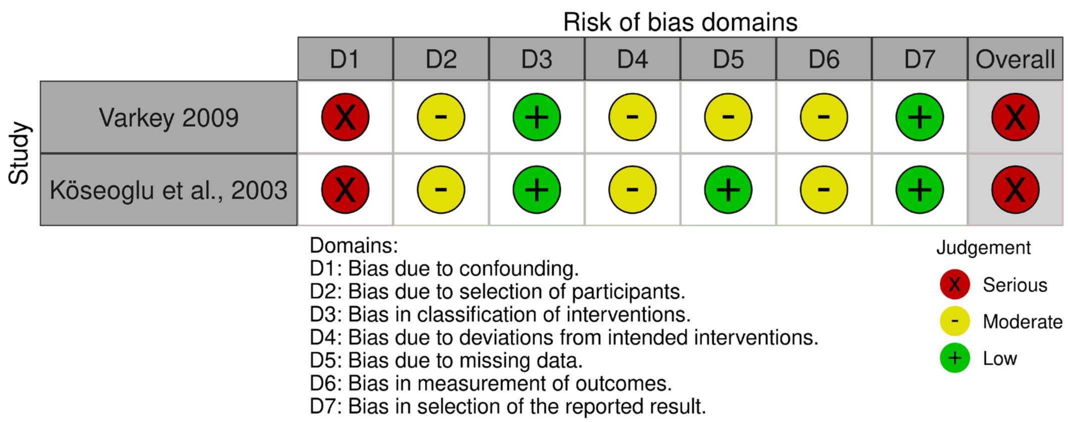

FIGURE 7 Risk of bias of the nonrandomized included studies (Risk of Bias in Non-Randomized Studies of Interventions). [Color figure can be viewed at wileyonlinelibrary.com]

intervention for migraine management, with clear dosing parameters that clinicians can immediately implement. This is particularly valuable for patients seeking alternatives or adjuncts to pharmacological treatments because it offers significant benefits with minimal side effects and can be integrated into existing treatment plans. The identification of an optimal exercise dose provides practical guidance for health professionals when designing exercise programs for this population. Specifically, we recommend that a total program duration of approximately 900–950 min be achieved, which can be practically implemented as 3 weekly sessions of 30 min each over 10–11 weeks with and intensity of 50%–70% of the $VO2_{peak}$ or 13–16 in a RPE scale. This intensity reflects a "somewhat hard to hard" effort, usually characterized by a noticeably increased breathing rate in which the patient can still maintain a conversation but would struggle to sing or speak in long sentences. Regarding the types of aerobic exercise, the included studies used a range of modalities, most commonly brisk walking and stationary or outdoor cycling, but also running and, in some protocols, swimming. This variety suggests that patients can choose among several accessible activities, allowing clinicians to tailor recommendations according to individual preferences, fitness levels, and feasibility.

This concrete prescription provides clinicians with an evidence-based framework that balances optimal therapeutic effect with feasible patient adherence. The provision of supervised, tailored exercise programs may be particularly helpful in maximizing adherence and effectiveness, taking into account common barriers to exercise, such as fear of movement and timing of exercise.[50,51] These recommendations are particularly applicable in supervised settings, where adherence and progression can be more closely monitored. In unsupervised settings, individualized guidance may be necessary to promote adherence and reduce risk. Although the included studies reported no adverse effects, it is important to note that individual responses to exercise may vary. Clinicians are encouraged to implement proactive strategies (e.g., gradual progression, adequate hydration, and nutritional support) to minimize the risks and increase the benefits of aerobic exercise in people with migraine. Future research should explore how individual factors, such as comorbidity or personal preferences, may influence exercise response. In this sense, our results show that the heterogeneity found in the meta-analyses is reduced when we perform sensitivity analyses according to the type of migraine (chronic or episodic, with or without aura) or sex. These factors could influence the exercise-related outcomes, and future research should consider them to determine individualized exercise for these specific patient populations.

Strengths and limitations

This study is notable for investigating the dose–response relationship between aerobic exercise and clinical outcomes in people with migraine, including both pain intensity and attack frequency. The use of dose–response models allowed the identification of an optimal "therapeutic window," a crucial and novel contribution to the field. Furthermore, the inclusion of a large number of studies and participants strengthens the statistical robustness and generalizability of the findings, which are relevant for the implementation of nonpharmacological strategies in the multidisciplinary management of migraine. On the other hand, this study has several limitations that should be considered when interpreting the results. First, the significant heterogeneity observed among the included studies reflects substantial differences in intervention characteristics, exercise modalities (ranging from walking to cycling programs), and participant demographics across studies, which may influence the generalizability of our dose–response findings to specific patient subgroups. This may have influenced the estimated effect sizes and the shape of the dose–response relationship. In addition, the small sample size for a meta-analysis and dose–response modeling could affect statistical power. Second, the lack of standardization in the measurement of walking intensity across trials, due to the use of different methods, makes it difficult to identify the optimal intensity level for maximum therapeutic benefit. In addition, measurements of cumulative exercise duration do not always take into account aspects such as adherence, intensity, or interruptions. Third, the analyses include pre–post comparisons without control groups, which limit causal inference and may overestimate effect sizes. Fourth, our operational definition of "dose" as total minutes does not capture key variables such as session frequency or intrasession intensity, which could influence the shape and interpretation of dose–response curves. Finally, the generalizability of the results may be limited by the specific clinical populations and types of aerobic exercise described in the included studies, which could restrict their applicability to broader migraine populations.

Considerations for future research

Although our study focused on the total duration (minutes) of aerobic exercise, it is important to recognize that intensity plays a critical role in the clinical response to physical activity. Most of the included trials reported moderate-intensity aerobic exercise, defined by a percentage of VO_2peak or by subjective scales such as the Borg RPE scale. However, this lack of standardization in intensity measurement may introduce variability in the results. Because the physiological effects of exercise differ as a function of intensity, future studies should employ more consistent and objective measures of exercise intensity.

Another important limitation is the assumption of full adherence across sessions. Our cumulative dose calculations did not consider possible session breaks, missed sessions, or symptom-triggered withdrawal, which are common in people living with migraine. Thus, although our recommendation of 900–950 min represents an optimal cumulative target, clinicians should apply it flexibly, using gradual progression strategies and monitoring patient response to avoid dropouts. We strongly recommend that future research in this field includes detailed reports on adherence rates and reasons for adherence (e.g., fatigue).

CONCLUSION

Aerobic exercise appears to be effective in reducing both pain intensity and migraine frequency in people with migraine. Specifically, the greatest observed effect on both variables occurred at a cumulative dose of 900–950 min of aerobic exercise during the program. Dose–response analyses revealed a U-shaped relationship, with reduced benefits outside this optimal range. However, these results should be interpreted with caution, as they are based on very-low certainty evidence due to high heterogeneity, risk of bias, and possible publication bias. These findings highlight the importance of identifying a minimum effective dose for clinically meaningful benefits, particularly in the context of nonpharmacological interventions. As people with migraine may find it difficult to follow standard physical activity guidelines, a gradual and individualized approach is advisable. The proposed dose should be considered hypothesis generating and may guide future studies aimed at refining dosing strategies.

AUTHOR CONTRIBUTIONS

Daniel C. Ogrezeanu: Data curation; writing – original draft. **Rodrigo Núñez-Cortés:** Investigation; methodology; writing – original draft. **Joaquín Salazar-Méndez:** Writing – review and editing. **Iván Cuyul-Vásquez:** Writing – review and editing. **Rubén López-Bueno:** Writing – review and editing. **Francisco José Ferrer-Sargues:** Writing – review and editing. **Lars Louis Andersen:** Writing – review and editing. **Joaquín Calatayud:** Investigation; methodology; writing – review and editing. **Luis Suso-Martí:** Conceptualization; formal analysis; investigation; methodology; project administration; writing – original draft.

CONFLICT OF INTEREST STATEMENT

Daniel C. Ogrezeanu, Rodrigo Núñez-Cortés, Joaquín Salazar-Méndez, Iván Cuyul-Vásquez, Rubén López-Bueno, Francisco José Ferrer-Sargues, Lars Louis Andersen, Joaquín Calatayud, and **Luis Suso-Martí** declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

REFERENCES

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38:1-211.
2. Ferrari AJ, Santomauro DF, Aali A, et al. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024;403:2133-2161.
3. Chen Z, Kong X, Yang C, Li XY, Guo H, Wang ZW. Global, regional, and national burden and trends of migraine among youths

and young adults aged 15–39 years from 1990 to 2021: findings from the global burden of disease study 2021. *J Headache Pain*. 2024;25:131.
4. Ashina M, Katsarava Z, Do TP, et al. Migraine: epidemiology and systems of care. *Lancet*. 2021;397:1485-1495.
5. Busch V, Gaul C. Exercise in migraine therapy—is there any evidence for efficacy? A critical review. *Headache*. 2008;48:890-899.
6. Varangot-Reille C, Suso-Martí L, Romero-Palau M, Suárez-Pastor P, Cuenca-Martínez F. Effects of different therapeutic exercise modalities on migraine or tension-type headache: A systematic review and meta-analysis with a replicability analysis. *J Pain*. 2022;23:1099-1122.
7. Song T-J, Chu MK. Exercise in treatment of migraine including chronic migraine. *Curr Pain Headache Rep*. 2021;25:14.
8. Reina-Varona Á, Madroñero-Miguel B, Gaul C, et al. Therapeutic exercise parameters, considerations, and recommendations for migraine treatment: an international Delphi study. *Phys Ther*. 2023;103:pzad080.
9. La Touche R, Fierro-Marrero J, Sánchez-Ruíz I, et al. Prescription of therapeutic exercise in migraine, an evidence-based clinical practice guideline. *J Headache Pain*. 2023;24:68.
10. Woldeamanuel YW, Oliveira ABD. What is the efficacy of aerobic exercise versus strength training in the treatment of migraine? A systematic review and network meta-analysis of clinical trials. *J Headache Pain*. 2022;23:134.
11. Reina-Varona Á, Madroñero-Miguel B, Fierro-Marrero J, Paris-Alemany A, la Touche R. Efficacy of various exercise interventions for migraine treatment: a systematic review and network meta-analysis. *Headache*. 2024;64:873-900.
12. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
13. Rohatgi A. WebPlotDigitizer. 2022. https://automeris.io/WebPlotDigitizer
14. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14:135.
15. Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res*. 2018;27:1785-1805.
16. Shi J, Luo D, Weng H, et al. Optimally estimating the sample standard deviation from the five-number summary. *Res Synth Methods*. 2020;11:641-654.
17. Pairo Z, Parnow AH, Sari-Aslani P, et al. Effect of moderate intensity aerobic exercise on migraine headache indexes and quality of life improvement in women with migraine. *Q Horiz Med Sci*. 2016;22:291-297.
18. Ahmadi Z, Tadibi V, razazian n. The effect of 8-week aerobic exercise on migraine headache indices and blood nitric oxide level in women with migraine. *Sport Physiol*. 2015;7:33-50.
19. Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions*. Wiley, 2019.
20. Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions*. Wiley. Epub ahead of Print January 1, 2019. doi:10.1002/9781119536604
21. Hopkins WG, Marshall SW, Batterham AM, Hanin J. Progressive statistics for studies in sports medicine and exercise science. *Med Sci Sports Exerc*. 2009;41:3-13.
22. Furuya-Kanamori L, Barendregt JJ, Doi SAR. A new improved graphical and quantitative method for detecting bias in meta-analysis. *Int J Evid Based Healthc*. 2018;16:195-203.
23. Crippa A, Orsini N. Dose-response meta-analysis of differences in means. *BMC Med Res Methodol*. 2016;16:91.
24. Crippa A, Discacciati A, Bottai M, Spiegelman D, Orsini N. One-stage dose–response meta-analysis for aggregated data. *Stat Methods Med Res*. 2019;28:1579-1596.
25. Crippa A, Orsini N. Multivariate dose-response meta-analysis: the dosresmeta *R* package. *J Stat Softw*. 72:1-15. Epub ahead of print 2016. doi:10.18637/jss.v072.c01
26. Varkey E, Cider Å, Carlsson J, Linde M. A study to evaluate the feasibility of an aerobic exercise program in patients with migraine. *Headache*. 2009;49:563-570.
27. Köseoglu E, Akboyraz A, Soyuer A, Ersoy A. Aerobic exercise and plasma beta endorphin levels in patients with migrainous headache without aura. *Cephalalgia*. 2003;23:972-976.
28. Darabaneanu S, Overath CH, Rubin D, et al. Aerobic exercise as a therapy option for migraine: a pilot study. *Int J Sports Med*. 2011;32:455-460.
29. Oliveira AB, Ribeiro RT, Mello MT, Tufik S, Peres MFP. Anandamide is related to clinical and cardiorespiratory benefits of aerobic exercise training in migraine patients: a randomized controlled clinical trial. *Cannabis Cannabinoid Res*. 2019;4:275-284.
30. Hanssen H, Minghetti A, Magon S, et al. Effects of different endurance exercise modalities on migraine days and cerebrovascular health in episodic migraineurs: a randomized controlled trial. *Scand J Med Sci Sports*. 2018;28:1103-1112.
31. Alipouri M, Amiri E, Hoseini R, Hezarkhani LA. Effects of eight weeks of aerobic exercise and vitamin D supplementation on psychiatric comorbidities in men with migraine and vitamin D insufficiency: a randomized controlled clinical trial. *J Affect Disord*. 2023;334:12-20.
32. Varkey E, Cider Å, Carlsson J, Linde M. Exercise as migraine prophylaxis: a randomized study using relaxation and topiramate as controls. *Cephalalgia*. 2011;31:1428-1438.
33. Oliveira AB, Bachi ALL, Ribeiro RT, Mello MT, Vaisberg M, Peres MFP. Exercise-induced change in plasma IL-12p70 is linked to migraine prevention and anxiolytic effects in treatment-naïve women: a randomized controlled trial. *Neuroimmunomodulation*. 2017;24:293-299.
34. Luedtke K, Starke W, Korn KV, Szikszay TM, Schwarz A, May A. Neck treatment compared to aerobic exercise in migraine: a preference-based clinical trial. *Cephalalgia Rep*. 2020;3:2515816320930681.
35. Hanssen H, Minghetti A, Magon S, et al. Superior effects of high-intensity interval training vs. moderate continuous training on arterial stiffness in episodic migraine: a randomized controlled trial. *Front Physiol*. 2017;8:1086.
36. Krøll LS, Hammarlund CS, Linde M, Gard G, Jensen RH. The effects of aerobic exercise for persons with migraine and co-existing tension-type headache and neck pain. A randomized, controlled, clinical trial. *Cephalalgia*. 2018;38:1805-1816.
37. Narin SO, Pinar L, Erbas D, Oztürk V, Idiman F. The effects of exercise and exercise-related changes in blood nitric oxide level on migraine headache. *Clin Rehabil*. 2003;17:624-630.
38. Eslami R, Parnow A, Pairo Z, Nikolaidis P, Knechtle B. The effects of two different intensities of aerobic training protocols on pain and serum neuro-biomarkers in women migraineurs: a randomized controlled trial. *Eur J Appl Physiol*. 2021;121:609-620.
39. Varangot-Reille C, Suso-Martí L, Romero-Palau M, Suárez-Pastor P, Cuenca-Martínez F. Effects of Different Therapeutic Exercise Modalities on Migraine or Tension-Type Headache: A Systematic Review and Meta-Analysis with a Replicability Analysis. *J Pain*. 2022;23:1099–1122. doi:10.1016/j.jpain.2021.12.003
40. La Touche R, Fernández Pérez JJ, Proy Acosta A, et al. Is aerobic exercise helpful in patients with migraine? A systematic review and meta-analysis. *Scand J Med Sci Sports*. 2020;30:965-982.
41. Lemmens J, De Pauw J, Van Soom T, et al. The effect of aerobic exercise on the number of migraine days, duration and pain intensity in migraine: a systematic literature review and meta-analysis. *J Headache Pain*. 2019;20:16. doi: 10.1186/s10194-019-0961-8
42. Boyer N, Dallel R, Artola A, Monconduit L. General trigeminospinal central sensitization and impaired descending pain inhibitory controls contribute to migraine progression. *Pain*. 2014;155:1196-1205.

43. Fernández-de-Las-Peñas C. Physical therapy and exercise in headache. *Cephalalgia*. 2008;28:36-38. doi:10.1111/j.1468-2982.2008.01618.x
44. He W, Wang Y, Zhang Y, Zhang Y, Zhou J. The status of knowledge on migraines: The role of microglia. *J Neuroimmunol*. 2023;381:578118. doi: 10.1016/j.jneuroim.2023.578118
45. Irby MB, Bond DS, Lipton RB, Nicklas B, Houle TT, Penzien DB. Aerobic exercise for reducing migraine burden: mechanisms, markers, and models of change processes. *Headache*. 2016;56:357-369.
46. Peterlin BL, Rapoport AM, Kurth T. Migraine and obesity: epidemiology, mechanisms, and implications. *Headache*. 2010;50:631-648. doi:10.1111/j.1526-4610.2009.01554.x
47. Bond DS, Roth J, Nash JM, Wing RR. Migraine and obesity: epidemiology, possible mechanisms and the potential role of weight loss treatment. *Obes Rev*. 2011;12:e362-371.
48. Koltyn KF, Brellenthin AG, Cook DB, Sehgal N, Hillard C. Mechanisms of exercise-induced hypoalgesia. *J Pain*. 2014;15:1294-1304. doi:10.1016/j.jpain.2014.09.006
49. Hindiyeh NA, Krusz JC, Cowan RP. Does exercise make migraines worse and tension type headaches better? Accessed February 5, 2025. https://pubmed.ncbi.nlm.nih.gov/24234818/
50. Amin FM, Aristeidou S, Baraldi C, et al. The association between migraine and physical exercise. *J Headache Pain*. 2018;19:83.
51. Koho P, Orenius T, Kautiainen H, et al. Association of fear of movement and leisure-time physical activity among patients with chronic pain. Accessed February 5, 2025. https://pubmed.ncbi.nlm.nih.gov/21874214/

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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