SYSTEMATIC REVIEW

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Effect of aerobic exercise on cardiopulmonary fitness among people with knee osteoarthritis: a systematic review and meta-analysis

Shan Su¹, Clare Chung-Wah Yu^{1*}, Emma Feng-Ming Zhou¹, Jing-Yuan Liu² and Siu-Ngor Fu¹

Abstract

Background Although aerobic exercise is widely recommended to enhance cardiopulmonary fitness and mitigate cardiovascular risk, the efficacy and effectiveness of aerobic exercise interventions have not been comprehensively evaluated among people with knee osteoarthritis (OA). This systematic review and meta-analysis aimed to synthesize the current evidence on the impact of aerobic exercise on cardiopulmonary fitness in people with knee OA.

Methods PubMed, Embase, Scopus, and Web of Science were searched from inception to March 1, 2024, for randomized controlled trials (RCTs). Eligible RCTs included those with an aerobic exercise intervention (e.g., aerobic walking, cycling, aquatic aerobics), a primary outcome of maximum oxygen consumption (VO₂ max), and participants with knee OA. The aerobic exercise programs were compared to control interventions (e.g., education, light-intensity exercise, usual activities, and routine care). Secondary outcomes included distance (m) walked during the six-minute walk test (6MWD), and Patient-Reported Outcome Measures (i.e., pain score and disability score). The overall level of evidence was assessed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results Out of 988 studies, 5 RCTs with 459 people with knee OA were included in the analysis. Aerobic exercise programs included walking, cycling, jumping, stepping, and aquatic aerobics. Pooled mean differences and 95% confidence intervals (Cls) were 0.90 ml/kg/min (95% Cl 0.43 to 1.38; moderate evidence), 46.97 m (95% Cl 33.71 to 60.23; high evidence), 5.59 points (95% Cl 2.93 to 8.25; low evidence), and 3.03 points (95% Cl 1.05 to 5.01; moderate evidence) for VO_2 max, 6MWD, pain and disability, respectively.

Conclusion These results support the hypothesis that aerobic exercise can elicit improvements in cardiopulmonary fitness for people with knee OA. Future research should focus on optimizing current exercise regimens for people with knee OA and exploring how to improve adherence while minimizing symptom exacerbation by other exercise modalities, e.g., Nordic walking and inspiratory muscle training.

Systematic review registration CRD42022340966, 07/07/2022, PROSPERO.

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Keywords Knee osteoarthritis, Aerobic exercise, Cardiopulmonary fitness

Introduction

Knee osteoarthritis (OA) is a prevalent condition among older adults, affecting approximately 33% of people over the age of 60 years [1]. This condition is associated with reduced cardiopulmonary fitness, as evidenced by a substantial decline in maximum oxygen consumption (VO₂ max) by 25-38% compared to those without knee OA [2–5]. Additionally, people with knee OA have an 18-24% higher risk of cardiovascular disorders and mortality compared to the general population [6, 7]. Despite the critical role of physical activity in maintaining fitness and reducing cardiovascular risk, only about 13% of people with knee OA meet the World Health Organization (WHO) recommendation of at least 75-150 min of moderate-to-vigorous-intensity physical activity per week [8, 9]. Persistent knee pain is a significant barrier to physical activity in this population [10, 11], leading to reduced engagement in physical activity and further declines in cardiopulmonary fitness. This decline contributes to an increased risk of cardiovascular morbidity and mortality, posing a significant burden on the healthcare system [12]. Given these findings, there is a compelling need for targeted interventions to enhance cardiopulmonary fitness in people with knee OA alongside traditional pain management strategies.

Aerobic exercise, which involves activities that elevate the heart rate and oxygen consumption, is a cornerstone of physical activity recommendations [13]. Common forms of aerobic exercise include cycling, swimming, and running, all known to improve cardiopulmonary fitness [14, 15]. For people with knee OA, exercise prescription requires careful consideration. High-intensity or high-impact exercise may exacerbate joint symptoms [16, 17], while insufficient exercise may not yield significant fitness improvements. Non-weightbearing exercises, which are the activities where the body does not bear its own weight, such as cycling and swimming, offer jointfriendly alternatives to traditional weightbearing activities like running. These low-impact exercises are less likely to induce joint pain, potentially improving adherence and leading to sustained therapeutic benefits [18]. Research supports the efficacy of non-weightbearing exercises in this population [18]. For example, a randomized controlled trial demonstrated that non-weightbearing strength training effectively alleviated pain and enhanced physical function in obese people with knee OA [19]. Similarly, a systematic review concluded that non-weightbearing strengthening exercises yielded a larger pooled effect size for pain relief compared to weightbearing exercises, suggesting superior outcomes in people with knee OA [18]. Despite these findings, the impact of both weightbearing and non-weightbearing aerobic exercises on cardiopulmonary fitness in people with knee OA remains inadequately understood. Factors such as exercise regimens, adherence levels, and disease severity may influence the efficacy of different exercise modalities. Therefore, a comprehensive systematic review is warranted to evaluate the overall effects of current aerobic exercise programs on cardiopulmonary fitness in people with knee OA.

Consequently, this review systematically evaluates the effects of aerobic exercise on cardiopulmonary fitness in people with knee OA. Our primary outcome is $\rm VO_2$ max. Secondary outcomes include distance (m) walked during the six-minute walk test (6MWD), and Patient-Reported Outcome Measures (i.e., pain score, and disability score).

Materials and methods

Search strategy

This review followed the PRISMA 2020 guidelines for reporting systematic reviews [20] and was registered in PROSPERO (No. CRD42022340966, 07/07/2022). An electronic search was conducted using PubMed, Excerpta Medica Database, Scopus, and Web of Science, from inception to the March 1, 2024. Search terms were listed in Table 1. The search terms were modified to fit individual database searches (details in Additional file 1). Additionally, manual searches of the reference lists of the included studies and Google Scholar were conducted to identify any additional relevant articles.

Selection criteria

The inclusion criteria encompassed randomized controlled trial (RCT) involving people with primary knee OA (occurs without any identifiable underlying cause, such as injury or another medical condition), aerobic exercises (such as walking, cycling, swimming), a control group (e.g., education, usual activities, diet, light exercise), and a primary outcome (VO $_2$ max). The exclusion criteria included studies without primary outcomes (VO $_2$ max), those lacking full text, non-English/Chinese articles, and non-experimental studies (e.g., review, comments, guidelines). The flow chart of the selection was shown in Fig. 1.

Risk of bias

The Cochrane Risk of Bias tool 2 (RoB-2) was utilized to evaluate the risk of bias in the retrieved studies [21]. This assessment considered various domains, including selection bias, performance bias, detection bias, and reporting bias. Each study was systematically reviewed by two reviewers independently (SS and ZFM). Any

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Table 1 Search terms

| Search | Keywords |
|--------|---|
| 1 | Osteoarthritis OR arthritis |
| 2 | Knee OR knee joint OR tibiofemoral joint |
| 3 | 1 AND 2 |
| 4 | exercise OR aerobic OR endurance OR circuit-based OR swim OR swimming OR run OR running OR jog OR jogging OR walk OR walking OR cycle OR cycling OR step OR stepping OR resistance OR landed OR land-based OR aquatic |
| 5 | Aerobic Capacity OR Aerobic Power OR Cardiopulmonary Fitness OR Functional Capacity OR Oxygen Consumption OR VO ₂ OR Oxygen Uptake OR Oxygen Consumed |
| 6 | 3 AND 4 AND 5 |
| 7 | Limited in Humans, English OR Chinese |

discrepancies were resolved through discussion, and if

consensus could not be reached, another author (YCW) was consulted.

Quality of evidence

The quality of evidence was assessed using the five Grading of Recommendations Assessment, Development and Evaluation (GRADE) considerations: risk of bias, inconsistency, imprecision, indirectness, and publication bias. The GRADEpro software was used to determine the levels of evidence [22]. In order to ensure objectivity and reliability, two reviewers (SS and ZFM) screened and selected the studies and rated the quality of the evidence independently. Any discrepancies raised were solved by discussion and consultation with another group member (YCW) if any agreement was not attained.

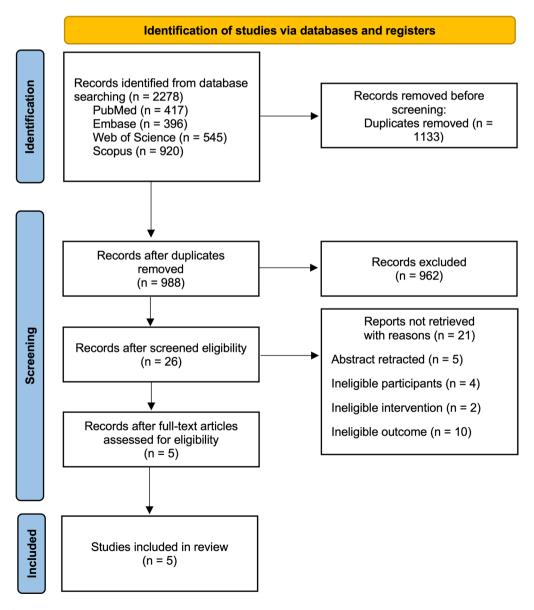


Fig. 1 PRISMA flow diagram

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Data extraction

Data extraction was conducted after article screening and selection by inclusion and exclusion criteria. The basic data, i.e., study code, sample size, age, gender, body mass index, and knee OA definition were extracted. To analyze the interventions, key components of the aerobic exercise protocols—frequency, intensity, time, and type (FITT principles)—were extracted. Additionally, the exercise protocols were evaluated to determine whether they adhered to the ACSM's guidelines for aerobic exercise prescription, which recommend at least 150-300 min/ week moderate-intensity aerobic exercise or 75 min/week vigorous-intensity aerobic exercise or 75-150 min/week moderate-to-vigorous-intensity aerobic exercise [13]. To assess the implementation of exercise interventions, data on adherence rates, adverse events, and dropout records were extracted. Finally, the Consensus on Exercise Reporting Template (CERT) tool was used to systematically assess and report the completeness of exercise intervention descriptions across studies [23].

Statistical analysis

Statistical analysis was conducted using RStudio, along with R packages such as "meta", "metafor", "forestplot" [24–27]. The results of primary and secondary outcomes reported in the published papers were analyzed. The mean scores and standard deviations for baseline and post-exercise time point were extracted from the studies. For Patient-Reported Outcome Measures assessing pain (e.g., pain scale 1–6, Arthritis Impact Measurement Scales [AIMS] pain scale 0–10, Knee Injury and Osteoarthritis Outcome Score [KOOS] pain scale 0-100, The Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC] pain scale 0-20) and disability (e.g., disability scale 1-5, KOOS disability scale 0-100, WOMAC disability scale 0-68), the extracted results were transformed into a standardized scale ranging from 0 (worst pain/disability) to 100 (no pain/disability).

The mean differences (MD) from baseline to post-exercise point, along with the standard deviations, were calculated for the exercise and the control group. For each trial, the mean changes and standard deviations of both groups were used in meta-analysis to calculate the pooled MD and 95% confidence interval (CI). The Q value and I-square (I²) were calculated to assess heterogeneity. If the I² value was lower than 50%, the fixed-effect model meta-analysis was applied; otherwise, the random-effect model meta-analysis was performed.

Results

Description of studies

The search strategy identified 988 papers, of which 5 RCTs met the inclusion criteria and were included in the review [28–32]. Details of the included studies are

presented in Table 2, and a list of the excluded studies with reasons can be found in Additional file 2.

Risk of bias and quality of evidence

Risk of bias findings are presented in Fig. 2. Overall, one study had 'high' risk of bias [29], three studies had 'some concerns' regarding the risk of bias [30-32] and one study had 'low' risk of bias [28]. All studies reported using an intention-to-treat approach to preserve the benefits of randomization and provide an unbiased estimate of treatment effect. Objective, reliable, and valid measures were employed to evaluate cardiopulmonary fitness. All studies reported comparable baseline values. Blinding of participant was not possible in any of the studies. Most studies did not implement allocation concealment or blinding of outcome assessors. One study reported their statistical methods within the result part [31]. Additionally, when applying the GRADE approach, the overall quality of evidence was assessed as high for 6MWD, moderate for cardiopulmonary fitness and disability, and low for pain (Table 3).

Interventions

The aerobic exercise interventions included aerobic walking, cycling, step-aerobic jumping, aquatic aerobics, and combined aerobic exercises (e.g., walking, cycling, aquatic aerobics). The duration of the interventions across all studies ranged from 10 weeks to 18 months, with a consistent frequency of 3 sessions per week, and session durations of 25 to 60 min. One study used vigorous intensity [30], and four moderate to vigorous intensity [28, 29, 31, 32]. Control interventions included health education [28], usual care [29, 31], and low-intensity cycling [30]. One study did not report the details of control group [32]. All studies met the criteria of ACSM's guidelines for aerobic exercise.

Implementation of intervention

The details of exercise intervention implementation were shown in Table 4. Three studies reported adverse events data in the experimental group, including falls, contact injuries with the pedal, and musculoskeletal pain [28-30]. Specifically, two falls occurred during walking, one of which resulted in a distal radius fracture [28]. Other adverse events did not lead to serious outcomes, and participants resumed exercise after an individualized period of rest [29, 30]. One sudden death and two cases of musculoskeletal pains occurred in the control group [28, 29]. Two studies did not report the adverse events [31, 32]. The attendance rate ranged from 68 to 92% in the experimental groups and 91 to 95% in the control groups [28–31]. The data on dropout reasons include loss to follow-up and failure to receive the allocated intervention [28-31]. The dropout rate ranged from 0 to 19% in the

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Table 2 Details of included studies

| Study | Population | Knee OA definition | Exercise | Control | FITT | Atten- dance rate (%) | Adverse event (n) | Drop- outs (n) | Results |
|---------------------------------|--|---|--|-----------------------------|--|--------------------------------|---|--------------------------|---|
| Et- tinger et al. 1997 | EG: 144 (99 F), 69±6 yo; CG: 149 (102 F), 69±6 yo | TFJ OA (KL 1–2), knee pain on most days | 3-month facility- based and 15-month home- based walking | Education | 60 min 3/week 50-70% HRR; 18 months | 68% in EG; 91%~95% in CG | 2 falls in EG group; 1 sud- den death in CG | EG (27) CG (22) | † VO_{2 peak}* †6MWD* Pain (1–6)* Disability (1–5)* |
| Man- gione et al. 1999 | EG: 19 (14 F), 71.1±7.7 yo, BMI 26.63±5.18; CG: 20 (12 F), 71±6.2 yo, BMI 29.08±5.07 | Knee OA (ACR clinical/ radiological diagnosis), knee pain | Vigorous intensity cycling | Light intensity cling | 25 min; 3/week; 70%HRR; 10 weeks | 92.2% in both groups | 1 fall during warm- up; 1 hit the pedal | 0 | ↑VO _{2 peak} ↑6MWD ↓AIMS-pain (0–10) |
| Keefe et al. 2004 | EG: 16 (6 F), 60.25 ± 8.74 yo; CG: 18 (11 F), 57.56 ± 14.27 yo | Knee pain due to OA | Walking, biking, aquatic aerobics | Routine care | 30 min; 3/week; 50–85% HRR; 12 weeks | 85–92% among groups | N.A. | CG (2) | ↑VO _{2 peak} ↓AIMS pain (0–10)* |
| Koli et al. 2015 | EG: 38 (38 F), 58±4 yo, BMI 27.1±3.1; CG:40 (40 F), 59±4 yo, BMI 26.7±4.2 | TFJ OA (KL1- 2), knee pain on most days | Step-aero- bic jump | Usual activities | 55 min; 3/week; 13.9 ± 0.5 (Borg scale 6-20) 12 months | 68% in EG | 6 MSK injury in EG; 2 in CG | EG (4) | ↑VO _{2 max} * ↓KOOS pain (0-100)* ↓KOOS dis- ability (0-100) |
| Ha et al. 2018 | EG: 9 (9), 60.89±5.06 yo, BMI 25.18±4.31; CG: 8 (8), 61.25±1.91 yo, BMI 24.63±5.33 | Physician di- agnosed knee OA (unclear criteria) | Aquatic aerobics | N.A. | 60 min; 3/week; 13–14 (Borg scale 6-20); 12 weeks | N.A. | N.A. | N.A. | ↑VO _{2 peak} ↓WOMAC pain (0–20) ↓WOMAC disability (0–68) |

Abbreviations. 6MWD: distance walked during the six-minute walk test; ACR: American College of Rheumatology; AIMS: The Arthritis Impact Measurement scale; BMI: body mass index; CG: controlled group; EG: experimental group; F: female; FITT: frequency, intensity, time, and type; HRR: heart rate reserve; KL: Kellgren and Lawrence grade; KOOS: Knee Injury and Osteoarthritis Outcome Score; N.A.: Not applicable; OA: osteoarthritis; TFJ: tibiofemoral joint; VO₂: oxygen consumption; yo: year old; WOMAC: The Western Ontario and McMaster Universities Osteoarthritis Index. ↑ indicates improved function, while ↓ indicates reduced symptom. * indicates statistically significant change

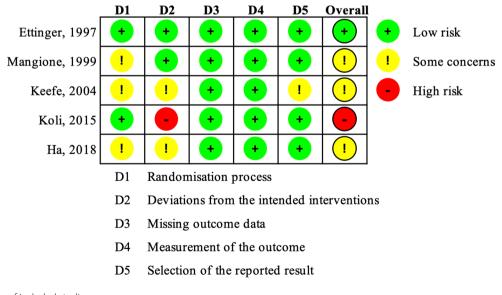


Fig. 2 Risk of Bias of included studies

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Table 3 GRADE quality of evidence

| Quality assessn | nent | | | | | | Nº of | Absolute | Qual- |
|---|-----------------|----------------------|----------------------|--------------|-------------|-----------------------|-----------------------|------------------------------|-----------------------------------|
| Outcomes | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | patients (studies) | Effect MD (95% CI) | ity of the evidence (GRADE) |
| VO ₂ max (ml/ kg/min) Exercise testing | RCT | serious ^a | not serious | not serious | not serious | none | 459 (5 studies) | 0.90 (0.43 to 1.38) | ⊕⊕⊕○ Moderate |
| 6MWD (meters) The six-minute walk test | RCT | serious ^a | not serious | not serious | not serious | strong association | 332 (2 studies) | 46.97 (33.71 to 60.23) | ⊕⊕⊕⊕ High |
| Pain (0-100) Self-rated questionnaire | RCT | serious ^a | serious ^b | not serious | not serious | none | 459 (5 studies) | 5.59 (2.93 to 8.25) | O OO Low |
| Disability (0-100) Self-rated questionnaire | RCT | serious ^a | not serious | not serious | not serious | none | 386 (3 studies) | 3.03 (1.05 to 5.01) | ⊕⊕⊕⊖ Moderate |

Abbreviations

6MWD: distance walked during the six-minute walk test; CI: confidence interval; MD: mean difference; VO₂ max: maximum oxygen consumption; RCT: randomized controlled trial

Explanations

High quality: Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low quality: We are very uncertain about the estimate

experimental group, with the number of dropouts ranging from 0 to 27 participants, and from 0 to 15% in the control group, with the number of dropouts ranging from 0 to 22 participants. One study did not disclose attendance rate or dropout data [32]. Furthermore, four studies indicated that the exercise programs were adjusted as needed to ensure safe and effective implementation [28–31].

Severity of knee OA

Two studies reported the severity of knee OA (i.e., Kell-gren and Lawrence grade 1–2) [28, 29]. In contrast, other studies did not investigate whether radiological severity affected the outcome [30–32].

Analgesic medication

One study provided data on analgesic medication for participants by questionnaire [29]. Koli (2015) reported the comparable usage of analgesic medication at baseline between the intervention group and the control group. No study reported changes of analgesic medication usage pre- and post-intervention.

Statistics of meta-analysis

VO_2 max (Fig. 3)

Five studies provided data on 459 participants. Betweenstudy heterogeneity was $I^2 = 0\%$. The pooled effect showed an improvement in VO_2 max with a MD of 0.90 (95% CI 0.43 to 1.38).

6WMD (Fig. 4)

Two studies provided data on 332 participants [28, 30]. Between-study heterogeneity was $I^2 = 0\%$. The pooled effect showed an improvement in cardiopulmonary fitness with a MD of 46.97 (95% CI 33.71 to 60.23).

Pain score (Fig. 5)

Five studies provided data on 459 participants. Two studies [28, 31] reported a statistically significant reduction in pain post exercise. The other 3 studies showed that the exercises reduced the pain but these reductions were not statistically significant [29, 30, 32]. Pooled results of these five studies demonstrated a statistically significant effect on pain reduction with MD of 5.59 (95% CI 2.93 to 8.25). Between-study heterogeneity was $\rm I^2$ = 69%.

Disability score (Fig. 6)

Three studies provided data on 386 participants. One study indicated significant improvement of functional disability [28]. Pooled results in the fixed-effect model of three studies demonstrated significant improvement with a MD of 3.03 (95% CI 1.05 to 5.01). The between-study heterogeneity was $I^2 = 30\%$.

^a Most studies had "some concerns" for RoB; ^b I² = 69%, substantial heterogeneity GRADE Working Group grades of evidence

Table 4 Consensus on exercise reporting template (CERT)

| | | | How | | | | | | | | | |
|----------------------|---|-----------------|-------------------|-------------------------------------|-----------------|-----------|--|-------------------|--------------------------------------|--------------|--|-----------------|
| Study | What | Who I/G U/S) | 1/G (S/US) | Adherence/ Adverse event | Motivation | | Progress: Exercise rule, how replicable | Home exercise/ | Where | When/ How | When/ Tailor/How/Start How level | How well: |
| | | | | | | | | no exercise | | much | | plan, actual |
| Ettinger et al. 1997 | Indoor tract, heart rate monitor | Z. Y. | G to I/S to US | Exercise leader to participants/Yes | ∀ . Z | N.A./N.A. | Yes | N.A./Yes | Central facil- ity and home | Yes | Tailor/HRmax/N.A. | Yes/ Yes |
| Mangione et al. 1999 | Mangione et al. 1999 Cycle ergometer, heart rate monitor, VAS | Ä. | N.A./S | Researcher/Yes | N.A. | N.A./N.A. | Yes | N.A./N.A. | In center | Yes | Tailor/HRmax/N.A. | N.A./ Yes |
| Keef et al. 2004 | Bike, pool, Nordic tract, heart rate monitor | Yes | g/S | N.A./N.A. | N.A. | N.A./Yes | Yes | N.A./N.A. | Ä. | Yes | Tailor/HRmax/N.A. | N.A./ Yes |
| Koli et al. 2015 | Foam fence, step bench, Yes VAS, Borg scale | Yes | N.A./S | Exercise trainer/Yes | N.A. | N.A./Yes | Yes | N.A./N.A. | Ϋ́. | Yes | Tailor/Borg scale/N.A. | Yes/ Yes |
| Haet al. 2018 | Pool, Borg scale | N.A. | N.A/S | N.A./N.A. | N.A. | N.A./N.A. | N.A. | N.A./N.A. | Pool | N.A. | Tailor/Borg scale/ N.A. N.A. N.A. N.A. | N.A. A.A. |
| A 1-1 | | | | | | | | | | | | |

G. Group; HRmax: Maximum heart rate; I: Individual; S: Supervised; N.A.: Not applicable; US: Unsupervised; VAS: Visual Analogue Scale

Discussion

This review demonstrates that aerobic exercise improves VO_2 max, 6MWD, patient-reported pain and disability in people with knee OA.

Effectiveness on cardiopulmonary fitness

This review supports the hypothesis that aerobic exercise can improve cardiopulmonary fitness in people diagnosed with knee OA. However, the magnitude of the observed improvements in cardiopulmonary fitness was small. Notably, both $\rm VO_2$ max and 6MWD failed to reach the minimal clinically important difference (MCID) of 1 ml/kg/min [33] and 79 m [34]. In contrast, previous studies have reported more substantial improvements in these measures among different populations, such as older adults demonstrating an average increase of nearly 4 ml/kg/min in $\rm VO_2$ max [14], and long-COVID-19 survivors exhibiting an enhancement of approximately 76 m in 6MWD [35]. Several factors may explain these differences.

The interpretation of the results presented in this study necessitates a critical examination of the exercise regimens employed. All included aerobic exercise protocols adhered to the ACSM's guidelines for moderate-to-vigorous-intensity aerobic exercises, which are widely recognized for their efficacy in enhancing cardiopulmonary fitness [13]. Notably, the findings indicated that only aerobic walking and step-aerobic jump yielded statistically significant improvements in cardiopulmonary fitness, while modalities such as cycling, aquatic aerobics, and combined aerobics did not demonstrate similar enhancements. A plausible explanation for this discrepancy lies in the inherent characteristics of the exercise performed. Aerobic walking and step-aerobic jumping are classified as weightbearing exercises that engage a greater number of major muscle groups, requiring sustained cardiovascular effort. Specifically, during walking, the most activated muscles include the gluteus maximus, gluteus medius, quadriceps, hamstrings, gastrocnemius, and soleus [36]. This extensive muscle engagement likely contributes to their superior impact on VO2 max. In contrast, nonweightbearing exercises, such as cycling and aquatic aerobics, while beneficial for joint health and often preferred for their low injury risk, may not elicit the same level of cardiovascular stimulus. For instance, during ergometer cycling, the primary muscles activated are the quadriceps, gastrocnemius, and soleus [37], which results in less overall muscle engagement compared to weightbearing activities. Additionally, research indicates that cycling has a lower fat oxidation rate-approximately 30% less—compared to walking at equivalent intensities [38]. This suggests that non-weightbearing exercises may lead to lesser overall cardiovascular adaptations, despite achieving similar heart rates. The findings of this

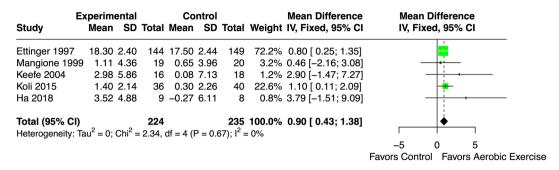


Fig. 3 Pooled mean difference on VO₂ max

| | Exper | imental | | (| Control | | | Mean Difference | Mean Difference |
|-------------------|------------------------|----------------|----------|-----------|------------------------|-------|--------|-----------------------|------------------------------------|
| Study | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| Ettinger 1997 | 459.33 | 58.52 | 144 | 411.18 | 59.54 | 149 | 96.2% | 48.16 [34.64; 61.68] | - |
| Mangione 1999 | 52.56 | 108.64 | 19 | 35.82 | 108.85 | 20 | 3.8% | 16.74 [-51.54; 85.02] | • |
| Total (95% CI) | | | 163 | | | 169 | 100.0% | 46.97 [33.71; 60.23] | — |
| Heterogeneity: Ta | au ² = 0; C | $0.71^2 = 0.7$ | 78, df = | 1 (P = 0. | .38); I ² = | 0% | | | |
| | | | | | | | | | –50 0 50 |
| | | | | | | | | | Favors Control Favors Aerobic Exer |

Fig. 4 Pooled mean difference on the distance walked during the six-minute walk test

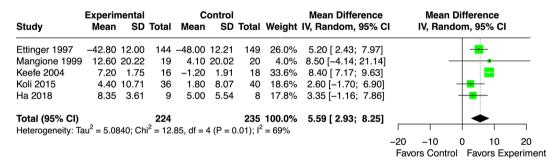


Fig. 5 Pooled mean difference on pain score

| | Experin | nental | | С | ontrol | | | Mean Difference | Mean Difference |
|---------------------------------|------------------------------------|----------|-------|-----------|----------|-------|--------|------------------------|---|
| Study | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| Ettinger 1997 | -43.00 | 12.00 | 144 | -47.50 | 12.21 | 149 | 51.0% | 4.50 [1.73; 7.27] | _ |
| Koli 2015 | 1.00 | 7.65 | 36 | -0.20 | 4.84 | 40 | 46.1% | 1.20 [-1.71; 4.11] | — — |
| Ha 2018 | 8.01 | 13.15 | 9 | 1.84 | 11.35 | 8 | 2.9% | 6.17 [-5.48; 17.82] | |
| Total (95% CI Heterogeneity: |) Tau ² = 2.6 | 857: CI | 189 | | P (P = 0 | | | 3.03 [1.05; 5.01] | <u> </u> |
| riotorogonotty. | 144 – 2.0 | ,007, 01 | – 2 | o, ui – 1 | - (1 – 0 | ,, . | - 0070 | | -15 -10 -5 0 5 10 15 Favors Control Favors Experiment |

Fig. 6 Pooled mean difference on disability score

study underscore the critical role of exercise modality in achieving significant cardiopulmonary benefits for people with knee OA. While existing literature has suggested that non-weightbearing exercises may provide superior outcomes in terms of pain relief and physical function [18], this review indicates the potential advantages of incorporating weightbearing aerobic exercises into rehabilitation programs aimed at improving cardiopulmonary fitness in people with mild knee OA.

Adherence to exercise regimens is essential to achieve the desired cardiopulmonary benefits. Suboptimal

adherence can dilute the "dose" of exercise, resulting in diminished outcomes. In the reviewed studies, attendance rates were modest among two effective studies, with Ettinger et al. (1997) and Koli et al. (2015) reporting only 68% adherence, which translates to an average of two sessions per week [28, 29]. This attendance rate may be insufficient to yield clinically meaningful improvements in cardiopulmonary fitness. There is consistent evidence indicating that adherence to exercise regimens is critical for managing knee OA. For instance, a systematic review highlighted that adherence to self-directed exercise

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during and after physical therapy is associated with better long-term outcomes for people with knee OA [39]. Moseng et al. (2020) reported that participants completing their exercise programs had a responder rate of 55%, compared to only 28% among non-completers [40]. This suggests that consistent participation in exercise is essential for achieving the desired therapeutic effects in OA management. A barrier to adherence is the occurrence of activity-related adverse events, such as musculoskeletal pain. Although these adverse events may not be serious, the fear of symptom exacerbation or injury can significantly reduce motivation and participation. The nature of the exercise modalities may also influence adherence and outcomes. Weightbearing exercises are often linked to higher levels of musculoskeletal stress, which can result in discomfort or injury. This risk is of particular concern for people with knee OA, as the potential for pain or injury may hinder them from engaging in these activities. In contrast, non-weightbearing exercises typically impose less stress on the joints and may be perceived as more tolerable. This perception could enhance adherence rates, as participants may feel more confident in their ability to engage in these activities without exacerbating their conditions. In the current review, adherence rates for weightbearing exercises were reported at 68% [28, 29], while non-weightbearing exercises demonstrated significantly higher adherence rates, ranging from 85% to 92% [30, 31]. This disparity underscores the potential advantages of non-weightbearing modalities in promoting sustained participation in exercise programs.

The severity of knee OA may also play a critical role in determining the effectiveness of aerobic exercise. For example, people with mild knee OA may be more responsive to exercise therapy than those with advanced knee OA. A recent study showed that people with a shorter duration of OA symptoms tend to benefit more from exercise therapy than those with longer disease durations [41], supporting the idea that exercise efficacy may diminish as the severity of OA increases. Additionally, people with mild knee OA may be able to tolerate higher-impact exercises, while those with more advanced OA may need to focus on low-impact activities to minimize joint stress. For example, a randomized controlled trial demonstrated that progressive high-impact exercise improved femoral neck strength in postmenopausal women with mild knee OA, indicating that such exercises can be safe and effective for this population [42]. Conversely, high-impact exercises may not be appropriate for those with severe OA due to the risk of exacerbating joint pain and stiffness. Kuptniratsaikul et al. found that aquatic exercise significantly improved pain and function in obese people with mild-to-moderate knee OA, emphasizing the importance of low-impact modalities for those with more severe symptoms [43].

Future research

Despite the promise of aerobic exercise to improve cardiopulmonary fitness, more research is needed to explore optimal exercise modalities tailored to different stages of knee OA. It is essential to consider that the benefits of exercise modalities may vary based on individual profiles, including specific health conditions, levels of physical fitness, and personal preferences. Therefore, a tailored approach that considers both the cardiovascular benefits of weightbearing exercises and the joint-friendly nature of non-weightbearing exercises may be most effective in optimizing overall health outcomes for people with knee OA. For instance, Nordic walking, which employs two handheld poles to provide reciprocal support [44], exemplifies an exercise modality that can offer both cardiopulmonary and joint-friendly benefits. Research indicates that Nordic walking can increase heart rate by 20% more than normal walking [45] and reduce the loading on the spine and lower limbs [46, 47], making it an applicable intervention for people with knee OA, especially those with mild knee OA. In addition to conventional aerobic exercise, inspiratory muscle training—a type of exercise that provides resistance during the inhalation phase—may also bring cardiopulmonary benefits without involving the lower limbs. Evidence suggests that it can promote cardiopulmonary fitness in older adults [48] and patients with cardiopulmonary disease [49, 50]; it leads to a moderate improvement in VO₂ max [51] by increasing inspiratory muscle strength and endurance, thereby improving respiratory efficiency [52]. The research suggests that inspiratory muscle training is a potential alternative for improving cardiopulmonary fitness in people with knee OA, especially those with more advanced OA, as it provides cardiovascular benefits without adding knee joint stress. These alternative exercise modalities show potential to improve exercise adherence and intensity while minimizing the risk of exacerbating symptoms. Further research is needed to optimize exercise prescriptions and tailor interventions to the specific needs and characteristics of people with knee OA.

Strengths and limitations

This review has a strength in the use of the CERT tool [23], which provides a structured and systematic framework for reporting key exercise components. The CERT tool evaluates the details of exercise intervention implementation, facilitating comparisons between studies and supporting the translation of research findings into practical applications for patient care. In addition, the review thoroughly examines the impact of various aerobic exercises (e.g., aerobic walking, cycling, step-aerobic jumping, aquatic aerobics, and combined aerobics) on cardio-pulmonary fitness in people with knee OA, providing a nuanced understanding of their benefits and limitations.

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By highlighting the challenges of achieving clinically meaningful improvements, the review underscores the importance of balancing cardiopulmonary benefits with symptom management. The review critically addresses the issue of suboptimal adherence to weightbearing exercise programs, highlighting the real-world challenges of implementing exercise interventions. By identifying gaps in the current literature and proposing strategies to improve adherence and minimize symptoms, the review offers practical insights for future research and clinical practice. However, the review has limitations, including potential bias from the dropout rates, a lack of long-term follow-up data, and variability in the risk of bias findings across studies. First, while one study reported a dropout rate of 17% and found no significant difference between those who dropped out and those who remained in terms of age, gender, and race [28], other studies suggest that participants may have withdrawn due to factors such as allocation issues or loss to follow-up [29, 31]. The nonrandom nature of dropouts compromises the validity of the data, as individuals experiencing adverse events or showing less improvement may be more likely to withdraw. This could skew the outcomes in favor of those who completed the exercise training, potentially overestimating the effectiveness of the interventions. Second, a lack of reported long-term follow-up data poses challenges in assessing the durability of the effects of aerobic exercise interventions. Included studies focused on shortterm outcomes, leaving uncertainty about whether the observed improvements are sustained over time. Third, the variability in risk of bias findings across studies must be acknowledged. While Ettinger et al. (1997) demonstrated a low risk of bias, providing robust and reliable findings, other studies raised concerns due to issues such as inadequate randomization, deviations from intended interventions, and selective reporting [29-32]. These methodological limitations introduce uncertainty into the evidence base, particularly regarding the effectiveness of certain exercise types and the generalizability of the findings. Moreover, the variability of control groups complicates the interpretation of aerobic exercise effects, as many do not provide the same cardiovascular stimulus. For instance, while education and usual activity controls may have their own benefits, they generally do not provide the cardiovascular stimulus as much as aerobic exercise interventions do. But light-intensity cycling [30], which may not elicit the same magnitude of cardiopulmonary adaptations as more intense aerobic activities, may still bring some cardiopulmonary benefits [13]. Consequently, the variation in control groups across studies may have contributed to inconsistencies in the reported effects of aerobic exercise on outcomes. Lastly, VO₂ max was not the primary outcome in the included studies. This may indicate that the sample sizes were insufficient

to accurately detect its effects, limiting the ability to draw definitive conclusions about the impact of aerobic exercise on cardiopulmonary fitness in people with knee OA. Future research should prioritize rigorous methodologies, standardized control conditions, and consider VO2 as a primary outcome to enhance the validity and applicability of findings in improving cardiopulmonary fitness for people with knee OA.

Conclusion

This review demonstrates that aerobic exercise enhances cardiopulmonary fitness in people with knee OA, although the observed effects were small and not clinically significant. Given the challenges with adherence and symptom management, future research should focus on optimizing aerobic exercise regimens and improving adherence while minimizing symptom exacerbation. Exploring alternative exercise modalities, such as Nordic walking and inspiratory muscle training, may offer promising solutions.

Abbreviations

6MWD Distance walked during the six-minute walk test **ACSM** The American College of Sports Medicine AIMS Arthritis Impact Measurement Scale CERT Consensus on Exercise Reporting Template Confidence interval

FITT Frequency, intensity, time, and type

GRADE Grading of Recommendations Assessment, Development and

> **Evaluation** I-square

Knee Injury and Osteoarthritis Outcome Score KOOS

MD Mean difference

MCID Minimal clinically important difference

OA Osteoarthritis

Randomized controlled trial RCT RoB-2 Cochrane Risk of Bias tool 2 VO₂ max Maximum oxygen consumption WHO World Health Organization

WOMAC Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary Information

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Additional file 1: Search strategy by databases.

Additional file 2: Reason(s) for exclusion during full-text screening.

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Author contributions

AF, CY, SS were responsible for defining the research question, designing the review; SS generated the systematic review terms, analyzed and interpretated the data, drafted and revised the manuscript; SS and EZ co-worked on conducting screening, data extraction and assessing bias; JYL reviewed and revised the manuscript. All authors contribute to review, edit, and revise the manuscript and approve the final submitted version.

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Data availability

All data generated or analyzed during this study are included in this article and the supplementary files.

Declarations

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Consent for publication

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Competing interests

The authors declare no competing interests.

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