



Does knee pain mediate the association between regular physical exercise and functional independence in older adults with knee osteoarthritis?

¿El dolor de rodilla media la asociación entre el ejercicio físico regular y la independencia funcional en adultos mayores con osteoartritis de rodilla?

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Received: 01-09-26

Accepted: 15-10-26

How to cite in APA

Pereira da Silva, R., Fabrizzi, F., & Marrese Bersotti, F. (2027). ¿El dolor de rodilla media la asociación entre el ejercicio físico regular y la independencia funcional en adultos mayores con osteoartritis de rodilla? *Retos*, 86, 24-35. <https://doi.org/10.47197/retos.v86.120073>

Abstract

Introduction: knee osteoarthritis was frequently associated with pain and limitations in daily functioning among older adults. Regular physical exercise was associated with lower pain and better function, but the role of pain in this relationship remained uncertain.

Objective: the study examined whether knee pain statistically mediated the association between regular physical exercise and functional independence in older adults with knee osteoarthritis after adjustment for age and body mass index.

Methodology: a cross-sectional observational study included 193 older adults with radiographically confirmed knee osteoarthritis. Regular exercise participation was exposure, knee pain intensity was the potential mediator, and functional independence measured with the lawton instrumental activities of daily living scale was the outcome. age and body mass index were covariates. Regression-based mediation analysis used heteroskedasticity-consistent standard errors and 10,000 bootstrap resamples.

Results: regular exercise was associated with lower knee pain and higher lawton scores. greater pain showed an inverse but non-significant adjusted association with functional independence. the direct association between exercise and functional independence remained significant after accounting for pain. The estimated indirect effect through pain was positive, but its 95% bootstrap confidence interval included zero.

Discussion: the findings agreed with previous research reporting favorable associations of exercise with pain and function, but lower current pain did not clearly account for the exercise-functional independence relationship. Other pathways may therefore have contributed.

Conclusions: regular physical exercise is associated with lower knee pain and greater functional independence, but the hypothesized indirect pathway through pain is not statistically supported.

Keywords

Activities of daily living; exercise; functional independence; knee osteoarthritis; mediation analysis; pain.

Resumen

Introducción: La osteoartritis de rodilla se asocia con dolor y limitaciones funcionales en adultos mayores. El ejercicio regular se asocia con menor dolor y mejor función, pero el papel del dolor en esta relación sigue siendo incierto.

Objetivo: Examinar si el dolor media estadísticamente la asociación entre ejercicio regular e independencia funcional, ajustando por edad e índice de masa corporal.

Metodología: Se realizó un estudio observacional transversal con 193 adultos mayores con osteoartritis de rodilla confirmada radiográficamente. El ejercicio regular se consideró la exposición, el dolor de rodilla el posible mediador y la independencia en las actividades instrumentales de la vida diaria, evaluada mediante la escala de Lawton, el desenlace. Mayores puntuaciones indican mayor independencia. Se ajustó por edad e índice de masa corporal. La mediación se analizó mediante regresión, con errores estándar robustos frente a la heterocedasticidad y 10.000 remuestreos bootstrap.

Resultados: El ejercicio se asocia con menor dolor y mayores puntuaciones de Lawton. El dolor muestra una asociación ajustada inversa, no significativa, con la independencia. La asociación directa permanece significativa al considerar el dolor. El efecto indirecto es positivo, pero su intervalo de confianza bootstrap del 95% incluye cero.

Discusión: Los hallazgos coinciden con investigaciones previas, pero un menor dolor actual no explica claramente la asociación entre ejercicio e independencia funcional. Otras vías pueden contribuir.

Conclusiones: El ejercicio regular se asocia con menor dolor y mayor independencia funcional, sin respaldo estadístico para la vía indirecta a través del dolor.

Palabras clave

Actividades de la vida diaria; análisis de mediación; dolor; ejercicio; independencia funcional; osteoartritis de rodilla.



Introduction

Knee osteoarthritis is a prevalent musculoskeletal condition among older adults and is frequently associated with persistent pain, reduced mobility, and limitations in daily functioning. (Hunter & Bierma-Zeinstra, 2019) Pain is one of its most clinically relevant manifestations because it may interfere with walking, transfers, household activities, community participation, and other tasks required for independent living. (Hunter & Bierma-Zeinstra, 2019; Heuts et al., 2004) As populations age, identifying potentially modifiable factors associated with preserved autonomy in older adults with knee osteoarthritis has become increasingly important for clinical practice and public health. (Roberts et al., 2017; Wang et al., 2020)

Regular physical exercise is widely recommended as a core non-pharmacological strategy for the management of knee osteoarthritis. (Bannuru et al., 2019; Fransen et al., 2015) Different exercise modalities may be associated with improvements in pain, muscle function, mobility, physical capacity, and participation in daily activities. (Fransen et al., 2015; Roberts et al., 2017) Exercise may also influence pain through peripheral and central mechanisms, including changes in periarticular muscle function, tolerance to joint loading, endogenous pain inhibition, and nociceptive processing. (Hall et al., 2020) Accordingly, individuals with knee osteoarthritis who remain regularly active may present lower pain intensity than their less active counterparts.

Functional independence represents another important outcome in the management of older adults with knee osteoarthritis. Instrumental activities of daily living comprise relatively complex activities required for autonomous community living, including transportation, shopping, food preparation, medication management, communication, household activities, and financial management. (Lawton & Brody, 1969) The Lawton Instrumental Activities of Daily Living Scale is commonly used to evaluate this construct, with higher scores indicating greater functional independence. (Lawton & Brody, 1969)

Loss of instrumental independence is multifactorial. Pain may contribute by restricting mobility, increasing difficulty with weight-bearing activities, and promoting avoidance of activities perceived as painful. (Heuts et al., 2004) However, independence also depends on factors such as muscle strength, balance, aerobic capacity, cognitive function, comorbidities, environmental resources, psychological characteristics, and social support. (McAuley et al., 2011; Vermeulen et al., 2011; Wang et al., 2020) Consequently, lower pain and greater functional independence among physically active individuals do not necessarily indicate that these two associations represent a single pathway.

One plausible hypothesis is that knee pain constitutes an intermediate statistical pathway between regular exercise participation and functional independence. Individuals reporting less pain may be better able to undertake transportation, shopping, household activities, and other instrumental tasks independently. (Lawton & Brody, 1969; Wang et al., 2020) Conversely, greater pain may restrict movement and participation, potentially contributing to loss of autonomy. (Heuts et al., 2004; Hunter & Bierma-Zeinstra, 2019) Whether pain statistically accounts for the association between regular exercise participation and instrumental independence, however, remains uncertain.

Mediation analysis provides a framework for decomposing an exposure-outcome association into direct and indirect components. (Preacher & Hayes, 2008) In the present context, exercise participation can be conceptualized as the exposure, knee pain as a potential mediator, and functional independence as the outcome. The indirect effect represents the component of the exercise-functional independence association statistically transmitted through pain, whereas the direct effect represents the remaining association after inclusion of pain in the model. (Preacher & Hayes, 2008)

Importantly, the temporal assumptions required for causal mediation cannot be established in a cross-sectional observational study. (Maxwell & Cole, 2007) A cross-sectional mediation model can therefore identify whether the observed covariance structure is compatible with a hypothesized indirect pathway, but it cannot demonstrate that exercise preceded pain reduction or that pain reduction subsequently produced better functional independence.

Age and body mass index (BMI) may additionally influence relationships among exercise, pain, and functional status. Older age is associated with reduced physical reserve and greater vulnerability to functional decline, whereas elevated BMI may contribute to mechanical loading, symptoms, and disability

in knee osteoarthritis. (Hunter & Bierma-Zeinstra, 2019; Vermeulen et al., 2011) These variables should therefore be considered when estimating associations within the proposed model.

Accordingly, this study aimed to examine whether knee pain statistically mediates the association between regular physical exercise and functional independence in older adults with knee osteoarthritis after adjustment for age and BMI. We hypothesized that regular exercise participation would be associated with lower knee pain, that greater knee pain would be associated with lower Lawton scores, and that lower pain would statistically account for part of the positive association between regular exercise participation and functional independence.

Method

Study Design

This observational cross-sectional study examined the statistical pathway linking regular physical exercise, knee pain, and functional independence in older adults with knee osteoarthritis. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for cross-sectional studies. (von Elm et al., 2007)

Given the cross-sectional design, the mediation analysis was intended to determine whether the observed covariance structure was compatible with the hypothesized indirect pathway rather than establish temporal or causal mediation.

The study protocol was approved by the Research Ethics Committee of the University of São Paulo (CAAE No. 04867418.6.0000.5390). All participants provided written informed consent.

Setting

Participants were evaluated in São Paulo, Brazil, within the research framework of the Physical Activity Sciences Laboratory, School of Arts, Sciences and Humanities, University of São Paulo.

Participants

The analytical sample comprised 193 older adults with radiographically confirmed knee osteoarthritis. A total of 168 participants regularly practiced physical exercise, whereas 25 did not regularly exercise.

Eligibility required medical documentation and radiographic evidence of knee osteoarthritis according to the Kellgren–Lawrence classification (Kellgren & Lawrence, 1957). Participants were classified according to regular exercise participation. Those classified as regular exercisers had performed aerobic, stretching, or resistance exercise one to three times per week for more than one year. Participants classified as non-exercisers had not participated in physical activity or rehabilitation during the preceding 12 months. Exclusion criteria included previous lower-limb surgery, fibromyalgia, corticosteroid or intra-articular hyaluronic acid use during the preceding 12 months, oral anti-inflammatory medication use during the preceding 2 months, physiotherapy involving the spine, hip, or lower limbs during the preceding 6 months, regular walking for 30 minutes or longer per day, heart failure, and physical dependence.

Study Size

The study included all 193 participants with complete information for regular exercise participation, knee pain, Lawton score, age, and BMI. No separate a priori sample-size calculation was performed specifically for the mediation model.

Exercise Exposure

Regular exercise participation was coded as 0 = no regular exercise and 1 = regular exercise.

The exercising participants practiced aerobic, stretching, or resistance exercise at frequencies ranging from one to three sessions per week.

Exercise participation collapsed into a binary exposure for the primary mediation analysis because the principal objective was to evaluate the general exercise-pain-functional independence pathway. Retain-

ing nine modality-by-frequency subgroups would have substantially increased model complexity relative to the size of the non-exercise reference group. Exercise modality and weekly frequency were therefore retained for characterization but were not modeled as separate exposures in the primary mediation analysis.

Knee Pain

Knee pain intensity was assessed using an 11-point Numeric Rating Scale (NRS) ranging from 0, representing no pain, to 10, representing the greatest pain imaginable.

NRS pain was retained as a continuous variable, with higher scores indicating greater knee pain, and constituted the proposed mediator (M).

Functional Independence

Functional independence was assessed using the Lawton Instrumental Activities of Daily Living Scale. (Lawton & Brody, 1969) The scale evaluates instrumental tasks required for relatively autonomous community living.

The total Lawton score was analyzed as a continuous outcome, with higher scores indicating greater functional independence. The observed score range was 9-27.

The continuous score was retained to preserve between-participant information and avoid unnecessary loss of statistical power. Because the scale is upper bounded, its distribution was specifically evaluated for a ceiling effect.

Covariates

Age and BMI were specified as a priori as covariates because both may plausibly influence exercise participation, osteoarthritis-related symptoms, and functional status. (Hunter & Bierma-Zeinstra, 2019; Vermeulen et al., 2011)

Age was expressed in years. BMI was calculated as follows:

$$BMI = \frac{\text{body mass (kg)}}{\text{height (m)}^2}$$

Covariates were not selected according to univariable statistical significance and were included consistently across the primary mediation equations.

Potential Sources of Bias

Potential confounding by age and BMI was addressed by including both variables as a priori covariates in all regression models. Because exercise participation was observational rather than experimentally assigned, self-selection into regular exercise and residual confounding by unmeasured clinical, behavioral, and functional characteristics could not be eliminated.

Pain and Lawton scores were retained as continuous variables in the primary analysis to minimize information loss.

Statistical Analysis

Continuous variables were summarized using descriptive statistics including mean, standard deviation, median, interquartile range, minimum, and maximum, as appropriate. Categorical variables were summarized using absolute and relative frequencies.

Distributions were examined using graphical and numerical diagnostics. A Lawton ceiling effect was quantified as the proportion of participants attaining the maximum possible score.

Preliminary associations among pain, Lawton score, age, and BMI were examined using Pearson correlations, with Spearman correlations used as complementary robustness analyses when appropriate.

Multicollinearity was evaluated using variance inflation factors.

A regression-based mediation model was used to examine whether knee pain statistically accounted for part of the association between regular exercise participation and functional independence. Exercise

participation was the exposure (X), knee pain the potential mediator (M), and Lawton score the outcome (Y).

Path a represented the association between regular exercise participation and knee pain after adjustment for age and BMI. Path c represented the total adjusted association between exercise and Lawton score. The outcome model simultaneously included exercise and pain, allowing estimation of path b, representing the pain-Lawton association, and c' , representing the direct exercise-Lawton association after accounting for pain.

$$M_i = \beta_0 + aX_i + \beta_1Age_i + \beta_2BMI_i + \varepsilon_i$$

$$Y_i = \beta_0 + cX_i + \beta_1Age_i + \beta_2BMI_i + \varepsilon_i$$

$$Y_i = \beta_0 + c'X_i + bM_i + \beta_1Age_i + \beta_2BMI_i + \varepsilon_i$$

$$Indirect\ effect = a \times b$$

$$c = c' + ab$$

All principal regression coefficients were reported as unstandardized estimates with 95% confidence intervals. Because diagnostic analyses indicated heteroskedasticity in models with Lawton score as the outcome, HC3 heteroskedasticity-consistent standard errors were used. (Long & Ervin, 2000)

The indirect effect was evaluated using 10,000 nonparametric bootstrap resamples with replacement. A percentile bootstrap of 95% confidence interval was calculated for $a \times b$. Statistical evidence for an indirect effect was considered present when this confidence interval excluded zero. Inference regarding mediation was therefore based primarily on the bootstrap confidence interval for the indirect effect rather than on significance testing of the component paths alone. (Hayes & Scharkow, 2013; Preacher & Hayes, 2008)

Potentially influential observations were evaluated using residual and influence diagnostics. Observations were not excluded solely because they were statistically influential unless objective evidence indicated erroneous or implausible data.

No imputation was required because complete data was available for all variables included in the primary mediation model.

As a sensitivity analysis addressing the bounded and ceiling-prone distribution of the Lawton score, proportional-odds ordinal logistic regression models were fitted using the same covariate structure as the corresponding primary outcome models.

Statistical significance for regression coefficients and secondary analyses was defined as two-sided $p < .05$. Analyses were performed in Python.

Results

Participant Characteristics

All 193 participants had complete data for the variables included in the primary mediation analysis. Of these, 168 (87.0%) regularly exercised and 25 (13.0%) did not.

The overall mean age was 73.24 ± 6.93 years, mean BMI was 27.80 ± 4.79 kg/m², mean knee pain was 3.76 ± 3.67 points, and mean Lawton score was 24.08 ± 3.88 points.

Participants engaged in regular exercise were descriptively younger and presented lower knee pain and higher Lawton scores than non-exercising participants. Participant characteristics are presented in Table 1.

Table 1. Participant Characteristics According to Regular Exercise Participation

Characteristic	Total (n = 193)	Exercise (n = 168)	No exercise (n = 25)
Age, years	73.24 ± 6.93	72.18 ± 6.44	80.32 ± 5.92
Body mass, kg	68.75 ± 11.98	69.02 ± 11.49	66.88 ± 15.05
Height, cm	157.36 ± 8.12	157.71 ± 8.03	154.96 ± 8.44
BMI, kg/m ²	27.80 ± 4.79	27.79 ± 4.50	27.92 ± 6.53
Knee pain, NRS 0-10	3.76 ± 3.67	3.28 ± 3.48	6.96 ± 3.36
Lawton score	24.08 ± 3.88	24.82 ± 2.71	19.12 ± 6.35

Note. Values are mean ± standard deviation. BMI = body mass index; NRS = Numeric Rating Scale. Higher Lawton scores indicate greater functional independence.

Preliminary Associations and Model Diagnostics

Knee pain was inversely associated with Lawton score in the unadjusted analysis ($r = -.269$, $p < .001$). A similar relationship was observed using Spearman correlation ($\rho = -.239$, $p < .001$).

Pain was positively correlated with age ($r = .219$, $p = .002$), whereas Lawton score was inversely correlated with age ($r = -.266$, $p < .001$). Neither pain nor Lawton score showed a meaningful correlation with BMI.

Sixty-two participants (32.1%) achieved the maximum Lawton score of 27, indicating substantial clustering at the upper limit. Seventy-six participants (39.4%) reported an NRS pain score of zero.

All VIF values in the final mediation model were below 1.30, indicating no relevant multicollinearity. Diagnostic analyses indicated heteroskedasticity in models with Lawton score as the outcome; HC3 standard errors were therefore retained for regression inference.

Exercise and Knee Pain: Path a

The mediator model explained 12.3% of the variance in knee pain ($R^2 = .123$; adjusted $R^2 = .109$).

After adjustment for age and BMI, regular exercise participation was associated with an approximately 3.26-point lower NRS pain score than no regular exercise ($B = -3.258$, robust SE = 0.839, 95% CI [-4.902, -1.614], $p < .001$).

3.4 Total Exercise-Functional Independence Association: Path c

The total-association model explained 25.0% of the variance in Lawton score ($R^2 = .250$; adjusted $R^2 = .238$).

Regular exercise participation was associated with an adjusted Lawton score approximately 5.28 points higher than that of non-exercising participants ($B = 5.284$, robust SE = 1.374, 95% CI [2.592, 7.977], $p < .001$).

Pain-Lawton Association and Direct Exercise Association

The outcome model explained 26.1% of the variance in Lawton score ($R^2 = .261$; adjusted $R^2 = .245$).

Greater knee pain showed the hypothesized inverse association with functional independence, but the adjusted pathway did not reach conventional statistical significance. Each 1-point increase in knee pain was associated with an estimated 0.116-point lower Lawton score ($B = -0.116$, robust SE = 0.065, 95% CI [-0.244, 0.012], $p = .076$).

The direct association between exercise and Lawton score remained statistically significant after inclusion of knee pain ($B = 4.907$, robust SE = 1.390, 95% CI [2.182, 7.632], $p < .001$). Regression estimates for the mediation pathways are presented in Table 2.

Table 2. Adjusted Regression Estimates for the Mediation Pathways

Path	B	Robust SE	95% CI	p
a: Exercise → Knee pain	-3.258	0.839	[-4.902, -1.614]	< .001
b: Knee pain → Lawton	-0.116	0.065	[-0.244, 0.012]	.076
c: Exercise → Lawton	5.284	1.374	[2.592, 7.977]	< .001
c': Exercise → Lawton, controlling for pain	4.907	1.390	[2.182, 7.632]	< .001



Note. Exercise participation was coded 0 = no regular exercise and 1 = regular exercise. All models were adjusted for age and BMI. HC3 heteroskedasticity-consistent standard errors were used.

Indirect Effect Through Knee Pain

The estimated indirect association between regular exercise and functional independence through knee pain was positive ($a \times b = 0.377$), consistent in direction with the hypothesized exercise $\rightarrow$ lower pain $\rightarrow$ greater independence pathway.

However, the percentile 95% bootstrap confidence interval based on 10,000 resamples included zero $[-0.030, 0.833]$. Thus, the hypothesized indirect effect through knee pain was not statistically supported. The total, direct, and indirect effects are summarized in Table 3.

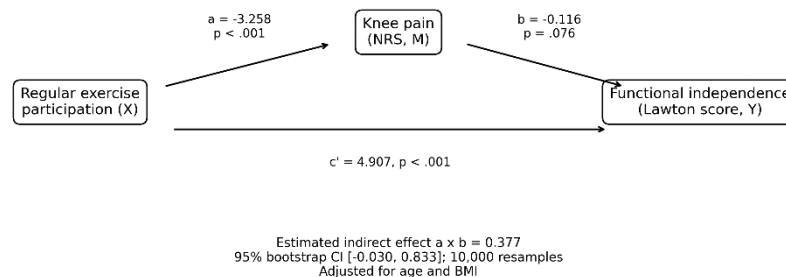
Table 3. Total, Direct, and Indirect Associations Between Regular Exercise and Functional Independence

Effect	Estimate	95% CI	Interpretation
Total association, c	5.284	[2.592, 7.977]	Statistically supported
Direct association, c'	4.907	[2.182, 7.632]	Statistically supported
Estimated indirect effect, $a \times b$	0.377	$[-0.030, 0.833]^a$	Not statistically supported

Note. All associations were adjusted for age and BMI. ^a Percentile bootstrap 95% confidence interval based on 10,000 resamples.

The adjusted mediation model is illustrated in Figure 1.

Figure 1. Adjusted cross-sectional mediation model examining knee pain as a potential statistical mediator of the association between regular exercise participation and functional independence. Values are unstandardized regression coefficients adjusted for age and BMI. The estimated indirect effect was $a \times b = 0.377$, 95% bootstrap CI $[-0.030, 0.833]$, based on 10,000 resamples.



Sensitivity Analysis

Sensitivity analyses using ordinal logistic regression yielded conclusions consistent with the primary linear models.

Regular exercise participation was associated with greater odds of being in a higher Lawton functional-independence category after adjustment for age and BMI (OR = 9.44, 95% CI [3.75, 23.77], $p < .001$).

After knee pain was added to the model, regular exercise remained associated with higher Lawton categories (OR = 7.68, 95% CI [2.96, 19.94], $p < .001$).

Greater knee pain was associated with lower odds of being in a higher Lawton category, although the association did not reach conventional statistical significance (OR = 0.94 per NRS point, 95% CI [0.87, 1.01], $p = .077$). Thus, the principal interpretation was unchanged when the bounded distribution of the Lawton score was explicitly considered.

Discussion



Regular physical exercise was strongly associated with both lower knee pain and greater functional independence in older adults with knee osteoarthritis after adjustment for age and BMI. However, the hypothesized indirect pathway linking exercise participation to functional independence through lower pain was not statistically supported. The bootstrap confidence interval for the estimated indirect effect included zero, while the direct exercise-Lawton association remained substantial after pain was included in the model. Together, these findings indicate that current knee pain did not statistically account for a clearly detectable proportion of the exercise-functional independence association.

These findings can be contextualized by studies examining different functional outcomes in knee osteoarthritis. Bersotti, Silva, Alonso, et al. (2025) reported differences in knee pain and Lawton scores across exercise modalities and weekly frequencies in a cross-sectional sample of 193 older adults. However, comparisons between exercise groups do not establish whether pain statistically mediates the association with instrumental independence. In a randomized trial, Bersotti, Silva, Barbanera, et al. (2025) reported improvements in pain and WOMAC physical function following strength training, without significant changes in Timed Up and Go performance. Similarly, Masyitah et al. (2025) observed improvements in WOMAC scores and Timed Up and Go performance following open and closed kinetic chain exercises in a quasi-experimental study. These differences highlight the importance of distinguishing self-reported osteoarthritis-related function, functional mobility, and independence in instrumental activities of daily living. Although these studies support favorable exercise-related outcomes, they do not demonstrate that pain reduction explains greater instrumental independence, reinforcing the relevance of evaluating the indirect association separately. The present study extends that analysis by examining an age- and BMI-adjusted statistical mediation model.

Exercise and Knee Pain

Regular exercise participation was associated with an adjusted difference of approximately 3.26 points on the 0-10 NRS, with exercising participants reporting less knee pain.

This finding is consistent with literature supporting exercise as an important non-pharmacological component of knee osteoarthritis management. (Bannuru et al., 2019; Fransen et al., 2015) Potential explanations include associations with periarticular muscle function, tolerance to joint loading, movement efficiency, endogenous pain modulation, and nociceptive processing. (Hall et al., 2020)

Importantly, the association persisted after adjustment for age and BMI. This is particularly relevant because the non-exercising participants were substantially older.

Nevertheless, the cross-sectional design prevents determination of directionality. Individuals experiencing less pain may be more capable of maintaining regular exercise, whereas individuals with greater symptoms may reduce or discontinue activity. (Heuts et al., 2004; Vivekanantham et al., 2023) The findings should therefore be interpreted as adjusted associations rather than evidence that exercise caused the observed differences in pain.

Pain and Functional Independence

Greater pain was associated with lower Lawton scores in the unadjusted analysis. However, after simultaneous adjustment for exercise participation, age, and BMI, the pain-Lawton association was attenuated and did not reach conventional statistical significance.

This finding suggests that the relationship between pain and instrumental independence overlaps with other characteristics associated with activity and aging.

Pain may restrict activities involving walking, prolonged standing, transportation, shopping, or other mobility-dependent tasks. (Heuts et al., 2004; Hunter & Bierma-Zeinstra, 2019) Nevertheless, instrumental independence is multidimensional and may also depend on muscle strength, balance, endurance, cognition, comorbidities, environmental resources, psychological characteristics, and social support. (McAuley et al., 2011; Vermeulen et al., 2011; Wang et al., 2020)

The Lawton ceiling effect may also have contributed. Approximately one third of the participants achieved the maximum score, potentially reducing discrimination among individuals with relatively preserved independence and attenuating the pain-Lawton pathway.

Indirect Pathway Through Pain

The estimated indirect effect was positive, as hypothesized: regular exercise was associated with lower pain, and lower pain was directionally associated with higher Lawton scores.

However, its bootstrap 95% confidence interval crossed zero. Consequently, the data did not provide statistically conclusive evidence for an indirect effect through current knee pain.

This distinction is important. A strong exercise-pain association and a strong exercise-function association do not establish that the former explains the latter. Mediation requires support for the indirect component itself. (Hayes & Scharkow, 2013; Preacher & Hayes, 2008)

The total adjusted exercise-Lawton association was 5.284 points, whereas the direct association after inclusion of pain remained 4.907 points. Thus, most of the observed associations remained outside the estimated pain pathway.

These quantities should not be interpreted causally. Nevertheless, they suggest that current pain intensity may represent, at most, a limited statistical pathway connecting regular exercise participation with functional independence in this sample.

Potential Alternative Pathways

The persistence of the exercise-Lawton association after accounting for pain suggests that other variables may contribute to the relationship.

Regular exercise may be associated with greater muscle strength, postural control, mobility, walking capacity, and aerobic fitness, all of which may facilitate instrumental activities of daily living independently of current pain intensity. (Roberts et al., 2017; Vermeulen et al., 2011; Wang et al., 2020)

Psychological and behavioral mechanisms may also be relevant. Regularly active older adults may differ in movement, confidence, self-efficacy, fear of activity, social participation, or other characteristics associated with independent functioning. (Heuts et al., 2004; McAuley et al., 2011)

Future mechanistic studies should therefore consider multiple parallel mediators, such as muscle strength, mobility, balance, aerobic capacity, psychological factors, and pain rather than if analgesia represents the primary pathway.

Clinical Implications

The findings suggest that the functional associations of regular exercise in older adults with knee osteoarthritis should not be conceptualized exclusively in terms of pain.

Symptom management remains clinically important, but greater functional independence may be associated with exercise even when differences in current pain do not statistically explain the functional association.

A rehabilitation approach focused solely on analgesia may therefore overlook other potentially important domains, including mobility, muscle performance, endurance, and participation. (Bannuru et al., 2019; Fransen et al., 2015; Wang et al., 2020)

However, the magnitude of the exercise-Lawton association should be interpreted cautiously. Regular exercise participation may also capture differences in overall health, mobility, motivation, comorbidity burden, and capacity to participate in exercise that were not represented by age and BMI alone.

Strengths

Strengths include the inclusion of 193 participants with complete primary-model data; explicit separation of total, direct, and indirect associations; use of a bootstrap procedure with 10,000 resamples for the indirect effect; prespecified adjustment for age and BMI; and use of HC3 robust standard errors after identification of heteroskedasticity.

Sensitivity analysis using ordinal logistic regression also yielded a pattern consistent with the primary analysis despite the bounded and ceiling-prone Lawton distribution.



Limitations

The most important limitation is the cross-sectional design. Mediation conceptually requires temporal ordering of exposure, mediator, and outcome, which cannot be demonstrated in the present data. (Maxwell & Cole, 2007) The analysis should therefore be interpreted as evaluation of a statistical indirect pathway compatible with the proposed hypothesis, not causal mediation.

Reverse directionality remains plausible. Greater independence may facilitate regular exercise, and lower pain may increase the likelihood that an individual remains physically active.

Residual confounding is another important limitation. Although age and BMI were included, other variables such as sex, osteoarthritis severity, disease duration, comorbidity burden, cognition, depressive symptoms, socioeconomic characteristics, medication, muscle strength, and mobility may influence both exercise participation and functional independence. (Hunter & Bierma-Zeinstra, 2019; McAuley et al., 2011; Wang et al., 2020) The models should therefore be interpreted as age- and BMI-adjusted associations rather than estimates fully adjusted for all plausible confounding.

Approximately 32.1% of participants achieved the maximum Lawton score. This ceiling effect may have reduced the instrument's ability to discriminate among participants with relatively preserved instrumental independence and may have attenuated the pain-Lawton pathway. Nevertheless, the ordinal regression sensitivity analysis yielded the same qualitative interpretation as the primary model.

The primary exposure also combined different exercise modalities and weekly frequencies. Therefore, the results characterize regular exercise participation in general rather than the effects of a specific exercise modality or dose.

Pain was measured using a single current NRS score. Osteoarthritis pain can fluctuate according to activity and time and may not be fully represented by a single assessment. (Vivekanantham et al., 2023)

Finally, because exercise participation was observational rather than experimentally assigned, selection effects cannot be excluded.

The generalizability of the findings should also be considered in relation to the characteristics of the sample, which consisted of older adults with radiographically confirmed knee osteoarthritis and generally preserved instrumental independence. The findings may not generalize to individuals with advanced functional dependence, substantially different disease severity, or other clinical populations.

Future Research

Longitudinal studies are needed to establish temporal ordering among exercise participation, subsequent changes in pain, and later functional outcomes.

Randomized exercise trials incorporating repeated mediator and outcome assessments would provide a stronger test of whether exercise-induced changes in pain precedes changes in functional independence.

Future studies should also evaluate multiple potential mediators, including muscle strength, mobility, balance, aerobic capacity, pain-related psychological factors, and self-efficacy.

Larger samples could additionally support modality- and frequency-specific mediation models and clarify whether resistance, aerobic, and stretching exercise are associated with functional independence through different pathways.

Conclusions

Regular physical exercise was associated with substantially lower knee pain and greater functional independence in older adults with knee osteoarthritis after adjustment for age and BMI. However, the hypothesized indirect association between exercise and functional independence through knee pain was not statistically supported because the bootstrap confidence interval for the estimated indirect effect included zero.



Greater pain showed the expected inverse relationship with Lawton score, but this association was attenuated after simultaneous adjustment for exercise, age, and BMI. In contrast, the direct exercise-functional independence association remained substantial after accounting for pain. Sensitivity analysis using ordinal modeling produced the same qualitative pattern.

These findings suggest that the association between regular exercise and functional independence may involve pathways beyond current pain intensity. Given the cross-sectional observational design, the direct and indirect associations should not be interpreted as evidence of causal mechanisms.

Acknowledgements

Thanks to all the participants who were interested in participating in this research and contributing to science.

Financing

There was no funding.

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