



The Effects of Physical Exercise on Pain Management in Patients with Knee Osteoarthritis: A Systematic Review with Metanalysis*

Os efeitos do exercício físico sobre o manejo da dor em pacientes com osteoartrose de joelho: Uma revisão sistemática com meta-análise

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Abstract

Objective The present study verified, through a systematic review with meta-analysis, the effects of a rehabilitation, physical training program for the treatment of pain and muscle strength in knee osteoarthritis (OA).

Methods We analyzed studies published between 2008 and 2018 referenced at the Medline (National Library of Medicine) database, selecting 7 randomized controlled clinical trials about exercise programs to improve pain and muscle strength in patients with knee OA with Physiotherapy Evidence Database (PeDro) score higher than 8. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) systematization was used to prepare this review, and a meta-analysis was carried out to obtain mathematical evidence the outcomes of physical exercise on pain.

Results The studies included in the analysis contained a total of 934 participants aged 40 to 73 years-old, with 34.90% males. Most of the exercise sets offered in OA treatment had a significantly positive outcome result in both criteria, but mainly for pain relief (statistically significant difference, $p < 0.003$).

Conclusion We infer that there was an improvement of pain in all articles that performed muscle strengthening, but there is still an obstacle to the protocols used.

Keywords

- ▶ pain
- ▶ muscle strength
- ▶ osteoarthritis of knee
- ▶ exercise and movement techniques

Resumo

Objetivo O presente estudo verificou por meio de uma revisão sistemática com metanálise os efeitos de um programa de reabilitação, através de um programa de

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Palavras-chave

- ▶ dor
- ▶ força muscular
- ▶ osteoartrite de joelho
- ▶ técnicas de exercício e de movimento

treinamento físico, para o tratamento da dor e força muscular na osteoartrose (OA) de joelho.

Métodos Foram analisados os estudos publicados entre 2008 e 2018, tendo como referência a base de dados Medline (National Library of Medicine), da qual foram selecionados 7 ensaios clínicos controlados randomizados que pontuaram acima de 8 na escala *Physiotherapy Evidence Database* (PEDro, na sigla em inglês), sobre programas de exercícios na melhora da dor e força muscular em paciente com OA de joelho. Foi usada a sistematização *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA, na sigla em inglês) para a elaboração desta revisão, e a realização de uma metanálise com o objetivo de evidenciar matematicamente os resultados do exercício físico sobre a dor.

Resultados Os estudos incluídos na análise continham um total de 934 participantes com idade entre 40 a 73 anos, sendo que 34,90% desses eram do sexo masculino. A maioria dos conjuntos de exercícios oferecidos no tratamento da OA tiveram resultado significativamente positivo em ambos os quesitos, mas principalmente para o alívio da dor (estatisticamente significativo $p < 0,003$).

Conclusão Inferimos que houve uma melhora da dor em todos os artigos que realizaram fortalecimento muscular, porém ainda há um óbice sobre os protocolos utilizados.

Introduction

Population aging has grown all over the world, increasing the health challenges, especially with regard to the large number of conditions affecting the elderly. Among them, osteoarthritis (OA) stands out.¹ According to Framingham, OA is the second cause of work absenteeism and the main cause of disability in the elderly.²

Osteoarthritis is as a degenerative and progressive non-inflammatory joint disease consisting of articular cartilage degradation and subchondral bone alterations.³ This condition affects the normal synchronous movement of the joint, resulting in pain, stiffness, muscular strength deficit, and joint instability, which can reduce the individual's functional mobility and lead to functional loss.⁴ However, it is believed that OA does not result from the aging process, but from biochemical changes and biomechanical stresses affecting joint cartilage.^{5,6}

As such, it is known that knee OA mostly affects females, since, anatomically, in females, the cartilage of this region is thinner, with smaller area and volume, resulting in an increased shear force at the site.⁷

In a randomized controlled trial, Nguyen et al.⁸ have shown that exercise therapy is successful in improving the physical performance of patients with knee OA and severe comorbidities. In line with this information, the updated 2014 guidelines from the Osteoarthritis Research Society International (OARSI) considered rehabilitation as the main treatment for OA. Through a meta-analysis, OARSI concluded that exercise therapy associated with strength training and aerobic activity reduced pain and improved the individual's physical function.^{8,9}

In a systematic review, Lange et al.¹⁰ evaluated the efficacy of resistance training in the management of knee OA. They observed a general improvement in the symptoms

and physical performance of the patients; in addition, these authors verified that more than half of the included studies reported success in the application of resistance training as physical function and muscular strength, which improved significantly when compared to the groups receiving standard care.^{9,10}

Tanakar et al.,¹¹ in a systematic review with meta-analysis of randomized clinical trials, pointed out that aerobic exercises associated with non-weight-bearing strengthening exercises were more effective in relieving pain in short-term activities. However, the literature reports that balance exercises, endurance training and aerobic exercises are associated with pain reduction, stiffness relief, and physical function improvement in patients with knee OA.¹²⁻¹⁵

As such, we need to understand the efficacy of physical training over knee OA impact factors. There are several evidences^{12,13,16,17} on the benefits of some knee OA rehabilitation methods, but the ideal treatment regimen for each condition is still in question. These rehabilitation methods include physical training using methods or programs to promote, maintain or restore the physical and physiological well-being of an individual.¹⁸

Thus, this study aims to verify controlled and randomized studies through a systematic review of the effects of a rehabilitation, physical training program for pain management and muscle strength in knee OA.

Methods

The most relevant studies originally published in English at the MEDLINE (National Library of Medicine), Scientific Electronic Library Online (SciELO), and Latin American and Caribbean Literature in Health Science database (LILACS) databases between January 2008 and December 2018 were included in our analysis. To select studies with the highest

scientific evidence, only randomized controlled clinical trials (RCTs) were used for the bibliographic review. The search for scientific papers contained the following combinations of keywords: *movement techniques exercise, knee osteoarthritis AND pain AND muscle strength AND proprioception training*, as well as their variations at Medical Subject Headings (MeSH).

Inclusion and exclusion criteria are shown in ► **Box 1**.

The studies were selected by two independent reviewers; those not related to the review subject or presenting some kind of bias were excluded. To verify the validity of eligible randomized trials, pairs of reviewers working independently and reliably determined the adequacy of randomization regarding exercise protocols performed by the control and intervention groups.

Next, the abstracts of the selected papers were analyzed to identify those meeting the inclusion and exclusion criteria. Papers that did not have any of the study outcomes, did not address knee OA, did not have a specific group, or did not perform any type of exercise, in addition to those that were study protocols, were excluded.

The relevant papers were submitted to a final evaluation according to their score in the Physiotherapy Evidence Database (PEDro) scale to help researchers quickly identify which ones have internal validity and enough statistical information for results interpretation. To be eligible for this systematic review, a minimum PEDro score of eight was required. In addition, the scale proposed by Jadad et al.¹⁹ was employed. This scale consists of 5 criteria, ranging from 0 to 5 points, and a score lower than 3 indicates that the study has low methodological quality and that its results will hardly be extrapolated for other scenarios.

Statistical Analysis

For data on exercise programs and knee pain symptom, a meta-analysis was performed using the Medcalc software, version 15.8 (BVBA, Ostend, Belgium). The Hedges' g statistical method was used to formulate a standardized mean difference under a fixed effects model. Next, the heteroge-

Box 1 Inclusion and exclusion criteria

Inclusion criteria
Study design: randomized controlled clinical trials
Intervention: exercise programs for pain and muscular strength improvement in patients with knee osteoarthritis
Only in human subjects
Language: English
Studies performed at the last 10 years
Exclusion criteria
Intervention: unclear, poorly described or inadequate
Publication form: only abstracts
Main variables analyzed
Knee pain
Muscle strength

neity statistical analysis is incorporated to calculate the summarized standardized mean difference under a random effects model using the random and fixed-effect statistical analysis, considering the heterogeneity of the studies. The 95% confidence interval (95% CI) was calculated for each study individually and then for the combination of selected studies. The mean and standard deviation values of each study were identified, and only *p*-values < 0.05 were considered significant.

Results

Based on the previously described keywords, 986 papers were selected from the MedLine, Lilacs, and ScieLo databases. After applying all inclusion and exclusion criteria, 35 papers were read and evaluated using the PEDro and the Jadad scales. Seven papers were considered relevant for our systematic review, as shown in ► **Figure 1**.

► **Tables 1 and 2** show the PEDro and Jadad scores of the 7 studies included in this systematic review, with a minimum score of 8 points in 11 papers and 3 points in 5 papers, respectively.

The studies included in the analysis contained a total of 934 participants aged 40 to 73 years-old, with 34.90% of the subjects being male. The studies evaluated the effectiveness of an exercise set for knee OA management, and some compared the exercises with other treatment techniques, which took place over a mean period of 12 weeks. The analyzed variables were pain and muscle strength, and most exercises sets for OA treatment led to significantly positive outcomes for both variables, but mainly pain, as shown in ► **Table 3**.

Metanalysis

Only five of the seven studies included in this review provided sufficient data to analyze knee pain after the exercise program. The metanalysis was performed based on those five papers, totalizing a sample with 520 volunteers. Among the reported outcomes, five of the seven papers used the Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire as a pain assessment method, whereas two papers demonstrated that exercises are effective when compared to other knee OA treatment techniques, as shown in ► **Figure 2** and ► **Table 4**. The forest plot chart evidences the analysis of the exercise program effect on knee pain. The results at the left side indicate favorable-influencing values of the exercise program in pain relief when compared to the control group, whereas the combined effect is represented by the rhombus. There is evidence of a statistical difference (*p* = 0.0031).

Discussion

The present study aimed to analyze the efficacy of an exercise program in the treatment of knee OA, with pain and muscle strength being the main outcomes addressed. Our results demonstrate that a rehabilitation program that includes strengthening of a particular muscle group has positive effects on pain.

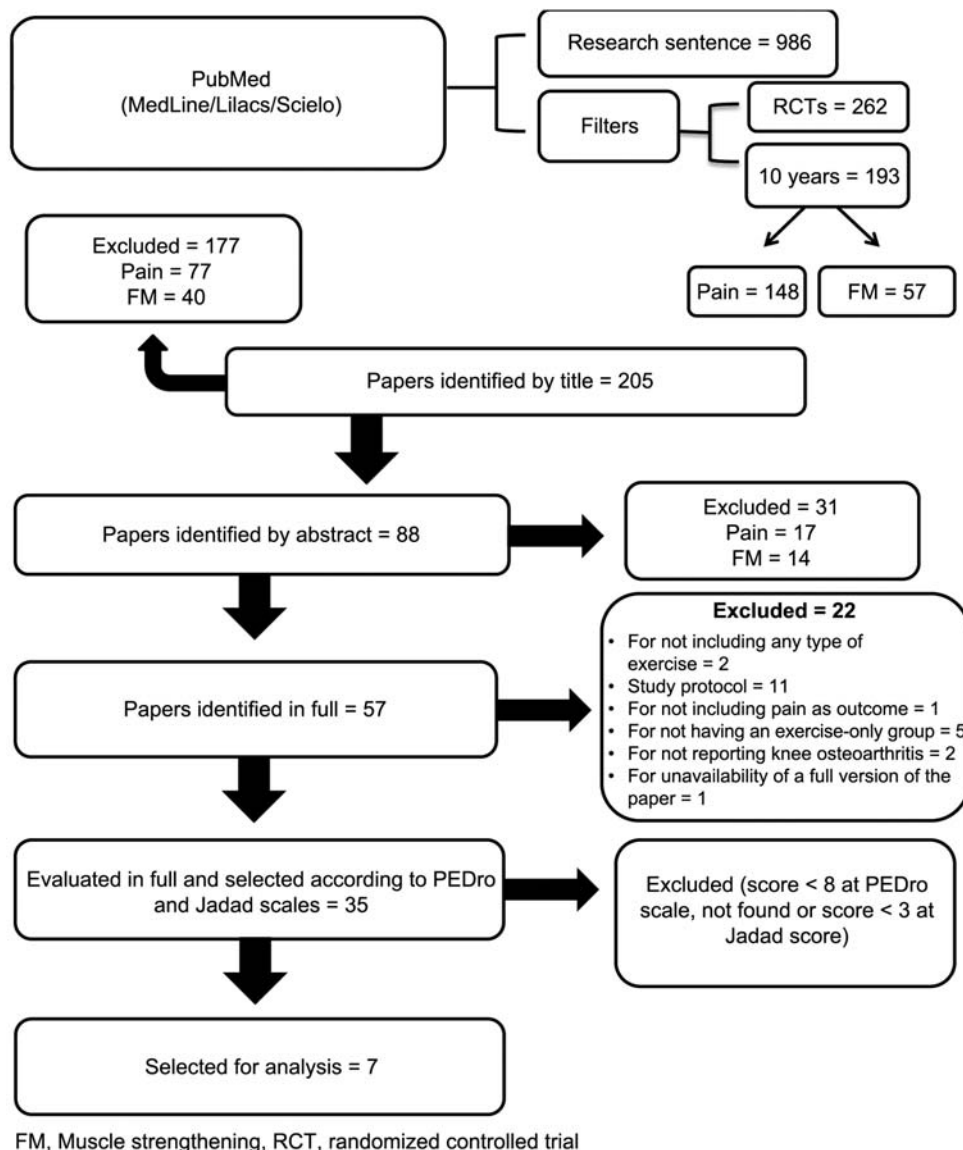


Fig. 1 Flow chart.

Table 1 Physiotherapy Evidence Database scale

PEDro Scale												
Study	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	Score
Boon-Whatt Lim et al., 2008 ³³	1	1	1	1	0	0	1	1	1	1	1	8/10
K.L. Bennell et al., 2010 ²⁵	1	1	1	1	0	0	1	1	1	1	1	8/10
G. Kelley Fitzgerald et al., 2011 ²⁰	1	1	1	1	1	0	1	0	1	1	1	8/10
Saccomanno MF et al., 2016 ²¹	1	1	1	1	0	0	1	1	1	1	1	8/10
Palmer S et al., 2014 ²²	1	1	1	1	1	0	1	0	1	1	1	8/10
Holsgaard-Larsen A et al., 2017 ²³	1	1	1	1	0	0	1	1	1	1	1	8/10
Jorge RT et al., 2015 ²⁴	1	1	1	1	0	0	1	1	1	1	1	8/10

Abbreviation: PEDro, Physiotherapy Evidence Database.

The quadriceps femoris, ischium cruralis, psoas major, gluteus maximus and medius, gastrocnemius, fascia lata tensor, long adductor, short adductor, gracilis, adductor magnus, and sartorius are the most evidenced muscles in this systematic review.²⁰⁻²⁵

Among the muscles cited in rehabilitation programs, the main focus is on the femoral quadriceps. Its strengthening is commonly indicated in the treatment and progression of OA because it has a static and dynamic chondroprotective effect on the knee joint, and its weakness can generate joint

Table 2 Jadad scale

Items	Boon-Whatt Lim et al., 2008 ³²	K.L. Bennell et al., 2010 ²⁴	G. Kelley Fitzgerald et al., 2011 ¹⁹	Sacco manno MF et al., 2016 ²⁰	Palmer S et al., 2014 ²¹	Holsgaard-Larsen A et al., 2017 ²²	Jorge RT et al., 2015 ²³
Was the study described as randomized?	1	1	1	1	1	1	1
Was there a description of randomization? Was it adequate?	1	1	1	1	1	1	1
Were there comparisons and results?	1	1	1	1	1	1	1
Was there a description of comparisons and results? Were they adequate?	1	1	1	1	1	1	1
Was there a description of withdrawals and dropouts?	1	1	1	1	1	1	1
TOTAL	5	5	5	5	5	5	5

overload, resulting in pain and instability.²⁶ According to O'Reilly et al.,²⁷ there is an inverse relationship between quadriceps muscle strength in OA patients and pain reports, that is, the higher the muscle strength, the lower the pain.^{27,28} However, the muscle at its greatest power may increase the shear force, or the compressive force, within the joint, which may increase the pain in the knee affected by OA; as such, when the joint is in a more flexed position, the muscle becomes more relaxed and these forces decrease over the joint, increasing the patient's comfort and reducing muscle activation.^{29,30} The literature still discusses the relationship between the femoral quadriceps muscle and knee OA, and it is controversial whether muscle weakness contributes to the pathology or the pathology causes muscle weakness.^{31,32}

The joint kinematic imbalance resulted from mechanical factors may also influence the cause and progression of knee OA because alignment plays an important role in determining articular loads distribution, minimizing the impact effect; so, it is postulated that increased muscle strength is a major cause of impact, pain reduction and disability. As such, one needs to understand the influence of poor joint alignment in the treatment of OA. Lim et al.³³ showed that quadriceps strengthening in a group of patients with severe knee misalignment caused worsening of pain compared to the control group, but not in the group presenting better joint alignment. In addition, these authors noted that quadriceps strengthening did not improve knee alignment, showing that a 3% increase in quadriceps strength worsened knee misalignment by 1 degree. This finding is not necessarily in line with our results, but it highlights the importance of observing the joint alignment before starting a strengthening program to obtain positive outcomes, especially regarding pain.³⁴

Range of motion is also an important issue in joint treatment success, since patients with chronic knee OA

may be subjected to immobilization or inactivity due to pain, resulting in joint capsule contractures and adaptive shortening.³⁵ Assuming that more elongated muscles have greater torque, the benefits of stretching programs exceed alignment and muscle balance. Hence, stretching therapy as an adjunctive treatment would be a favorable technique to be included in an exercise program for OA management. Both proprioceptive neuromuscular facilitation (PNF) and static stretching show excellent results, but PNF stretching was more effective than static stretching exercises.^{35,36} Only three of the papers included in the present review had stretching exercises in their programs.^{21,23,33}

Most studies included in this review address, in addition to strengthening, balance and proprioceptive techniques. However, only Fitzgerald et al.²⁰ evaluated these techniques separately, and found no significant evidence that these exercises improve pain and muscle strength in OA patients. This finding does not corroborate the study by Diracoglu et al.,³⁷ who compared kinesthesia and balance exercises or only strengthening exercises in women with knee OA, obtaining positive outcomes on muscle strength, quality of life, and the physical function scale, according to the WOMAC questionnaire.

To measure each of these outcomes, all authors opted for evaluation tools such as the WOMAC questionnaire and the visual analogue scale (VAS). The WOMAC questionnaire is an easy-to-apply, low-cost and specific instrument for knee OA composed of three domains, namely, pain, stiffness, and functionality.³⁸ Meanwhile, the VAS is a numerical instrument, with scores ranging from 0 to 10, with 10 cm in length, to validate pain sensation; greater VAS scores reflect increased pain levels.³⁰

Confronting each evaluation instrument, we can observe that when the evaluation of a specific question is required, as in OA, the VAS scale and the WOMAC questionnaire become

Table 3 Summary of studies and their main results on muscle strength and knee pain

Study	SAMPLE	SAMPLE	MEN	AGE	GROUPS	GI	GC	Duration	Analyzed variables	MUSCLE STRENGTH
Lim et al., 2008 ³³	107		48	53–73 years old	GI: 54 GC: 53	Quadriceps strengthening with weighted shin sleeves and Theraband	No intervention	12 weeks	Significant pain improvement in the group with better knee alignment	NA
K.L. Bennell et al., 2010 ²⁵	102		51	62–73 years old	GI: 51 GC: 51	Hip strengthening I (quadriceps adduction, external rotation, extension and isometry)	No intervention	12 weeks	Pain improvement in GI compared to GC	Significant hip and quadriceps strength improvement compared to the control group
G. Kelley Fitzgerald et al., 2011 ²⁰	183		61	63–73 years old	GI: 92 GC: 91	The agility and disturbance group received the same standard exercise program with the addition of training techniques on agility and disturbance	Standard exercise program: an exercise program including muscle stretching, strengthening and walking on a treadmill	4 years and 2 months	Both groups presented modest improvements, but with no significant differences between them	NA
Saccomanno MF et al., 2016 ²¹	165		44	40–70 years-old	GI: 53 GI: 2: 53 GC: 51	GI-1: three hyaluronic acid (HA) injections GI-2: HA injections + knee exercises	Knee exercises	6 months	At the 1 st month, GI-2 scores were significantly better compared to GI-1. GC and GI-2 presented a significant reduction at the 1 st and the 6 th month	NA
Palmer S et al., 2014 ²²	224		83	60–72 years old	GI: 73 GC-1: 74 GC-2: 77	Active TENS (continuous mode, – 110 Hz, 50 µs) + knee exercises	GC-1: fictional TENS + knee exercises GC-2: knee exercises (30 minutes of education + 30 minutes of exercises)	6 weeks	Each score from each group significantly improved over time	NA
Holsgaard-Jensen A et al., 2017 ²³	93		39	40–70 years old	GI: 47 GC: 46	Warming up (10 minutes), functional, proprioceptive training, resistance strengthening and cooling down	Information about analgesic and anti-inflammatory agents	8 weeks	There were no significant differences between groups	NA
Jorge RT et al., 2015 ²⁴	60		NA	40–70 years old	GI: 29 GC: 31	Warming up, 5 minutes at bike. Progressive resistance exercise (knee extension/flexion and hip adduction and abduction with light weights).	No intervention	13 weeks	Pain in the GI group was significantly lower in 45 and 90 days	Significant differences for hip adduction between groups from T0 until the end of the study

Abbreviations: GC, control group; GI, intervention group; NA, not analyzed; TENS, transcutaneous electrical neural stimulation; T0, initial time.

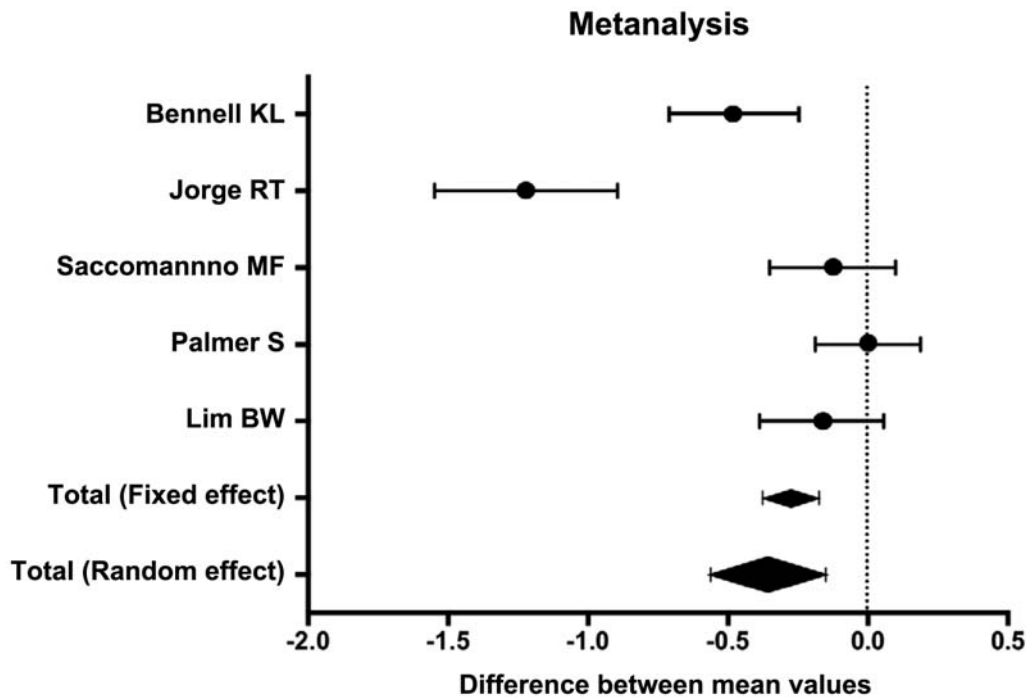


Fig. 2 Forest plot graph of the studies included in the fixed and random effect analysis; the standardized mean difference was set at a 95% confidence interval.

Table 4 Metanalysis data

Study	N1	N2	TOTAL	SMD	95% IC
Lim et al., 2008	54	53	107	-0.165	-0.549 to 0.219
Bennell et al., 2010	51	51	102	-0.481	-0.880 to -0.0824
Jorge et al., 2015	29	31	60	-0.122	-1.788 to -0.655
Saccomanno et al., 2016	51	53	104	-0.126	-0.516 to 0.263
Palmer et al., 2014	73	74	147	0.000	-0.326 to 0.326
Total (fixed effect)	258	262	520	-0.275	-0.450 to -0.101
Total (randomized effect)	258	262	520	-0.357	-0.712 to -0.00181
Significance level	$P = 0.0031$				

Abbreviations: IC, confidence interval; N1, sample from the intervention group; N2, sample from the control group; SMD, difference between average values.

very subjective; however, since WOMAC specifies momentary pain only in knee OA, it is most satisfactory for this type of evaluation.^{30,38}

Based on common evidence aspects, we conclude that for a rehabilitation program to be beneficial in the treatment of OA, it should satisfactorily evaluate knee joint misalignment and subsequently develop a treatment plan tailored to the needs of each patient. This evaluation will guide the therapist in the formulation of a physical training program focusing on the appropriate muscular group.

Our results indicate that an ideal program would include isometric and quadriceps femoris and crural ischial muscles isotonic strengthening exercises, especially quadriceps isotonic strengthening, crural and gastrocnemius ischial muscles dynamic stretching and proprioception and balance exercises.

The studies analyzed present some limitations, including the lack of a detailed description of the interventions, the load used, and the evolution of the exercises, mainly in relation to muscular stretches, thus hampering the final elaboration of an adequate physical training program. The duration of the intervention was very variable, not allowing us to reach a consensus about the ideal time to treat OA. The long-term benefits of therapy exercises and possible OA prevention are not yet known due to the lack of studies on these effects.

Another limitation observed is the absence of a gold standard instrument for muscle strength evaluation, such as the use of a dynamometer, compromising the quantitative analysis of this variable. We believed that the lack of such gold standard may be caused by reduced availability and high cost of evaluation devices.

Conclusion

This analysis shows that all papers examining the role of muscle strengthening in the treatment of OA reported pain improvement; however, the protocols used were not properly described, making it difficult to establish a specific physical exercise program for the treatment of knee OA. In addition, only two papers evaluated muscular strength, maybe due to the difficulty in measuring/using an appropriate instrument.

Conflicts of Interest

The authors declare that there is no conflict of interest.

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