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High- versus low-intensity resistance exercise in the treatment of pain in patients with knee osteoarthritis

Exercício resistido de alta versus baixa intensidade no tratamento da dor em pacientes com osteoartrite de joelho

Ejercicio de resistencia de alta versus baja intensidad en el tratamiento del dolor en pacientes con osteoartritis de rodilla

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Abstract

Objective: To compare the effects of two intervention protocols using a single low- (LIRE) or high- (HIRE) intensity resistance exercise on chronic pain and muscle strength in patients with knee osteoarthritis (KOA). **Methods:** Twenty patients with a clinical diagnosis of KOA were evaluated and randomized into two intervention groups: (HIRE: N=10, 75% of 1-RM; LIRE: N=10, 30% of 1-RM). Each group performed a single resistance exercise (knee joint extension on a leg extension machine) at high or low intensity twice a week. Strength for one repetition maximum (1-RM), functional strength, and pain were assessed before and after 12 weeks of intervention. **Results:** Pain decreased from pre- to post-test in both the ERBI group (effect size = -1.931) and the HIRE group (effect size = -3.299), and this reduction was significantly greater in the HIRE group ($p > 0.05$). Both HIRE and LIRE produced increases in 1-RM strength and functional strength after 12 weeks of intervention ($p < 0.05$). The percentage change between pre- and post-test for functional strength showed a negative correlation with the percentage change in pain only in response to high-intensity exercise ($p < 0.05$). **Conclusions:** ERAI is more effective than ERBI in reducing pain in patients with KOA. Increased functional strength is associated with greater pain reduction only in response to HIRE.

Keywords: Chronic pain. Exercise therapy. Resistance training. Osteoarthritis.

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Resumo

Objetivo: Comparar os efeitos de dois protocolos de intervenção usando um único exercício resistido de baixa (ERBI) ou alta (ERAI) intensidade sobre a dor crônica e a força muscular em pacientes com osteoartrite de joelho (OAJ). **Métodos:** Vinte pacientes com diagnóstico clínico de OAJ foram avaliados e randomizados em dois grupos de intervenção: (ERAI: N= 10, 75% de 1-RM; ERBI: N= 10, 30% de 1-RM). Cada grupo realizou um único exercício de resistência (extensão da articulação do joelho na máquina de extensão de perna) em alta ou baixa intensidade duas vezes por semana. A força para uma repetição máxima (1-RM), a força funcional e a dor foram avaliadas antes e depois de 12 semanas de intervenção. **Resultados:** A dor diminuiu do pré para o pós-teste tanto no grupo ERBI (tamanho do efeito = -1,931), quanto no grupo ERAI (tamanho do efeito = -3,299) e essa redução foi significativamente maior no grupo HIRE ($p > 0,05$). Tanto o HIRE quanto o LIRE produziram aumentos na força de 1-RM e na força funcional após 12 semanas de intervenção ($p < 0,05$). A variação percentual entre o pré e o pós-teste para a força funcional mostrou uma correlação negativa com a variação percentual na dor apenas em resposta ao exercício de alta intensidade ($p < 0,05$). **Conclusões:** O ERAI é mais eficaz do que o ERBI na redução da dor em pacientes com OAJ. O aumento da força funcional está associado a uma maior redução da dor somente em resposta ao ERAI.

Palavras-chave: Dor crônica. Terapia por exercício. Treinamento resistido. Osteoartrite.

Resumen

Objetivo: Comparar los efectos de dos protocolos de intervención que utilizan un único ejercicio de resistencia de baja (ERBI) o alta intensidad (ERAI) sobre el dolor crónico y la fuerza muscular en pacientes con osteoartritis de rodilla (OR). Métodos: Veinte pacientes con diagnóstico clínico de KOA fueron evaluados y aleatorizados en dos grupos de intervención: (ERAI: N= 10, 75% de 1-RM; ERBI: N= 10, 30% de 1-RM). Cada grupo realizó un único ejercicio de resistencia (extensión de la articulación de la rodilla en la máquina de extensión de piernas) de alta o baja intensidad dos veces por semana. Se evaluaron la fuerza para una repetición máxima (1-RM), la fuerza funcional y el dolor antes y después de 12 semanas de intervención. Resultados: El dolor disminuyó desde antes hasta después de la prueba tanto en el grupo ERBI (tamaño del efecto = -1,931) como en el grupo ERAI (tamaño del efecto = -3,299) y esta reducción fue significativamente mayor en el grupo ERAI ($p > 0,05$). Tanto ERAI como ERBI produjeron aumentos en la fuerza de 1 RM y en la fuerza funcional después de 12 semanas de intervención ($p <0,05$). El cambio porcentual entre la prueba previa y posterior para la fuerza funcional mostró una correlación negativa con el cambio porcentual en el dolor sólo en respuesta al ejercicio de alta intensidad ($p <0,05$). Conclusiones: ERAI es más efectivo que ERBI para reducir el dolor en pacientes con OR. El aumento de la fuerza funcional se asocia con una mayor reducción del dolor sólo en respuesta al ERAI.

Descriptores: Dolor crónico. Terapia de ejercicio. Entrenamiento de resistência. Osteoartritis.

Introduction

Knee osteoarthritis (KOA) is one of the most prevalent joint diseases and a leading cause of functional limitation and pain[1,2]. The joint wear, resulting from the clinical progression of the disease, contributes significantly to the limitation of sports practice and the performance of daily life activities[3,4].

The years living with disability due to KOA increased by 30.8% between 2007 and 2017, and the rise in life expectancy and obesity cases in the general population are expected to have a significant impact on the prevalence of KOA in the coming decades[5].

Muscle weakness and age are among the main risk factors for KOA[6,7]. The aging process is accompanied by a series of physiological changes that negatively impact the musculoskeletal health of individuals, which further potentiates the pain and functional disability associated with KOA[7,8]. Physical exercise plays a fundamental role as an adjunctive treatment for KOA, providing significant benefits in reducing symptoms, pain, and improving the patients' quality of life[9,10]. Exercise programs that encompass various modalities, such as aerobic, muscle strengthening and flexibility exercises, can reduce joint pain and stiffness, while enhancing physical function and functional capacity in KOA patients[11,12]. Moreover, physical exercise has also demonstrated positive effects on preserving muscle mass and improving joint biomechanics, contributing to reducing the impact on affected joints[13].

In this perspective, strength exercises or resistance training play a crucial role in reducing functional losses associated with aging, improving overall chronic conditions, daily life or sports activities, general physical conditioning, and the quality of life of patients[4,12].

Turner et al. reviewed 12 articles involving a total of 1428 participants and concluded that resistance training may have a positive and dose-dependent effect on reducing pain in KOA patients, although the optimal dose, represented by the type of exercise, volume and intensity, is not yet adequately established[14].

To our best knowledge, there is no consensus on the optimal dose of resistance exercise recommended for KOA patients. Therefore, the present study aimed to compare the effects of two intervention protocols using a single high- or low-intensity resistance exercise on chronic pain and muscle strength in patients with KOA.

Method

Study design

In this experimental study, patients with a clinical diagnosis of KOA were selected from those attending the Basic Health Unit. Out of the 36 volunteers, 26 met the eligibility criteria and were randomized into two intervention groups stratified by gender, age, and level of muscular pain: Low-Intensity Resistance Exercise (LIRE: N = 13) and High-Intensity Resistance Exercise (HIRE: N = 13). The participants underwent pre-test assessments, completed 12 weeks of intervention, and were re-evaluated at the post-test. During the intervention period, three participants from the HIRE group and

two from the LIRE group were excluded for not meeting the frequency criteria. One participant from the LIRE group withdrew for personal reasons.

Participants

The final sample of the present study consisted of 20 participants of both sexes (LIRE: N = 10, age = 64.8 ± 9.7 years, body mass = 67.5 ± 24,9 kg; HIRE: N = 10, age = 65.0 ± 10.0 years, body mass = 77.4 ± 15.9 kg).

Eligibility criteria

This study included men and women aged 45 to 70 years diagnosed with KOA, according to the criteria established by the American College of Rheumatology[6], who did not have clinical restrictions for the practice of physical exercise and who did not participate in any program of physical exercise in the six months that preceded the beginning of the data collection. Patients who underwent surgical procedures in the last three months and those with clinical restrictions to perform the proposed protocol in this study were excluded. Furthermore, data from participants who missed more than two consecutive sessions or four or more sessions during the intervention period were excluded from the analysis.

Interventions

The low-intensity exercise protocol consisted of performing knee joint extension exercise on the leg extension machine (TRG Fitness™, Blumenau, Santa Catarina), conducted in two sessions per week (Tuesdays and Thursdays) over 12 weeks. In the first two sessions, a single set of 15 repetitions was performed, followed by two sets of 15 repetitions in the subsequent two sessions, and three sets of 15 repetitions until the end of the 12-week intervention. The load used was equivalent to 30% of the one-repetition maximum (1-RM) strength, assessed in the pre-test and every 3 weeks during the intervention period. The exercise execution speed during the training sessions was three seconds for each repetition, with 1.5 seconds for the concentric phase and 1.5 seconds for the eccentric phase, monitored by a digital metronome (Sanny Personal Counter™, São Bernardo do Campo-SP, Brazil).

The high-intensity exercise protocol was identical to the low-intensity protocol in terms of volume, weekly frequency, and duration. However, the load used corresponded to 75% of the dynamic maximum strength assessed in the pre-test and every three weeks during the intervention period. Additionally, for load adjustment in the high-intensity protocol, it was established that whenever a participant could perform more than 20% of the number of repetitions established for the third set of exercises, the load was increased for the subsequent session.

Data collection

Pre- and post-test data collection was carried out by researchers who were blind to the interventions.

The assessment of maximum dynamic muscle strength in knee extension exercise (TRG Fitness™, Blumenau, Santa Catarina, Brazil) followed the recommendations of the American Society of Exercise Physiologists[15]. The exercise consisted of full knee joint extension (180º) from the starting position (90º), with subsequent return to the starting position.

The functional lower limb strength was assessed using the chair test, which involves rising from a chair without arm support, performing a full extension of the knee and hip joints, keeping the trunk upright, and returning to the starting position as many times as possible within 30 seconds[16].

Pain was assessed using the analogic visual scale[17] in the pre-test and post-test, immediately before and after each training session. The instrument consists of a scale with a score ranging from zero (no pain) to 10 (worst possible pain).

Ethical aspects

All study procedures, as well as its objectives, benefits, and potential risks, were thoroughly explained to eligible volunteers, and those who agreed to participate in the research signed an Informed Consent Form. This study was approved by the Ethics Committee for Research Involving Human Beings.

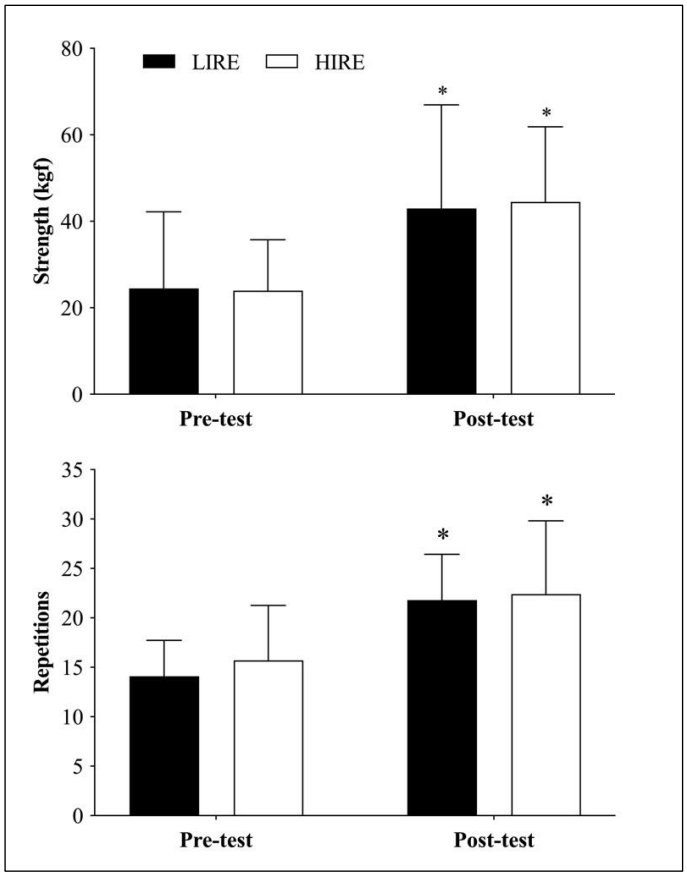
Data analysis

Data were assessed for normality using the Shapiro-Wilk test. A two-way repeated measures analysis of variance (2x2 ANOVA) was performed for within- and between-group analyses, followed by the Bonferroni multiple comparison test. An independent samples t-test was employed to compare the percentage differences between pre- and post-test for pain (Delta%) between the LIRE and HIRE groups. Correlation analyses (Pearson or Spearman) were performed between the pre- and post-test differences, expressed as percentage variation (Delta%), for maximum dynamic strength (1-RM), functional strength (chair test) and pain (Analogic visual scale). Additionally, effect sizes were computed for both paired groups (Glass's delta) and independent data (Edges's g). For all analyses, Statistical Package for the Social Sciences (SPSS™) version 26.0 was used, and the level of significance adopted for all analyses was 5%.

Results

Two-way ANOVA with repeated measures showed a significant increase in strength for 1-RM from pre- to post-test ($p<0.05$) in the LIRE group (Effect size: 0.803; 95% CI = 0.142 – 1.367) and in the HIRE group (Effect size: 1.273; 95% CI = 0.482 – 1.871), as shown in Figure 1. Additionally, an increase in functional strength, assessed by the Chair-test, was also observed in both the LIRE group (Effect size = 1.696; 95% CI = 0.766 – 2.349) and the HIRE group (Effect size = 0.931; 95% CI = 0.238 – 1.500). There were no statistically significant differences between groups, both in the pre-test and post-test for both variables ($p>0.05$).

Figure 1. Assessment of muscle strength (one maximum repetition) and functional strength (number of repetitions - chair-test) in patients with knee osteoarthritis performed in the pre-test and after 12 weeks of intervention (post-test).

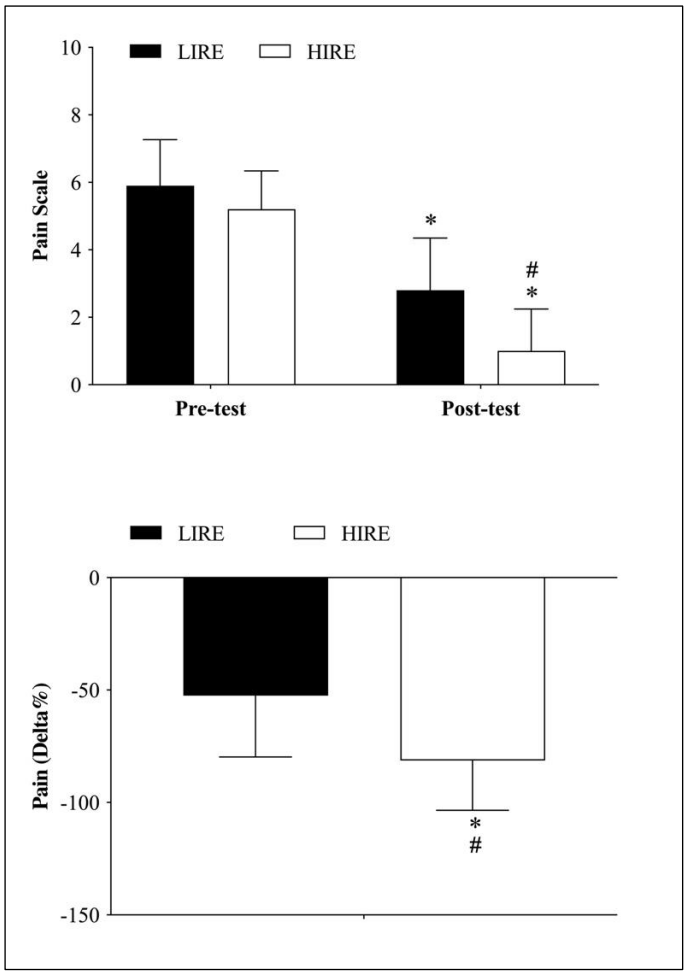


LIRE: Low intensity resistance exercise; HIRE: High intensity resistance exercise; *Statistically significant difference compared to the pre-test ($p<0.05$).

The evaluation of the pain response depending on the interventions is shown in Figure 2. Pain showed a statistically significant reduction from pre- to post-test in both the LIRE group (Effect size = -1.931; 95% CI = -2.946 – -0.524) and in the HIRE group (Effect size = -3.299; 95% CI = -4,849 – -1,101). A statistically significant difference between groups was evident only in the post-test ($p < 0.05$). A t-test for independent samples showed a statistically significant difference ($p < 0.05$) in pain reduction,

expressed as a percentage of the difference between pre- and post-test (Effect Size = 1.67; 95% CI = -2.66 – -0.68).

Figure 2. Evaluation of pain in patients with knee osteoarthritis (Visual Analog Scale) in the pre-test and post-test expressed in absolute values (a) and as a percentage variation from pre to post-test (b).

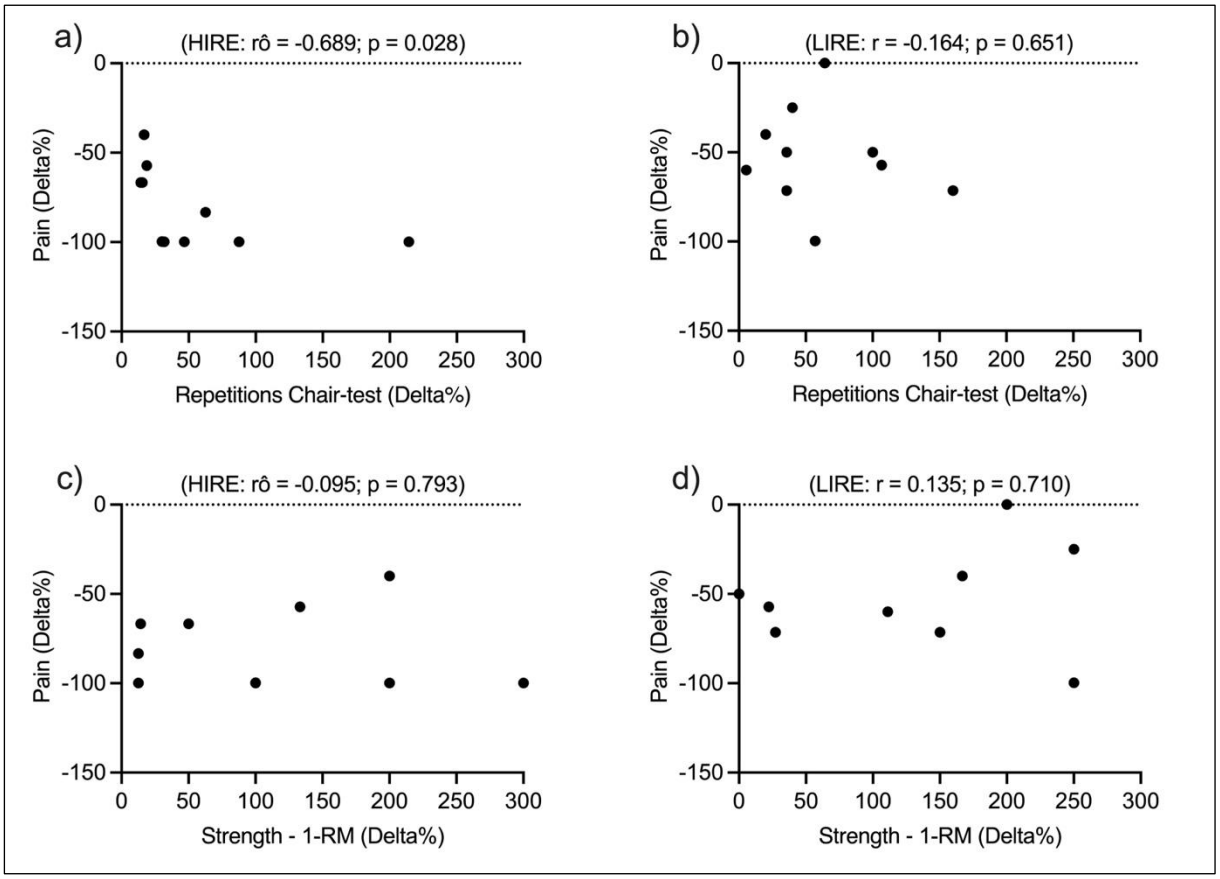


LIRE: Low intensity resistance exercise;HIRE: High intensity resistance exercise; *Statistically significant difference compared to the pre-test ($p<0.05$); # Statistically significant difference between groups ($p<0.05$); Delta%: Pain reduction, expressed by the percentage variation between pre- and post-test.

The analysis of the correlation between pain, strength for one maximum repetition, and functional strength (expressed as percentage variation from pre- to post-test) showed that pain had a statistically significant correlation ($p=0.017$) only with the variation in the number of repetitions in the chair test (Figure 3).

Figure 3. Correlations between the pain variation expressed as a percentage difference between pre- and post-test (Pain - Delta%), and the variation in strength for one maximum repetition (1-RM), functional strength (Chair-test), expressed as percentage variations from pre to post-test (Strength-Delta% and

Repetitions-Delta%, respectively) in patients with knee osteoarthritis.



HIRE: High-intensity resistance exercise, LIRE: Low-intensity resistance exercise. Functional strength - Chair-test: a) HIRE, b) LIRE. Strength for one repetition maximum (1-RM): c) HIRE, d) LIRE.

Discussion

The main finding of this study was that high-intensity exercise was more effective than low-intensity exercise in reducing pain in patients with KOA (-81,3% and -52.5%, respectively), although gains in maximal dynamic strength and functional strength were similar between interventions.

Another important aspect to highlight regarding the results of this study was that improvements in functional strength and maximal dynamic strength were similar in both interventions (high vs. low intensity). Adaptations to strength training in short intervention periods (8 to 12 weeks) are well described in the literature. The initial strength gains in the early phases of training are due to neural adaptations, such as improvements in intramuscular and intermuscular coordination, and they tend to be very similar regardless of training intensity and volume. A study by Zwart et al.[18] demonstrated that high and low-intensity resistance training were equally efficient in promoting improvements in isokinetic muscle strength and physical functioning and in reducing pain in patients with KOA. This authors also demonstrated that high-intensity resistance training, although well tolerated by patients with KOA, does

not lead to greater improvements in isokinetic muscle strength, pain, and physical function compared to low-intensity resistance training. These findings provide consistent evidence that both high- and low-intensity training can be viable strategies to promote muscle strength gain in short training periods (10 to 12 weeks).

In the present study, functional strength, assessed by the chair test, was positively correlated with pain reduction only in the high-intensity group. This relationship may be explained by other factors associated with high-intensity training, beyond strength gain. Although motor coordination and mobility were not specifically evaluated in this study, these factors could at least partly explain why the increase in functional strength, and not maximal dynamic strength, correlated with pain reduction. The chair test primarily assesses the strength associated with motor coordination, unlike the maximal dynamic strength test applied in this study, where the level of coordination required is quite low (knee extension with the leg extension machine).

High-intensity strength training has been suggested in the literature to be more efficient than low-intensity training in improving motor coordination and mobility. Strength gain and improvement in muscle function are dependent on the exercise dose[19] and high-intensity resistance training has proven to be efficient than low-intensity training to improve motor coordination and joint mobility[20]. These results reinforce the importance of high-intensity strength training as a more effective approach to improving motor coordination and mobility in patients with pain.

Out of the ten participants who completed the high-intensity protocol, five experienced 100% pain reduction, while in the low-intensity group, only one out of ten participants finished the experiment with complete pain remission. The mechanisms involved in pain reduction in patients with KOA include the release of neurotransmitters, such as endorphins, which act as natural analgesics and contribute to a decrease in pain perception. Resistance exercise has been associated with an increase in the production of neurotrophic factors, such as brain-derived neurotrophic factor (BDNF), which plays an important role in neuroplasticity and pain sensitivity modulation21.

Recent studies suggest that regular high-intensity resistance training sessions can lead to significant modulation in levels of proinflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor alpha - TNF-α[22,23]. High-intensity resistance exercise was also associated with a significant increase in BDNF levels, a neurotrophic biomarker that acts on pain sensitivity, modulation, and neural plasticity[24]. These modulations appear to be associated with intracellular signaling pathways influenced by exercise, directly impacting the balance between inflammatory and anti-inflammatory processes in the body[25]. Furthermore, resistance training can improve muscle function and joint stability, reducing stress on affected joints and alleviating pain associated with osteoarthritis[13]. Although the previously proposed mechanisms were not investigated in the present study, they may explain the

reduction in pain in response to the intervention protocols used.

Strength gain has been recognized as a crucial factor in increasing functional capacity, reducing pain, and improving the quality of life in patients with KOA. Resistance training can promote significant increases in muscle strength, positively affecting the performance of activities of daily living (ADLs), and the functionality of these patients. Messier et al.[26] showed that individuals with KOA who participated in a strength training program presented significant improvements in their ability to climb stairs, rise from a chair, and walk, indicating greater independence and autonomy in ADLs. These findings corroborate with the present study and reinforce the importance of strength gain as an effective intervention to promote functionality and quality of life in patients with KOA.

Another important aspect to highlight is that this study used only one exercise focused on quadriceps strength development. The choice of knee extension exercise was because quadriceps strength gain is associated with pain reduction and improved functional capacity in patients with KOA[27]. This type of intervention is characterized as low risk and easy to perform, contributing to adherence to the intervention protocol in the initial phase of treatment (12 weeks) and representing a significant improvement in the clinical condition of patients with KOA, expanding the possibility of practicing exercise and other activities in subsequent stages of treatment.

Our findings regarding pain reduction are consistent with other studies that used protocols involving various exercises[14,27,28]. This fact supports the indication of using a protocol with a single exercise in the treatment of pain in patients with KOA, especially in the initial phase, allowing for later progression to more complex exercise programs with higher load.

Conclusion

This study demonstrated that high-intensity resistance training using a single high-intensity resistance exercise is more effective than low-intensity resistance training in reducing pain. The improvement in functional strength, only in response to high-intensity training, is associated with a greater reduction in chronic pain in patients with KOA.

Authors' contributions

Category 1

Conception and design of study: DE SÁ, CA; GROSSL, FS; CORRALO, VS.

Acquisition of data: DE SÁ, CAS; GROSSL, FS; CORRALO, VS.

Analysis and/or interpretation of data: DE SÁ, CA; GROSSL, FS; VASCONCELOS, ABS; COPATTI, SL; CORBELLINI, F; CORRALO, VS.

Category 2

Drafting the manuscript: Authors' contributionsRevising the manuscript critically for important intellectual content: DE SÁ, CA; GROSSL, FS; VASCONCELOS, ABS; COPATTI, SL; CORBELLINI, F; CORRALO, VS.

Category 3

Approval of the version of the manuscript to be published (the names of all authors must be listed): DE SÁ, CA; GROSSL, FS; VASCONCELOS, ABS; COPATTI, SL; CORBELLINI, F; CORRALO, VS.

Data availability

Data will be available upon request to the corresponding author.

Declaration of conflict of interest

There is no conflict of interest to be declared by the authors.

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