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Exercise-Induced Hypoalgesia After Static Low-Angle Squat Exercise in Patients with Knee Osteoarthritis

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Abstract

The purpose of this study was to investigate exercise-induced hypoalgesia (EIH) on pressure pain thresholds (PPTs) after a static low-angel squat (SLAS) exercise in patients with knee osteoarthritis OA. Thirty-two patients with knee OA were recruited. Patients' demographic and clinical data were recorded. An algometer was used to measure the PPTs on the painful knee and biceps muscle and visual analog scale(VAS) was used for pain intensity. Subjects were instructed to perform a standardized single bout SLAS exercise. PPTs were assessed before and immediately after exercise. Pain intensity was assessed before, during and after quite exercise using VAS. Time up and go test (TUG) was used to measure mobility before and after exercise. The PPTs of the medial and lateral side of the knee showed a significant increase following SLAS exercise (p<0.001). The pressure pain thresholds of the biceps and quadriceps did not change (p>0.05). Pain intensity significantly increased during the low-angle squat exercise but decreased significantly post-exercise (p<0.001). The TUG scores decreased after exercise (p<0.001). The hypoalgesic effects of isometric low-angle squat exercise were moderate to large (Cohen's d -0.35 to -0.73) on pain and mobility after SLAS exercise in patients with knee OA. This study showed that the SLAS exercise induces local hypoalgesia in the exercising limb, reduces pain, and improves physical performance in patients with knee OA. These findings provide evidence on the mechanisms underlying the hypoalgesic effect of SLAS exercise, underscoring its potential as an effective intervention to alleviate pain and enhance function in clinical management of knee OA.

Keywords: Hypoalgesia, Exercise, Chronic pain, Osteoarthritis, Knee

Özet

Diz Osteoartriti olan Hastalarda İzometrik Squat Egzersizi Sonrasında Egzersize Bağlı Hipoaljezi

Bu çalışmanın amacı, diz osteoartriti (OA) olan hastalarda düşük açılı izometrik squat (DAİS) egzersizi sonrasında egzersiz kaynaklı hipoaljezi (EKH) etkisinin basınç ağrı eşiği (BAE) üzerindeki etkisini araştırmaktır. Diz osteoartriti olan 32 hasta çalışmaya dahil edildi. Hastaların demografik ve klinik verileri kaydedildi. Algometre kullanılarak ağrılı diz ve biseps kasındaki BAE'ler ölçüldü, ağrı şiddeti için görsel analog skala (GAS) kullanıldı.

Katılımcılara, standartlaştırılmış tek seanslık DAİS egzersizi yaptırıldı. BAE'leri egzersiz öncesi ve hemen sonrasında değerlendirildi. Ağrı şiddeti, egzersiz öncesi, sırasında ve sonrasında GAS kullanılarak değerlendirildi. Egzersiz öncesi ve sonrasında mobiliteyi ölçmek için Zamanlı Kalk ve Yürü testi (ZKYT) kullanıldı. Diz ekleminin medial ve lateral taraflarındaki BAE'ler, DAİS egzersizi sonrasında anlamlı bir artış gösterdi ($p<0.001$). Biseps ve kuadriseps kaslarındaki basınç ağrı eşiklerinde bir değişiklik gözlenmedi ($p>0.05$). Düşük açılı squat egzersizi sırasında ağrı şiddeti anlamlı şekilde artarken, egzersiz sonrasında anlamlı şekilde azaldı ($p<0.001$). ZKYT skorları egzersiz sonrasında azaldı ($p<0.001$). DAİS egzersizinin hipoaljezik etkileri, diz OA olan hastalarda ağrı ve mobilite üzerinde orta ile büyük (Cohen's d -0.35 ila -0.73) arasında değişen etkilere sahipti. Bu çalışma, DAİS egzersizinin egzersiz yapılan ekstremitede lokal hipoaljeziye neden olduğunu, ağrıyı azalttığını ve diz OA olan hastalarda fiziksel performansı iyileştirdiğini gösterdi. Bu bulgular, DAİS egzersizinin hipoaljezik etkisinin altında yatan mekanizmalara dair kanıt sağlayarak, diz OA'sının klinik yönetiminde ağrıyı hafifletmek ve fonksiyonu artırmak için etkili bir müdahale olma potansiyelini vurgulamaktadır.

Anahtar Kelimeler: Hipoaljezi, Egzersiz, Kronik ağrı, Osteoartrit, Diz

INTRODUCTION

Knee osteoarthritis (OA) one of the most prevalent joint disease in middle-aged and older populations. Knee OA is a major cause of musculoskeletal pain or disability complaints. Pain, as the primary symptom of knee OA, not only causes significant discomfort but also contributes to increased disability risk, greater healthcare utilization, and overall impairment in daily living. Given the multifaceted impact of pain in knee OA, there is a critical need to explore effective interventions that can alleviate pain and improve functional outcomes in affected individuals (1–4).

Exercise is recommended as a standard treatment for individuals diagnosed with knee osteoarthritis (OA) (5). Squat exercises represent a widely utilized strength and conditioning regimen, targeting numerous lower body muscles such as the quadriceps femoris, gluteus maximus and medius, adductor longus, hamstrings and triceps surae. Furthermore, squatting engages a multitude of supporting muscles, promoting postural stabilization of the trunk, with over 200 muscles activated during its execution (6). However, it is crucial to note that squat exercises can vary in depth, and performing deep squats with weight-bearing may pose risks to the knee joint (7). In recent years, a static squat exercise that is performed in the low angle, called "horse stance (Ma Bu)," has been put into practice which provides a reliable and safe isometric exercise based on the traditional Chinese exercise. With this regard, Zhao et al. (8) designed static low-angle squat (SLAS) exercise a new exercise approach that has a broad effect on the muscle around the back and knees. They demonstrated that static SLAS exercise led to significant reductions in proinflammatory factors including tumor necrosis factor-alpha and Interleukin-1β. These findings underline that SLAS is a reliable approach in the rehabilitation of individuals with knee OA (9).

Exercise-induced hypoalgesia (EIH) is a well-documented phenomenon observed in pain-free individuals following a single bout of aerobic or isometric exercise. EIH is characterized by a temporary reduction in sensitivity to painful stimuli, typically lasting up to 30 minutes post-exercise (10). The analgesic effects of exercise, including EIH, are mediated by endogenous opioid release, activation of descending pain inhibitory pathways, and anti-inflammatory responses (11). Exercise stimulates β-endorphin release and modulates central pain processing via the periaqueductal gray and rostroventral medulla. Additionally, it reduces proinflammatory cytokines, counteracting peripheral and central sensitization. These mechanisms are particularly relevant in knee OA, where chronic inflammation and altered pain processing exacerbate symptoms (12). Understanding how SLAS exercise influences these pathways could enhance its application as a non-pharmacological pain management strategy.

Researchers frequently quantify EIH by evaluating alterations in pain sensitivity, including raised pain thresholds or decreased pain intensity, both prior to and following a specified exercise protocols (13). This temporary decrease in pain sensitivity highlights the immediate pain-relieving effects of exercise, which can have implications for pain management strategies. Moreover, while clinically significant improvements in pain are typically observed following multiple sessions of exercise therapy, even a single session of exercise can influence pain sensitivity, underscoring the potential therapeutic benefits of acute exercise interventions (11,14). The acute effect of exercise on pain sensitivity exhibits greater variability within chronic pain populations, with some studies indicating no change, a reduction, or even an increase in pain sensitivity following a single bout of exercise (10,14–18). However, in individuals with knee OA, the effect of acute isometric exercise remains contentious, as both hypoalgesia and hyperalgesia have been reported (10). The aim of this study was to investigate the impact of static low-angel squat (SLAS) exercise on EIH in patients with knee OA.

METHOD

A cross-sectional pre-post study investigated EIH in patients with knee OA, using a single session of static low-angel squat exercise. This study was conducted between April-May 2022. The participants met the criteria for tibiofemoral joint osteoarthritis (OA) in at least one knee as per the American College of Rheumatology classification criteria (19). They experienced knee pain on most days of the past month, and knee osteophytes were evident on radiographic examination. Exclusion criteria comprised a history of lower limb joint replacement or fracture, rheumatoid arthritis and neuromuscular disorders. Prior to data collection, written informed consent was obtained from all participants.

Procedure

Demographic information and questionnaires were administered prior to the collection of measurements. Lequesne Index was used to assess pain and functional limitations in subjects. An algometer was used to measure the PPTs on the painful knee. All subjects were then instructed to perform a standardized a single bout static low-angle squat exercise. PPTs were assessed before and immediately after exercise. In additionally pain intensity was assessed before, during and after quite exercise using visual analogue scale (VAS, 100 mm). Time Up and Go test (TUG) was used to measure mobility before and after exercise.

The Lequesne Index is a questionnaire used to assess functional limitation and symptom severity in patients with osteoarthritis, particularly of the hip and knee. It consists of patient-reported questions evaluating three main components: pain, walking distance, and difficulties in daily activities. The total score is used to determine the severity of the condition, with higher scores indicating greater functional impairment (20).

Assessment of Pressure Pain Thresholds

Pain Pressure Thresholds (PPTs) evaluations were carried out utilizing a handheld pressure algometer (Force Dial FDK, Wagner Instruments, Greenwich, Connecticut), featuring a stimulation area of 1 cm^2. Gradual compression pressure escalation was applied, and participants were prompted to indicate when they experienced pain or discomfort, upon which the pressure was ceased. So, the pressure intensity defined the PPT values. Previous studies have reported excellent intra-rater and inter-rater reliability (intraclass correlation coefficients [ICCs] > 0.80) for PPT measurements in healthy individuals and patient populations with chronic pain (21). Assessments were conducted with the subject seated in a relaxed position on a chair lacking foot support, with both arms resting on the thighs (22). Four specific assessment sites were identified and marked: Site 1: Positioned in the middle of the dominant quadriceps muscle, 10 cm proximal to the base of the patella, Site 2: Located 3 cm medial to the midpoint of the medial edge of the patella, Site 3: Positioned 3 cm lateral to the midpoint of the lateral edge of the patella and Site 4: Located in the midpoint of the biceps brachii muscle. For each site, three PPTs assessments were conducted. Measurements were taken both before and after exercise, with the results recorded in kgPa.

Timed Up and Go Test

The Timed Up and Go (TUG) test is a reliable and valid tool for assessing functional mobility, balance, and fall risk in individuals with knee OA. The test measures the time taken for a participant to stand up from a chair, walk 3 meters, turn, walk back, and sit down. Longer completion times in knee OA patients are associated with reduced gait speed, quadriceps weakness, joint pain, and impaired dynamic balance, reflecting disease progression and mobility limitations. (23)

Static Low-Angle Squat Exercise

During the study, all individuals were instructed to perform isometric squat exercises for a duration of three minutes. Before initiating the exercise, all participants performed a standardized 10-minute warm-up using a bicycle ergometer at a self-selected moderate intensity.They were instructed to stand upright with their back against a wall, feet parallel and shoulder-width apart, and hands by their sides. Using a goniometer aligned with the lateral epicondyle of the right femur, they were directed to lower their backs down the wall until achieving a knee joint angle of 40° flexion for low-angle squatting (Figure 1) (24). Participants were then asked to maintain this posture for up to three minutes or until they experienced fatigue. Before initiating the exercise, each participant rated the intensity of leg pain on a visual analogue scale ranging from 0 to 100, where 0 indicated "no pain" and 100 represented "worst imaginable pain". Pressure pain thresholds (PPTs) were assessed both before and immediately after the three-minute wall squat exercises, with careful monitoring of the pain response throughout the procedure (22).

Figure 1. Isometric Low-Angle Squat Exercise Exercises

Statistical Analysis

All statistical analyses were performed with SPSS statistical software version 22 (IBM Corp., Armonk, NY, USA). Conformity of the data to normal distribution was analysed using the Shapiro-Wilk test in conjunction with visual inspection of histograms and box plots. Descriptive analyses were presented using median and interquartile range (IQR) for non-normality distributed and ordinal variables. The Wilcoxon and Friedman test were used to compare the change in pressure pain threshold, TUG scores and pain intensities. The effect size value used for the Wilcoxon Test was calculated with the formula $r=z/\sqrt{n}$. If the effect size is <0.3, it is interpreted as a weak effect, between 0.3-0.5 as a medium effect, and >0.5 as a large effect. The level of statistical significance was set at 0.05. The sample size was determined using Naugle's study datas (25). The calculation based on a difference in means (pre- to post-exercise) and, sample size determination indicated that 32 participants were required (effect size = 0.6 with 95% power and type I error rate of 5%).

Ethical approval and institutional permission

The study protocol was approved by the Süleyman Demirel University, Clinical Research Ethics Committee on May 24, 2022 (Approval Number: 152).

RESULTS

Thirty-two patients with knee OA (mean age = 57.93 ± 9.73 years, range = 53–62 years, average body mass index [BMI] = 29.1 ± 3.8 kg/m2, range = 19.4–34.7 kg/m2, 22 females) were included. According to K-L grading system, the number of Grade-2 patients were 10 (45.4%), the number of Grade-3 patients were 6 (27.7%), the number of Grade-4 patients were 6 (27.7%). 50% of these patients had bilateral knee OA. The clinical characteristics of all subjects are shown in Table 1.

Table 1. Participant characteristics

Parameters	**Median (IQR)**
Age (years)	59 (53-62)
Sex (%n)	
Female	10 (31.3)
Male	22 (68.8)
Bilateral knee OA (%n)	16 (50)
Unilateral knee OA (%n)	16 (50)
BMI	29 (26-35)
Education (years)	4 (4-8)
Duration of disease (months)	9(6-22)
Radiological grade (%n)	
Grade II	10 (45.4)
Grade III	6 (27.7)
Grade IV	6 (27.7)
Lequesne Index	11 (8-15)
Visual Analogue Scale -Rest	10 (0 -25)
Visual Analogue Scale -Activity	60 (42.5-80)

IQR, Interquartile Range; OA, Osteoarthritis; BMI, Body Mass Index

Pain at rest (VAS1; median [min-max]; 17.5[0-60]) level increased during squat (VAS2; (median [min-max]; 55[0-100]) and decreased after squat exercise (VAS3; median[min-max]; 0[0-50]) in individuals who performed single session SLAS squat exercise (p<0.001) (Figure 2). And also, all patients were able to complete the wall squat exercise in our study. No significant differences in PPT assessments were found between men and women (p>0.05) (Table 2).

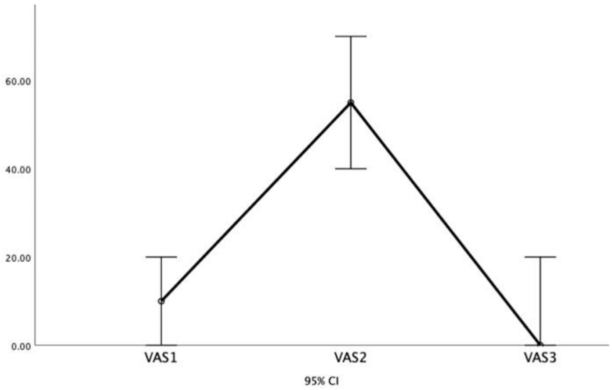

Figure 2. Pain Intensity Scores Before, During and After Static Low Angle Squat Exercise (VAS1; pain intensity before the SLAS exercise; VAS2; pain intensity during the SLAS exercise; VAS3; pain intensity after the SLAS exercise)

Table 2. Comparisons of PPTS Assessments of Women and Men

	Men Median (IQR)	**Women Median (IQR)**	**p value**
PPT1-Before	14 (14-22)	14 (12.30-15)	0.328
PPT1-After	15(12-22)	13(9-15)	0.215
PPT2-Before	18.50(18-22)	16.75(14.50-18)	0.144
PPT2-After	18(11-22)	15(11-18)	0.346
PPT3-Before	15(14-17)	14(13-17)	0.470
PPT3-After	14.50(12-18)	18(12-18)	0.407
PPT4-Before	12.50(10-13)	11.50(9.50-15)	0.885
PPT4-After	11.75(10-15)	15.50(9.50-17)	0.141

PPT; Pressure Pain Thresholds, PPT1, in the middle of the dominant quadriceps muscle, 10 cm proximal to the base of patella; PPT2, 3 cm medial to the midpoint of the medial edge of the patella; PPT3, 3 cm lateral to the midpoint of the lateral edge of the patella; PPT4, midpoint of the biceps muscle IQR; Inter Quartile Range

The mean PPT values in the middle of the dominant quadriceps muscle 10 cm proximal to the base of patella and 3 cm medial to the midpoint of the medial edge of the patella were higher after one session of SLAS exercise (p<0.05). The mean PPT values in the 3 cm lateral to the midpoint of the lateral edge of the patella and midpoint of the biceps muscle were noted relatively stable (Table 3).

In this study, the effect sizes for PPT1 (*d*=0.46) and PPT2 (*d*=0.44) suggest moderate improvements in pressure pain thresholds following a single session of SLAS exercise, indicating a potential reduction in pain sensitivity around the knee. The larger effect size for the TUG test (*d*=0.73) reflects a more substantial improvement in functional mobility, which may have meaningful implications for individuals with knee osteoarthritis, as enhanced mobility and reduced pain sensitivity could contribute to better overall function.

Table 3. Pressure Pain Thresholds Before and After Single Session Static Low-Angle Squat Exercise

PPT Site (kgPA)	Before		After		Effect size	p value
	Mean ± SD	**Inter Quartile Range**	**Mean ± SD**	**Inter Quartile Range**		
PPT1	14.53±4.11	12.30-15	13.00±4.88	10-15	0.46	**0.04***
PPT2	16.25±3.89	14.75-18.50	14.78±4.45	11-18	0.44	**0.04***
PPT3	14.28±4.24	13-17	15.25±4.32	12-18	0.35	0.08
PPT4	12.05±3.87	10-15	13.31±3.78	10-17	0.37	0.24
TUG (second)	10.91±1.91	6.59-13.45	19.09±1.77	5.89-12.60	0.73	**0.001***

PPT; Pressure Pain Thresholds; TUG; Time Up and Go Test; PPT1, in the middle of the dominant quadriceps muscle, 10 cm proximal to the base of patella; PPT2, 3 cm medial to the midpoint of the medial edge of the patella; PPT3, 3 cm lateral to the midpoint of the lateral edge of the patella; PPT4, midpoint of the biceps muscle; *Significantly differences in between exercise session(p<0.05), *Wilcoxon Test;

DISCUSSION AND CONCLUSION

In the present study, we investigate the effect of the SLAS exercise on EIH in patients with knee OA. Our study noted that the three-minute low angle wall squat exercise significantly increased PPTs of exercising muscles. While pain intensity of patients as increased during the SLAS, it was decreased after isometric the squat exercise. Thus, SLAS exercise evoked hypoalgesia in patients with knee OA. These results provide evidence of EIH in individuals with knee OA following isometric exercise highlighting the immediate analgesic effect of SLAS exercise.

In our study, it was observed that the EIH mechanism reduced pain and increased functional mobility in individuals with knee OA. Similarly, previous studies have reported that exercise contributes to pain modulation by enhancing the EIH response (25,26). Improvements in TUG time occurred following the activation of the EIH mechanism, and this finding is also supported by Goldoni et al. (27) The SLAS exercise is effective in pain management and improving functional capacity, and it may reduce fear of movement by enhancing joint stability. Lower extremity strengthening exercises have previously been shown to reduce pain and promote functional gains (28). Our study showed that increases in PPTs in exercising muscles immediately after a short-duration isometric exercise, which is in agreement with previous research conducted with healthy adults (29), patients with chronic whiplash (30). The results suggest that hypoalgesia following isometric exercise is associated with the activation of systemic pain inhibitory mechanisms (31,32). Additionally, our study found no significant relation between males and females in pressure pain threshold values. These findings are consistent with those of Hooger et al(33), reported similar observations of no sex-based differences in pressure pain sensitivity following submaximal isometric handgrips performed at 25% of maximum voluntary isometric contraction. Systemic hypoalgesic effect observed after various exercise modalities may be associated with conditioned pain modulation and influenced by the pain experience during exercise. Several researchers have noted a reduction in pain following a single session of exercise among healthy young adults. Different types of exercises, such as aerobic, resistance, and isometric exercises, have been investigated for their pain-relieving effects. In healthy individuals, aerobic exercise has shown small to moderate hypoalgesic effects, with effect sizes ranging from Cohen's d = -0.41 to -0.59. Isometric exercise and dynamic resistance exercise have demonstrated moderate to large hypoalgesic effects, with effect sizes ranging from d = -0.72 to -1.02 and d = -0.75 to -0.83, respectively (11,29).

The efficacy of exercise in individuals with chronic pain varies widely across different exercise modes, with effect sizes ranging from hypoalgesia to hyperalgesia (d = -0.43 to 1.92)(14). In our study involving patients with knee osteoarthritis (OA), the hypoalgesic effects of SLAS exercise were moderate (Cohen's d -0.35 to -0.46). In other study, 14 healthy women completed two sets of submaximal isometric handgrip exercises (40-50% maximum voluntary isometric contraction), leading to elevated pressure pain thresholds (PPTs) and reduced self-perceived pain ratings in both hands (34). Similarly, Burrows et al. (15) investigated the analgesic effects of resistance exercise in individuals with knee OA, finding increased pain thresholds at various body sites, including the knee.

Our study demonstrated increased lower body PPTs following a single bout of squat exercise, while upper body PPTs remained unchanged. The pain evoked during isometric squat exercises may trigger a descending pain inhibitory response, contributing to EIH (35). This mechanism, observed in healthy subjects, could explain the EIH response observed in our study. We found similar peak pain intensities during the low angle squat exercise at baseline and follow-up, suggesting that "pain inhibits pain" was one of the mechanisms affecting EIH. We can say these results suggest that SLAS exercise resulted in an immediate decrease in pain sensitivity, aligning with prior research demonstrating a systemic analgesic effect through isometric contractions (18,36). Similarly, Vaetger et al. (22) found that a three-minute wall squat exercise increased PPTs in both exercising and non-exercising muscles compared to quiet rest, with larger and more frequent EIH observed in the exercising muscle. Isometric contractions have also been shown to provide greater immediate analgesia than isotonic contractions in patients with patellar tendon pain. Participants experienced a significant reduction in pain during single-leg decline squats, isometric contractions reduced pain during single-leg decline squat from 7.0 to 0.17 on an 11-point scale (37).

In our study, we did not observe a significant difference in PPT3 and PPT4 measurements before and after the exercise. Several factors may explain this finding. First, the sensitivity of these specific measurements and their ability to detect changes in pressure pain thresholds in certain muscle groups may be limited. Second, the duration and intensity of the intervention might not have been sufficient to induce significant changes in these particular parameters. Additionally, individual variability in pain perception and possible learning effects could have influenced the results. In our study, while pain-VAS scores increased during the isometric squat exercises (from 17.5 to 11.93 on a 100 mm line), it decreased after a single bout SLAS exercise. And also, patients with knee OA displayed less pain and better physical performance after low angle isometric squat exercises in the current study. We think that patient's physical performance is better due to their low perception of pain. Low-angle isometric exercise presents a safe alternative that enhances knee stability, fortifies the medial femoral quadriceps muscle, and expands joint space without the risk of exacerbating existing damage.

EIH reduces pain, enhances freedom of movement, and improves functional performance. In our study, we observed that the EIH mechanism first reduced pain, followed by an improvement in TUG performance. Similarly, Rice et al. (11) reported that exercise suppresses pain, enhances mobility, and positively impacts TUG time. Additionally, Moezy et al. (38) demonstrated that in individuals with knee osteoarthritis, pain reduction following exercise was associated with shorter TUG times. Our findings indicate that pain reduction enhances functional mobility and that exercise provides both analgesic and physical performance benefits

Quadriceps strength is a crucial intrinsic factor influencing knee joint function and disability. Squats, commonly employed in strength and conditioning regimens, play a pivotal role in enhancing quadriceps strength. In knee OA rehabilitation, the emphasis typically lies on symptom management, particularly pain, and improving physical performance. The SLAS exercise presents a novel rehabilitation approach that stimulates EIH. This study indicates the first investigation into the effects of SLAS exercises on both pain modulation and physical performance. However, some limitations should be acknowledged. Firstly, we couldn't include pain-free controls. Secondly, in our study pain scores and PPT values were measured immediately following exercise, and we were unable to assess follow-up measures in our study. Additionally, the lack of a control group makes it difficult to attribute observed changes solely to the exercise intervention.Future research should include longer follow-up periods and control groups to validate our findings. Investigating the duration of the analgesic response through repeated measures over time could provide valuable insights into optimizing exercise interventions for pain management in knee osteoarthritis.

This study provides strong evidence that a single bout of SLAS exercise induces EIH, reduces pain, and enhances physical performance. The observed analgesic effects may be attributed to mechanisms such as opioid system activation and conditioned pain modulation. Our findings strongly support the potential of SLAS exercise as an effective rehabilitation strategy for pain management in individuals with knee osteoarthritis. Future studies with longer follow-up periods and controlled designs are necessary to further validate these findings and explore the long-term effects of SLAS exercise. This study highlights the clinical relevance of SLAS exercise, positioning it as a promising, evidence-based intervention for alleviating pain and improving functional outcomes in patients with knee OA.

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