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The Effects of High-Intensity Resistance Training Versus Isometric Training on Quadriceps Muscle Architecture and Strength in Obese Men with Early Knee Osteoarthritis

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ABSTRACT

Background and Purpose: *Exercise therapy has been extensively utilized as a nonpharmacologic therapy in clinical settings for managing knee osteoarthritis (KOA), and identifying the optimal exercise intensity is crucial to gain a sufficient training response without harmful side effects. The present study aimed to investigate the effects of high-intensity resistance training versus (HIRT) isometric training on quadriceps muscle architecture and strength in obese men with early KOA.*

Methods: *This study included 71 obese men over the age of 45 with primary KOA graded as 1 or 2 on the Kellgren-Lawrence scale. Participants were randomly allocated into two groups: the HIRT group (n=35) underwent 12 weeks of high-intensity resistance training (65–90% of one-repetition maximum) targeting the quadriceps, while the ISOM group (n=36) engaged in 12 weeks of quadriceps isometric training, consisting of 3 to 5 sets of 5 to 10 repetitions of 5-second unilateral knee extensions per session. Assessments included measurements of vastus lateralis muscle thickness, pennation angle, and fascicle length at rest using B-mode ultrasound. Maximal voluntary isometric contraction (MVIC) torque of the affected knee was evaluated with an isokinetic dynamometer. Knee pain and functional status were assessed using the Visual Analogue Scale (VAS) and the Western Ontario and McMaster Universities Arthritis Index (WOMAC).*

Results: *The findings of this study demonstrated that 12 weeks of HIRT resulted in more significant improvements in quadriceps muscle architecture and strength compared to isometric training in obese men with early KOA ($p<0.05$). Both training programs resulted in comparable significant improvements in knee pain and physical function with no significant difference between groups ($p>0.05$).*

Conclusions: *HIRT may be more effective than isometric training in improving quadriceps muscle strength and architecture among obese men with early KOA. Both HIRT and isometric training led to similarly significant improvements in knee pain and function. The findings indicate that either exercise regimen may be appropriately recommended for patients with early-stage KOA.*

Keywords: *knee osteoarthritis, high intensity resistance training, isometric, obesity*

INTRODUCTION

Knee osteoarthritis (KOA) is a prevalent degenerative condition with progressive cartilage breakdown, osteophytosis, and joint inflammation (Dantas et al., 2021). These pathological changes contribute to structural alterations in the knee, leading to persistent joint pain, instability, stiffness, muscle weakness, and significant impairment in mobility and quality of life (Sharma, 2021). KOA is the tenth leading cause of years lived with disability worldwide, (Dantas et al., 2021) presenting a major global public health concern, driven by its sharp rise in prevalence since 1990 and the anticipated continued growth through 2050 (Steinmetz et al., 2023).

The pathophysiology of KOA is influenced by various risk factors including gender, age, obesity, joint injuries and genetics (Katz et al., 2021). Obesity is the most prevalent modifiable risk factor

associated with the onset and progression of symptoms in KOA (Roos & Arden, 2016). It is estimated that two out of every three individuals with obesity are likely to develop symptomatic KOA in at least one knee (Murphy et al., 2008). Excess mechanical stress on the knee joint, combined with lower limb muscle weakness caused by obesity, accelerates cartilage breakdown and intensifies pain, worsening the condition. This leads to reduced functional ability and subsequent physical inactivity (Yázigi et al., 2018) which lowers daily energy expenditure, ultimately contributing to weight gain and an increase in body mass index (BMI) (Jiang et al., 2012). Pain and a sedentary lifestyle may further elevate the risk of obesity in these individuals. In this way a vicious cycle is created in which weight gain contributes to the progression of KOA, with the condition itself hinders effective weight management due to limited physical activity, resulting in a rising body mass index (BMI) (Çiftçi et al., 2025).

Obese individuals have been shown to exhibit lower maximum knee extensor muscle strength relative to their body mass compared to non-obese individuals (Abdelmoula et al., 2012). Earlier studies have shown that weakness in the quadriceps muscles may lead to the onset of KOA, as the knee joint becomes less capable of supporting body weight during walking (Hurley, 1999). The rate of disease progression is significantly accelerated due to quadriceps muscle weakness and subsequent increases in joint loads (Huang et al., 2018). Moreover, KOA is often associated with significant quadriceps muscle weakness, resulting in dynamic knee instability and physical impairment (Rice et al., 2011).

Muscle strength and overall joint mechanics are influenced by the architecture of the skeletal muscle which refers to the geometric configuration of the muscle fibers. To accurately assess muscle morphology and mechanical function, analyzing the architecture of skeletal muscle is a crucial factor. Ultrasound techniques are used noninvasively to objectively assess skeletal muscle architecture (Chauhan et al., 2013). Muscle thickness, cross-sectional area and pennation angle are critical parameters for force production and execution of movement (Ashnagar et al., 2021). To efficiently transmit force from muscle fibers to the tendon is related to the value of pennation angle, whereas the magnitude of force production is dependent on skeletal muscle thickness (Agyapong-Badu et al., 2014; Gaid et al., 2024). An increase in pennation angle (PA) reflects a higher concentration of contractile tissue within a given muscle volume, enhancing the muscle's force-generating capacity. Conversely, during muscle atrophy, the reduction in contractile tissue near the aponeurosis leads to a decline in PA (Ema, Wakahara, Miyamoto, et al., 2013).

According to existing literature, individuals with KOA exhibit reduced quadriceps muscle thickness compared to healthy subjects. These findings indicate that quadriceps muscle atrophy is involved in the abnormal muscle function, disruption of the normal movement patterns and knee joint and patellofemoral pain, highlighting the importance of assessing muscle morphology as a means of addressing such conditions (Kumar et al., 2023; Darabseh et al., 2024).

The current KOA treatment methods include pharmacotherapy, physical and surgical interventions (Duong et al., 2023). Exercise training has been extensively utilized as a nonpharmacologic therapy in clinical settings for managing KOA, owing to its effectiveness in alleviating symptoms with minimal adverse effects (Hochberg et al., 2012). Current guidelines have recommended strength training for the management of KOA (Kolasinski et al., 2020). Recent studies have demonstrated notable enhancements in disease-related symptoms, muscular strength, joint stability, and overall physical function following strength training (Lo et al., 2024; Xu et al., 2025). It has been shown that self-reported pain and physical function significantly improved in response to quadriceps muscle strengthening (Lange et al., 2008).

Strength training can be carried out using either isometric or isotonic exercises. Isometric exercises involve muscle contractions without any visible movement in joint angles, whereas isotonic exercises are characterized by muscle contractions accompanied by changes in muscle length and joint angle (Widodo et al., 2022). Given its low-impact nature and minimal joint strain, isometric exercise may be more appropriate for individuals with KOA who are vulnerable to joint injury or excessive joint loading (Yang et al., 2024). Nonetheless, studies indicate that isometric exercise is less effective than isokinetic exercise in improving strength and alleviating pain in in patients with KOA (Rosa et al., 2012a). Recent studies showed that eight weeks of isometric exercise significantly improved pain and quadriceps muscles strength in elderly women with early knee OA (Park et al., 2021). In an earlier study, we found that a 12-week isometric quadriceps training program led to improvements in knee pain, as well as in quadriceps strength and muscle architecture, among obese individuals with knee

OA (Mahmoud et al., 2017).
HIRT is typically characterized by exercising at an intensity over 60% to 80% of an individual's one-repetition maximum (1RM) (Bartholdy et al., 2017). Previous studies have produced mixed results regarding the effects of HIRT on KOA symptoms. Some have indicated that HIT might worsen symptoms like pain and swelling due to increased joint contact forces (Jan et al., 2008; Sharma et al., 2003). However, other studies have not supported these findings (Hurkmans et al., 2009; King et al., 2008). On the contrary, it has been found that short-term, HIRT was safe and well tolerated by older adults with KOA and improved clinical outcomes by enhancing muscle strength (Baker et al., 2001). More recently 12 weeks of HIRT at 70–80% of the 1-RM significantly improved pain, isokinetic muscle strength, and physical functioning (de Zwart et al., 2022).
Although resistance training is increasingly acknowledged for its role in the management of KOA, the optimal type and dose of resistance training remains unknown (Turner et al., 2020). Therefore, the purpose of the present study was to investigate the effects of HIRT versus isometric training on quadriceps muscle architecture and strength in obese men with early KOA. The hypothesis suggested that HIRT would give greater improvements than isometric training in terms of pain, physical function, quadriceps muscle architecture and strength in obese men with early KOA.

METHODS

Trial Design

This trial is a parallel-group RCT involving two groups. The study protocol was approved by the Standing Committee of Bioethics Research in Prince Sattam bin Abdulaziz University, Saudi Arabia (ID: SCBR-386/2025). Written informed consent was obtained from each participant. Study procedures followed the ethical standards set forth in the Declaration of Helsinki. The study procedures were carried out in the Department of Rehabilitation and Health Sciences, Prince Sattam Bin Abdulaziz University, Al-Kharj, Saudi Arabia between January 2025 and April 2025.

Participants:

Subjects were recruited from nearby clinics and hospitals and through advertisements shared by consumer organizations and on social media. The study enrolled 105 obese men diagnosed with degenerative KOA. The diagnosis was made based on the guidelines established by the American College of Rheumatology. Patients with primary knee osteoarthritis classified as grade 1 or 2 on the Kellgren-Lawrence scale, determined by weight-bearing radiographs, were included. According to the Kellgren-Lawrence classification, Grade I is characterized by questionable joint space narrowing and the potential presence of osteophytes, while Grade II indicates a possible reduction in joint space accompanied by clearly visible osteophyte formation (Kohn et al., 2016). Initial screening of participants was conducted via an electronic survey and phone interview, followed by radiographic screening for potentially eligible participants. An initial examination was carried out by a qualified physician for all participants, who were then advised to continue their existing medications, eating patterns, and physical activity levels throughout the study.
The inclusion criteria were as follows: i) age over 45 years; ii) having a body mass index (BMI) of more than 30 kg/m^2; iii) knee pain persisting for more than 3 months; and iv) presence of tibiofemoral osteophytes visible on weight-bearing X-rays; v) A mechanically aligned knee classified as either neutral (ranging from −2° valgus to 2° varus) or exhibiting varus alignment (up to 10° varus); vi) the more symptomatic knee was selected for training in case of bilateral KOA.
Participants were excluded if they had: i) knee or hip deformity; ii) previous knee surgery; iii) intra-articular injection within the past three months; iv) rheumatoid arthritis or systemic arthritic conditions; v) patellofemoral pain syndrome in the affected knee vi) engagement in knee strengthening or functional training in the past six months; vii) history of major organ system dysfunction; viii) unable to fulfill the study requirements.
A biostatistician generated an unstratified randomization sequence using Microsoft Excel (Microsoft Corporation, Redmond, WA). A person not involved with the trial sealed the assignments in opaque, numbered envelopes. Eligible participants were directed to an independent administrator who randomly allocated them to either of the two study groups. Study groups included the high-intensity quadriceps resistance training group (HIRT group) and the isometric quadriceps training group (ISOM group).

Sample size calculation
The calculation of the sample size was carried out according to an anticipated effect size of d = 0.80, in accordance with recommendations for clinical trials targeting pain and physical function in individuals with knee osteoarthritis (McAlindon et al., 2015). Using G*Power 3.0.10 software (University of Düsseldorf, Düsseldorf, Germany), a sample size of 34 participants per group was determined to achieve 90% statistical power at a two-sided alpha level of 0.05. To account for an expected 20% dropout rate, the sample size was increased to 40 participants per group, resulting in a total of 80 participants.

Anthropometrics assessments:
Body weight and height were recorded for all participants using a Detecto scale (USA), and BMI was determined by dividing weight in kilograms by the square of height in meters. Waist circumference was measured per standard protocol. Body composition measures—specifically body fat mass, fat percentage, and fat-free mass—were evaluated using the InBody 770 BIA device (Biospace, Cerritos, CA).

Pain evaluation
Pain was assessed using a 10 cm horizontal Visual Analog Scale (VAS), recorded at baseline and following 12 weeks of exercise intervention. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was employed to evaluate pain, joint stiffness, and physical function. WOMAC is a disease-specific, self-administered, multidimensional tool designed for patients with knee osteoarthritis. The physical function domain includes 17 items assessing the level of difficulty in performing daily activities. A composite physical function score, ranging from 0 to 68, was calculated by summing individual item scores, with higher values indicating worse function. The instrument also features subscales for pain and stiffness; the pain subscale consists of five items, yielding a total score between 0 and 20, where higher scores denote more severe pain (McConnell et al., 2001).

Muscle architecture
All ultrasonography measurements were carried out by experienced radiologist who was blinded to the identity of the subjects. During rest, vastus lateralis (VL) muscle thickness, pennation angle, and fascicle length in the affected knee were assessed in vivo at rest using a diagnostic ultrasound system (HI VISION Avius; Hitachi Aloka Medical Japan, Tokyo, Japan) equipped with a high-frequency linear array transducer (10–15 MHz). Ultrasonographic assessment was performed on the VL muscle, based on the widely accepted assumption that architectural changes in the VL are representative of the entire quadriceps femoris muscle group (Baroni et al., 2013a). The participant was placed in a supine position with the knee passively extended, while the popliteal region was supported and the muscles relaxed to facilitate image acquisition. To ensure consistent fluid distribution, participants rested in the supine position for at least 20 minutes prior to all measurements. Subsequently, a water-based gel was applied to the ultrasound transducer to facilitate acoustic coupling and to minimize muscle deformation that could result from excessive probe pressure. Ultrasound images were acquired at the midpoint of the VL, corresponding to 50% of the distance between the palpable center of the greater trochanter and the lateral epicondyle of the femur. To maintain consistency across repeated scans, the probe location was recorded on a flexible plastic template. For analysis, the average of three consecutive scans was used. Fascicle length was defined as the distance along the fascicular trajectory between the superficial and deep aponeuroses. In instances where the fascicle extended beyond the field of view, its full length was estimated through linear extrapolation. This involved measuring the straight-line distance from the visible end of the fascicle to the point of intersection between an extended fascicle line and a line projected from the superficial aponeurosis (Baroni et al., 2013a). Pennation angle was defined as the angle formed between the fascicle path and the deep aponeurosis of the VL muscle. Three pennation angles were measured per ultrasound image, and their mean value was used. Muscle thickness was defined as the average vertical distance between the superficial and deep aponeuroses, taken at both ends of each 45 mm-wide ultrasound images.

Quadriceps muscle strength

The machine was initially calibrated just before the start of each test session. Subjects were familiarized with the device and procedures involved through visiting the laboratory on at least one occasion before undergoing the testing procedure. Maximal isometric knee extension torque of the affected knee was measured using an isokinetic dynamometer (CSMI Humac 2009, cybex II, II+, version 129, USA) with at 70° knee flexion (full knee extension=0°) for all subjects as this angle is the optimum angle reported for maximal isometric strength of knee extensors (Pearson & Onambele, 2005). Participants were positioned in a seated posture with the backrest inclined at 85° relative to the horizontal plane (where 0° denotes full supine alignment) and instructed to grasp the lateral edges of the seat to ensure stability during testing. A padded cuff was affixed to the test limb proximal to the medial malleolus, securing the limb to an adjustable lever arm. The dynamometer's axis of rotation was meticulously aligned with the lateral femoral epicondyle to ensure accurate joint movement measurement. To mitigate compensatory or extraneous motion, stabilization straps were firmly applied across the waist, thorax, and contralateral thigh. Following an initial warm-up consisting of 10 unloaded isokinetic knee extensions, participants performed three submaximal isometric contractions at 70° of knee flexion, with efforts progressively increasing to approximately 50% of their estimated maximal capacity. After a standardized 1-minute rest period, participants were instructed to perform maximal voluntary isometric contractions (MVIC) of the quadriceps against the dynamometer's lever arm. Consistent verbal encouragement was provided throughout to promote maximal effort. Three MVIC trials were completed, with each contraction sustained for approximately 2 seconds and separated by a 60-second rest interval. The peak knee extension torque from each trial was recorded, and the highest value was used to determine maximal quadriceps strength.

Interventions

High-intensity resistance training

HIRT sessions were conducted 3 times weekly over 12 weeks. During the initial one to two sessions, participants were instructed in proper exercise techniques. Following this familiarization phase, one-repetition maximum (1RM) tests were administered to determine each participant's maximal lifting capacity, which was used to prescribe initial training loads. Participants performed three sets per exercise, beginning with 8 repetitions at 75% of their 1RM in the first week. The training load was progressively increased: 80% of 1RM for 8 repetitions in week two, 85% for 6 repetitions in week three, and 90% for 4 repetitions in week four. Updated 1RM values were obtained at the end of weeks five and nine to adjust exercise intensities for the subsequent training phases. In cases where participants reported pain during exercise exceeding a visual analogue scale (VAS) score of 5, the range of motion at the knee joint was reduced. If pain persisted, the resistance load was decreased (Peterson et al., 2011). Outcome measures, including pain intensity, functional activity, and muscle strength, were assessed before and after the intervention. Pain intensity was evaluated using the VAS.

Isometric quadriceps muscle training

The isometric training program was conducted three times per week, with at least one rest day between sessions. Each session consisted of 3 to 5 sets of 5 to 10 repetitions of 5-second unilateral isometric knee extensions. A 30-second rest period was provided between repetitions and a 1-minute rest between sets. To reduce the risk of muscle damage due to unfamiliar high-intensity exercise, the protocol was progressively intensified over 12 weeks, beginning with 3 sets of 5 repetitions in the first week and gradually increasing to 5 sets of 10 repetitions by week 12. To facilitate adaptation to the training load, initial sessions were performed at submaximal intensities—50% of maximal voluntary isometric contraction (MVIC) during week 1 and 60% MVIC during week 2. To prevent asymmetrical strength gains between limbs, both legs were trained. Each session was preceded by a standardized warm-up that included 5 minutes of cycling at 60–75 W, followed by 10 isotonic quadriceps contractions through a full range of motion without resistance, and three submaximal isometric contractions at 70° of knee flexion, performed at intensities below 50% of maximal effort.

Statistical analysis

Statistical analyses were performed using SPSS version 23. Descriptive statistics, including means

and standard deviations, were calculated, and 95% confidence intervals (CI) were used to describe key variables. Data analysis was performed using IBM SPSS Statistics version 23.0 (Chicago, IL). Results were presented as mean ± standard deviation (SD). The normality of continuous variables was assessed using the Shapiro–Wilk test. To evaluate the baseline comparability of parametric data between the two groups, an independent t-test was applied. A two-way mixed analysis of variance (ANOVA) with a 2 × 2 design (group × time) was employed to examine the effects of the intervention over time between the HIIT and control groups. Statistical significance was determined at a p-value of less than 0.05.

RESULTS

A total of 80 individuals with KOA were enrolled in the study, with 71 participants ultimately included in the final analysis, as illustrated in Figure 1. The HIRT group included 35 subjects and the ISOM group included 36 subjects. Baseline and demographic characteristics were similar between groups, with no statistically significant differences noted (refer to Table 1). Across all intervention groups, adherence to treatment sessions was high, with an overall attendance rate of 91% maintained throughout the study duration.

Changes in muscle architecture

A significant interaction of VL fascicle length, muscle thickness and pennation angle were observed pre- to post-intervention between the HIRT and the ISOM groups, $F(1, 71) = 45.13$, $p < 0.001$, $\eta 2 = 0.966$, $F(1, 71) = 47.14$, $p < 0.001$, $\eta 2 = 0.999$, $F(1, 71) = 46.17$, $p < 0.001$, $\eta 2 = 0.976$ respectively (Table 2). In comparison with baseline values, fascicle length, muscle thickness and pennation angle significantly increased in both the HIRT group ($p<0.001$) and in the ISOM group ($p<0.001$). Post-test fascicle length, muscle thickness and pennation angle values significantly increased in the HIRT group compared to the ISOM group ($p<0.001$).

Changes in quadriceps muscle strength

MVIC values showed significant interactions pre- to post-intervention between the HIRT and the ISOM groups, $F(1, 71) = 46.81$, $p < 0.001$, $\eta 2 = 0.992$ (Table 2). In comparison with baseline values, MVIC significantly increased in both the HIRT group ($p<0.001$) and in the ISOM group ($p<0.001$). Post-test MVIC values significantly increased in the HIRT group compared to the ISOM group ($p<0.001$).

Changes in pain and physical function

In comparison with baseline values, VAS values significantly increased in both the HIRT group ($p<0.001$) and in the ISOM group ($p<0.001$) (Table 2). There was no significant difference in the post-test VAS values between the HIRT group compared to the ISOM group ($p>0.05$). No significant interaction of VAS was observed pre- to post-intervention between the HIRT and the ISOM groups ($p=11$). WOMAC stiffness score showed no within- or between-group significant changes ($p>0.05$).

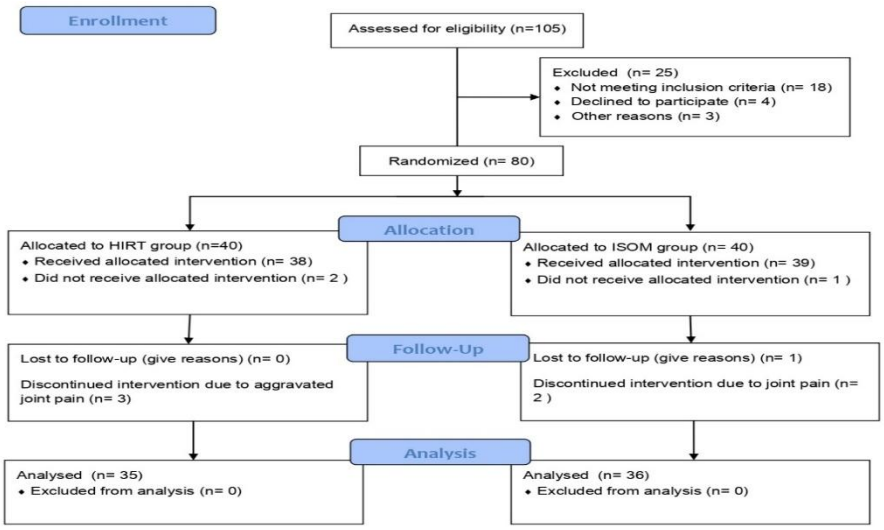

Fig. 1 The CONSORT flow diagram of the study.

Table 1. Demographic data of the study participants

Variable	HIRT Group (n=35)	ISOM Group (n=36)	P value
Age, years	Mean ±SD (CI 95%)		
	53.2 ±5.22 (45.11-57.44)	52.6 ±6.12 (44.20-58.55)	0.811*
Body weight, Kg	94.11 ±4.6 (92.84-96.41)	93.83 ±5.1 (91.99-95.23)	0.447*
BMI, Kg/m2	35.33 ±2.76 (34.78-36.1)	34.64 ±2.9 (34.25-36.34)	0.528*
Waist circumference, cm	107.88 ±3.42 (105.13-109.77)	106.56 ±3.79 (104.82-109.9)	0.992*
Body fat, %	42.77 ±2.12 (41.17-44.11)	42.16 ±2.3 (41.05-44.28)	0.864*
Symptom duration, years	7.6 ±4.8 (6.13-10.11)	8.2 ±4.14 (6.22-9.80)	0.422*
Affected knee (right/ left), n	16/19	19/17	0.866†
Kellgren-Lawrence grade (Grade 1/ Grade 2), n	11/24	9/27	0.426†
Current drug treatment, No. (%)			
-Non-steroidal anti-inflammatory drugs	11 (31)	9 (25)	0.633†
-Analgesics (paracetamol combinations)	16 (45.7)	19 (51.3)	
-Cyclooxygenase-2 inhibitors	6 (17.1)	4 (10.8)	
-Topical anti-inflammatory drugs	4 (11.4)	7 (18.9)	
-COX-2 inhibitors	2 (5.7)	2 (5.4)	
- Glucosamine/chondroitin products	7 (20)	8 (21.6)	

Data are presented as Mean ±SD, CI: Confidence Interval, BMI: Body Mass Index *: Non-significant changes between two groups p>0.05 (Independent t-test) †: Non-significant difference p>0.05 (Chi-square X^2 test).

Table 2. Effect of exercise training on the study outcome measures in both groups

Variable	HIRT Group (n=35) Mean ±SD (CI 95%)		ISOM group (n=36) Mean ±SD (CI 95%)		Group _ time interaction	
	Pre	Post	Pre	Post	p	η^2Partial
VAS, (range 0-10)	4.3 ±1.3 (3.1-5.4)	2.44 ±1.5† (2.17-3.6)	4.1 ±1.5 (3.5-5.1)	2.47 ±1.5† (2.2-3.8)	0.11	-
WOMAC pain score, (range 0-20)	7.8 ±1.9 (5.3-9.1)	5.3 ±1.6† (3.9-6.8)	7.6 ±1.8 (5.2-8.8)	5.6 ±1.8† (4.1-7.1)	0.09	-
WOMAC physical function score, (range 0-68)	23.2 ±6.4 (19.3-27.7)	17.2 ±5.8† (13.5-21.3)	22.8 ±6.3 (18.7-26.9)	18.4 ±5.1† (15.6-22.6)	0.22	-

WOMAC stiffness score, (range 0-8)	2.1 ±0.5 (1.7-2.4)	2.0 ±0.5 (1.7-2.3)	2.0 ±0.4 (1.6-2.4)	2.0 ±0.4 (1.6-2.4)	0.63	-
Fascicle length, cm	9.2 ±0.6 (8.7-9.4)	12.6 ±0.7† (11.9-13.1)	9.4 ±0.7 (8.9-9.8)	10.8 ±0.7†‡ (9.6-10.8)	P<0.001*	0.966
Muscle thickness, cm	3.2±0.3 (2.9-3.4)	3.9±0.4† (3.5-4.2)	3.3±0.4 (3.1-3.6)	3.5±0.4†‡ (3.2-3.8)	P<0.001*	0.999
Pennation angle, degrees	17.6 ±2.5 (15.7-19.2)	22.8 ±2.4† (19.9-24.6)	18.8 ±2.6 (16.3-20.1)	20.4 ±2.6†‡ (18.3-22.6)	P<0.001*	0.976
MVIC, N.m	133.8 ±15.3 (116.2-141.7)	181.5 ±19.1† (165.6-194.8)	136.3 ±16.5 (119.1-144.3)	155.7 ±17.1†‡ (141.2-173.7)	P<0.001*	0.992

BMI: Body mass index; CI: Confidence interval; VAS: visual analogue scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; MVIC: Maximum voluntary isometric contraction; η^2Partial: Effect size of the difference;
†: Significant changes within the group at p<0.05 (paired t-test);
‡: Significant changes of post-tests between the two groups at p<0.05;
*: Significant changes from pre- to post-intervention among study and control groups at p<0.05

DISCUSSION

This is the first study to directly evaluate and compare HIRT with isometric training in obese men with early KOA. Consistent with our hypothesis, the findings of the current study showed that 12 weeks of HIRT led to more significant improvements in quadriceps muscle architecture and strength compared to isometric training in obese men with early KOA. Both training programs resulted in comparable significant improvements in knee pain and physical function.

Muscle architecture

This study revealed that both HIRT and isometric training led to significant improvement in muscle architecture parameters in terms of VL muscle fascicle length, pennation angle and thickness. However, HIRT yielded greater improvements across all measured architectural parameters compared to isometric training. Nonetheless, existing research presents mixed results regarding muscle fascicle length changes following various forms of resistance training. A 12-week isometric exercise program resulted in significant increase in VL muscle fascicle length, pennation angle and muscle thickness in obese individuals with KOA (Mahmoud et al., 2017). Moreover, 11% and 13% increase in VL muscle fascicle length and pennation angle respectively were observed after 14 weeks of dynamic resistance training in elderly people. The training protocol included leg press and leg extension exercises, performed three times per week, consisting of two sets of 10 repetitions at 80% of the five-repetition maximum (Reeves et al., 2004). Eight weeks of isometric training have been shown to significantly increase VL muscle thickness and pennation angle in healthy young men and women (Alegre et al., 2014). Likewise, a 5-wk program of HIRT increased VL muscle fascicle length and pennation angle by 9.9 ± 1.2 and 7.7 ± 1.3%, respectively in young adults (Seynnes et al., 2007). Also, significant increases in VL muscle fascicle length, pennation angle and muscle thickness has been observed following an 8-week high intensity concentric and eccentric resistance training program in sixty healthy young women (Coratella et al., 2022). The inconsistency in findings regarding muscle architectural adaptations to resistance training remains uncertain. However, it may be influenced by potential measurement errors associated with ultrasound techniques, variations in the specific regions of the muscle where architectural parameters were assessed, or differences in the characteristics of the study populations (Baroni et al., 2013b; Ema, Wakahara, Mogi, et al., 2013).

Mechanisms of muscle fiber growth involve radial longitudinal sarcomere addition. Radial muscle growth occurs through the addition of sarcomeres in parallel, which is reflected by an increase in pennation angle and physiological cross-sectional area at the whole muscle level. In contrast, longitudinal growth involves the addition of sarcomeres in series, leading to longer muscle fascicles

(Jorgenson et al., 2020).
The superior improvements in muscle architecture observed in the HIRT group compared to the ISOM group may be attributed to higher metabolic stress during dynamic contractions (Hinks et al., 2023). Repeated dynamic movements can cause microdamage to sarcomeres, initiating a repair and adaptation process known as the repeated bout effect (Hyldahl et al., 2017). This adaptive process likely involves an increase in muscle protein content, which helps reinforce the sarcomeres and enhances their resistance to subsequent mechanical stress (McHugh, 2003).

Muscle strength
The results of this study demonstrated that HIRT produced greater gains in muscle strength, as measured by MVIC, compared to isometric training (35% vs. 14%). These outcomes are consistent with our earlier research, where a 12-week isometric training program led to an 18% increase in MVIC (Mahmoud et al., 2017). Likewise, earlier studies have shown that isokinetic training leads to more substantial improvements in quadriceps strength compared to isometric training in individuals with KOA (Rosa et al., 2012b). Nevertheless, although isometric exercise has proven to be beneficial in the management of KOA, it has not been shown to produce significantly greater improvements in pain reduction, physical function, or muscle strength when compared to isotonic exercise (Yang et al., 2024).
Evidence indicates that both high- and low-intensity resistance training are comparably effective in enhancing muscle strength, improving physical function, and reducing pain in individuals with KOA. Furthermore, although HIRT is well tolerated by patients, it does not confer significantly greater benefits than low-intensity training with respect to muscle strength, pain reduction, or functional outcomes (de Zwart et al., 2022). These results provide robust evidence that both training intensities represent viable and effective strategies for promoting muscle strength gains within relatively short intervention durations of 10 to 12 weeks.
Mechanisms proposed to explain improvements in muscle strength in response to resistance training include neuromuscular adaptations, hypertrophy reflected by increased muscle cross-sectional area, and modifications in the stiffness of connective tissues (Hughes et al., 2018). Furthermore, greater muscle strength improvement in response to HIRT compared to isometric training in the current study may be due to several mechanisms. First, greater muscle architectural adaptations reported in the HIRT group which indicate more sarcomerogenesis. Muscle strength improvement is directly related to increased muscle thickness (Hinks et al., 2023), which was more pronounced in the HIRT group. Increased serial sarcomerogenesis enables muscles to produce higher force across the full range of joint motion by maintaining individual sarcomeres nearer to their optimal length. Furthermore, enhanced force generation during joint angular shortening is achieved as each sarcomere experiences reduced and slower shortening, thereby preserving an optimal force-velocity relationship (Hinks et al., 2023). Second, the high training intensity may enhance the rate of increase in force at the onset of contraction (RFD) due to increased neural drive (Hughes et al., 2018). Third, the substantial mechanical stress imposed on muscle fibers and connective tissues during HIRT may induce hormonal responses that activate hypertrophic signaling pathways, including those involving insulin-like growth factor, testosterone, and growth hormone (Schoenfeld, 2010). Last, studies indicated that resistance exercise induces a load-dependent activation of mammalian target of rapamycin complex 1 (mTORC1) signaling, which is associated with subsequent increases in muscle hypertrophy observed after training (Baar & Esser, 1999).

Pain and physical function
The findings of the current study revealed that both the HIRT and ISOM groups exhibited significant improvements in WOMAC and VAS scores. According to the American College of Sports Medicine (ACSM) guidelines, resistance training is effective in reducing pain and improving physical function in individuals with osteoarthritis (Riebe et al., 2018). Moreover, increases in quadriceps strength are correlated with reductions in pain and enhancements in functional capacity among patients with KOA (Bennell et al., 2014).
A previous study has demonstrated that implementing a quadriceps isometric contraction exercise protocol leads to reductions in joint pain and enhancements in functional capacity in individuals with KOA (Huang et al., 2018). A recent meta-analysis concluded that isometric exercise serves as an effective therapeutic intervention for managing KOA, demonstrating significant benefits in pain

reduction, physical function enhancement, and muscle strength improvement in affected individuals (Yang et al., 2024). In the same domain, eight-week isometric exercise program led to significant improvements in multiple subscales of the Knee injury and Osteoarthritis Outcome Score (KOOS)—including pain, symptoms, activities of daily living (ADL), sport and recreation (SR), and knee-related quality of life (KQoL)—among elderly women with early-stage KOA (Park et al., 2021). Similarly, HIRT resulted in complete pain reduction in 50% of subjects with KOA. However, among individuals with KOA, HIRT did not result in a significantly greater reduction in WOMAC knee pain compared to low-intensity strength training (Messier et al., 2021).

Evidence suggests that isometric training enhances the molecular weight and viscosity of hyaluronic acid (HA) within the joint fluid, thereby improving joint lubrication and contributing to pain relief. This form of exercise also supports joint cartilage protection and modulates inflammation by optimizing chondroitin sulfate concentration and regulating joint fluid pH (Miyaguchi et al., 2003). Furthermore, isometric training has been shown to significantly reduce inflammatory cytokines such as IL-6, TNF-α, CRP, and RSTN in individuals with KOA, indicating its effectiveness in mitigating inflammatory responses (Park et al., 2021). Isometric exercise also notably increases the density of the infrapatellar fat pad while decreasing tissue oxygenated and deoxygenated hemoglobin concentrations, thereby promoting better blood circulation and tissue oxygenation in individuals with KOA (Katayama et al., 2021).

The mechanisms underlying pain reduction through HIRT in individuals with KOA involve several physiological processes. One key mechanism is the exercise-induced release of neurotransmitters, such as endorphins, which function as natural analgesics and contribute to diminished pain perception. Additionally, resistance training has been linked to elevated levels of neurotrophic factors, notably brain-derived neurotrophic factor (BDNF), which is essential for neuroplasticity and modulation of pain sensitivity (Shin et al., 2016). Emerging research further indicates that regular HIRT sessions can significantly alter the concentrations of proinflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) (Church et al., 2016). Moreover, HIRT has been shown to substantially increase BDNF levels, reinforcing its role in neural adaptation and pain modulation (Church et al., 2016). These physiological changes are believed to be mediated by exercise-induced intracellular signaling pathways that influence the equilibrium between inflammatory and anti-inflammatory responses in the body (Pereira Nunes Pinto et al., 2017).

In clinical settings, effect size trends indicate that isotonic exercises may offer a slight advantage over isometric exercises in terms of therapeutic outcomes. However, each modality possesses distinct characteristics that inform their clinical application. Isometric exercises, characterized by static muscle contractions without changes in muscle length, impose minimal joint load, making them particularly appropriate for individuals in the acute phase of KOA or those with heightened joint pain sensitivity. Conversely, isotonic exercises, which involve dynamic joint movement, may be more suitable for patients with greater exercise tolerance and can facilitate progressive overload to optimize improvements in functional capacity (Yang et al., 2024). Considering the scarcity of comparative research, there is a need for more high-quality randomized controlled trials to assess the distinct therapeutic benefits of isometric and isotonic exercises. Future studies should also explore the effectiveness of integrated treatment approaches that combine both exercise modalities in the management of KOA.

The strengths of this study include its randomized controlled design, which adhered to rigorous methodological standards. Additionally, the exercise intervention was fully supervised, ensuring high participant adherence. One limitation of the study is the absence of a non-treatment control group, which raises the possibility that the observed symptomatic improvements may, in part, be attributed to the therapeutic setting or participants' expectations of benefit, rather than the exercise intervention per se. Regarding the assessment of muscle architecture, measurements were limited to the VL, which may not fully reflect the structural characteristics of the entire quadriceps muscle group. Moreover, given that the isometric training was conducted at only one knee joint position, it cannot be conclusively stated that the observed adaptations represent the optimal achievable outcomes. For ethical and medical reasons, participants continued their prescribed medication regimens and dosages throughout the study, which may have influenced or confounded the observed effects of the exercise intervention.

CONCLUSIONS

The findings of the present study demonstrated that HIRT is more effective than isometric training in improving quadriceps muscle strength and architecture among obese men with early KOA. Both HIRT and isometric training led to similarly significant improvements in knee pain and function. The findings indicate that either exercise regimen may be appropriately recommended for patients with early-stage KOA.

AUTHORS' CONTRIBUTIONS

Samah M. Ismail made the conception and design, data extraction, risk of bias assessment, and drafting of the manuscript.
Mohamed Salah El-Sayed made contributions to literature search and drafting of the manuscript
Ahmed S. Ahmed as the corresponding author, made substantial contributions to the conception and design of the study, literature search and interventional procedures.
Ahmad M. Osailan revised the whole manuscript content.
Waleed S. Mahmoud was responsible for statistical analyses and interventional procedures.
Mohammed M. Hegazy made equal contributions to literature search and interventional procedures.
Nadia L. Radwan made equal contributions to literature search and interventional procedures.
Mohamed A. Shendy made equal contributions to literature search and drafting of the manuscript

CONFLICTS OF INTEREST:

The authors have no conflicts of interest to report.

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