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Original Research Article

Acute and Adaptive Analgesic Effects of Passive Heat Therapy or High-Intensity Interval Exercise in Patients with Severe Lower-Limb Osteoarthritis: A Mixed-Methods Exploratory Study

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Abstract

Background: The purpose of the study was to examine the acute and adaptive analgesic effects of two separate therapies - hot-water immersion and upper-limb high-intensity interval exercise (HIIE) - in patients with severe lower-limb osteoarthritis. **Methods:** Eligible and consenting participants scheduled for hip or knee arthroplasty were randomized to hot-water immersion (Heat, *n*=27); 20-30 min immersed in 40°C water followed by ~15 min light resistance exercise) or upper-limb high-intensity interval exercise (HIIE, *n*=25; 6-8 x 60 s intervals on a cross-trainer or arm ergometer at ~100% peak $\dot{V}O_2$, 60-90 s recovery); all for 36 sessions (3 sessions per week for 12 weeks). Joint pain (0-10 scale; 0 = no pain, 10 = worst pain) and accelerometry were assessed during and following acute exposure and across the intervention. **Results:** Joint pain decreased by 3 arbitrary units (AU) and 2 AU during an acute exposure of heat therapy and HIIE ($p \le 0.035$); this acute analgesic effect was still evident in the final week of the intervention. These acute analgesic effects did not translate to reduced joint pain adaptively across the intervention (p=0.684), or improved daily step count in the 24-h following acute exposure (p=0.855) or across the intervention (p=0.604). **Conclusions:** The findings from this study highlight the acute analgesic effects of hot-water immersion and HIIE, and that patients with severe lower-limb osteoarthritis can participate in high-intensity upper-limb exercise, relatively pain free. **Significance:** This research reports several novel findings: 1) acute hot-water immersion has a potent analgesic effect in people with severe lower-limb osteoarthritis; 2) this acute effect is lost within one hour of exposure; 3) people with severe lower-limb osteoarthritis can perform cardiovascularly meaningful exercise via HIIE using predominantly the upper limbs, while decreasing joint pain; 4) reassuringly, the acute analgesic effect of hot-water immersion or HIIE persists across 12-wk of repeated exposure.

Key Words: Hot-Water Immersion, Joint Replacement, Osteoarthritis, Pain, Surgery, Upper-Limb Exercise.

Introduction

Osteoarthritis is a prevalent condition characterized by a breakdown of articular cartilage and subsequent joint degradation[1]. These pathological changes are associated with pain and dysfunction within the affected joint. The knee and hip are the two most common sites of osteoarthritis, with an estimated lifetime risk of developing symptomatic knee and hip osteoarthritis of 45% and 25% respectively[2, 3]. The disabling pain in these weight-bearing joints often means exercise is avoided and physical activity limited[4, 5]. This avoidance of exercise accelerates osteoarthritis progression and contributes to poorer general health, exacerbation of osteoarthritis-related pain and disability and the development of comorbid conditions[6].

Passive heat therapy (e.g., sauna: 80-100°C or spa bathing: ~40°C) is a contemporary area of research, inducing some acute cardiovascular and metabolic responses similar to exercise (e.g., increased heart rate, shear stress and core temperature)[7]. The non-impact nature of heat therapy makes it an appealing therapeutic option for patients with osteoarthritis. No research has directly looked at the effects of passive heat therapy on pain in osteoarthritis patients, however heat has exhibited pain-relieving benefits in other forms of arthritis, such as fibromyalgia, rheumatoid arthritis and ankylosing spondylitis[8, 9]. In response to heat stress, the sympathetic nervous system and hypothalamic-pituitary-adrenal axis are activated, triggering an increase in noradrenaline[10,11]. The consequential increase in neurohormonal and anti-inflammatory factors may account for some of the pleasure-inducing and analgesic effects of acute sauna exposure[10-14]; regular and ongoing exposure may improve these long term. Furthermore, either acute or longer-term reductions in pain may translate to increased physical activity levels, potentially slowing osteoarthritis progression and improving overall health.

Although acute exercise may transiently cause discomfort or pain, when performed regularly, aerobic exercise is an effective intervention for the long-term management of pain / immobility etc. associated with osteoarthritis[15]. Prolonged (>1 h) exercise activates opioid and non-opioid systems, increasing pain thresholds and decreasing pain sensitivity[16-20]. Similarly, exercise-induced hypoalgesia appears to have an intensity-related dose response, with higher-intensity exercise, even as short as 30 s of vigorous exercise, showing a larger effect than moderate-intensity exercise[21, 22]; however, the mechanisms modulating exercise-induced hypoalgesia remain equivocal[16]. A time efficient and effective alternative for patients with limiting lower-limb pain and function may be to utilize high-intensity interval exercise incorporating the upper limbs. To our knowledge, no study has investigated the acute or adaptive analgesic effects of upper-limb high-intensity interval exercise in people with osteoarthritis.

The purpose of the study was to examine the acute analgesic effect of two separate therapies - hot-water immersion and upper-limb high-intensity interval exercise (HIIE) - in patients with severe lower-limb osteoarthritis. Secondary objectives were to: i) assess if any acute analgesic effect, if present, was different across 12 weeks of regular exposure, ii) determine if regular exposure translates to an adaptive analgesic effect, iii) explore inflammatory markers associated with adaptive pain relief and iv) characterize the impact of pain relief on daily physical activity. We hypothesized that both hot-water immersion and HIIE would decrease pain across an acute session and that this effect would persist across the 12-week intervention.

Methods

Ethical Approval

Ethical approval for the study was obtained from the Health and Disability Ethics Committee of New Zealand (Ref: 18/NTA/148) and the study was prospectively registered with the Australia New Zealand Clinical Trial Registry (ACTRN12618001358235). Written, informed consent was obtained for all participants, and all procedures conformed to the standards set by the Declaration of Helsinki.

Experimental Design

The design presented here consists of two exploratory analyses from a previously reported randomized controlled trial (see Figure 1)[23]. The trial compared hot-water immersion (Heat, with light calisthenics) with upper-limb HIIE and a control group (Home; not included in the studies presented here) in patients with severe lower-limb osteoarthritis. Study one examined the acute analgesic effect of Heat or HIIE *during* exposure; secondary goals were to compare the adaptive effects of these therapies on joint pain, inflammatory cytokines and physical activity across a 12-week intervention. Study two was conceived after recruitment for study one had commenced, following large analgesic effects being reported. The purpose of study two was to quantify the duration of any analgesic effect, *following* acute exposure. Secondary goals were to assess if any beneficial analgesic effect translated to altered physical activity and to examine whether any analgesic effect was different in week three when exposure duration had increased from week one (i.e., Heat 20 vs. 30 min; HIIE – 6 vs. 8 intervals).

Eligible and consenting participants underwent an initial baseline assessment prior to randomization (detailed below). Participants randomized to Heat or HIIE attended an initial session where physiological and psychophysical (including pain) measures were collected to characterize responses to an acute exposure (Figure 1); this was repeated in the third (study two only) and final weeks of the intervention. Participants then attended three sessions per week, for up to 12 weeks, to assess the adaptive responses to these therapies. Upon completion of the intervention, pre-intervention measurements were repeated.

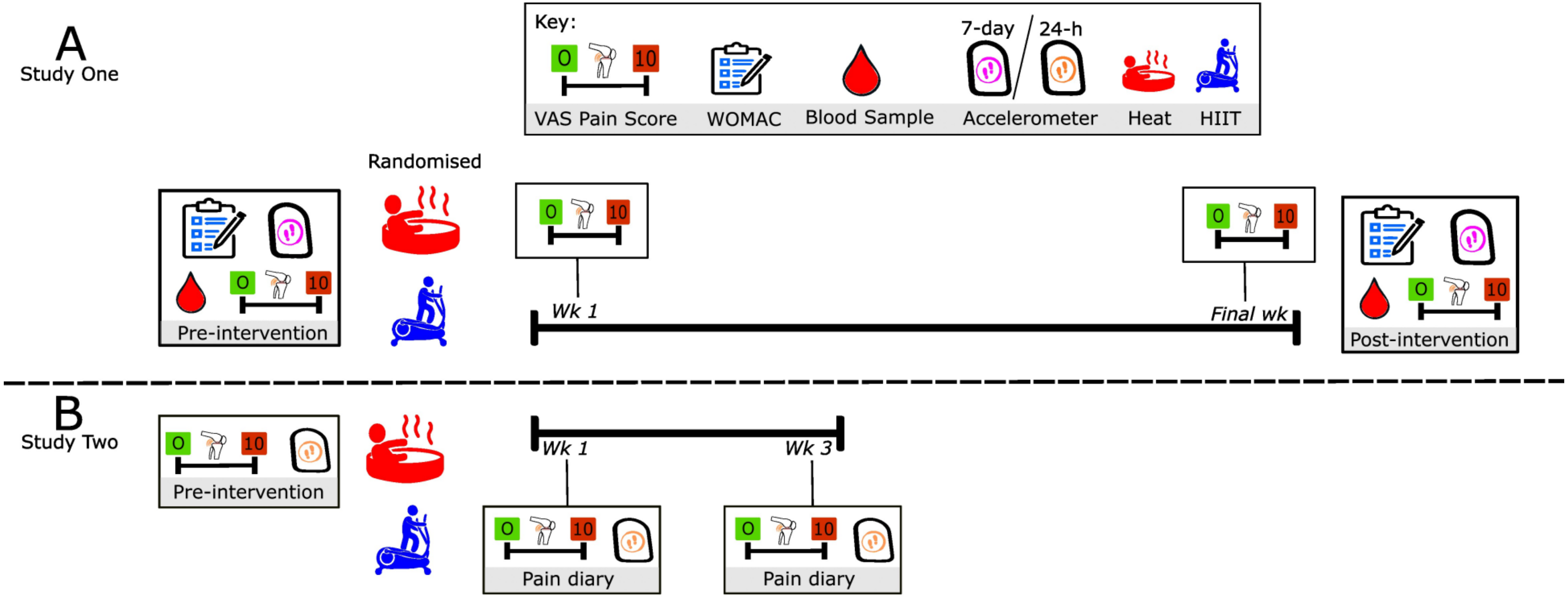

Figure 1. A) Study one - Schematic representation of acute (week one and final week; Heat (n=27) and HIIE (n=25) only) and adaptive (pre-intervention and post-intervention) experimental measures. B) Study two: A subset of participants (Heat n=18; HIIE n=13) completed an extended pain diary pre-intervention and following a session in week 1 and 3, where joint pain was rated during an exposure, then every hour for the first three hours post-exposure and three-hourly thereafter; joint pain was also recorded immediately prior to an overnight sleep, upon waking and one-hour post-waking. Heat = hot-water immersion / passive heat therapy; HIIE = high-intensity interval exercise; VAS = visual analogue scale; WOMAC = Western Ontario and McMaster Universities Arthritis Index. * = acute exposure not assessed.

Study participants

Patients with end-stage hip or knee osteoarthritis who were scheduled for total hip / knee arthroplasty within the next 12 months at Dunedin Public Hospital (Dunedin, New Zealand) were recruited for this study. Participants were excluded if they met any of the following criteria of the primary study[23]: 1) a contraindication to non-physician supervised maximal exercise testing[24]; 2) stable or unstable angina; 3) a recent myocardial infarction (i.e., < 3 months); 4) an implantable cardioverter defibrillator and/or pacemaker; 5) revision arthroplasty; 6) staged bilateral total joint replacement; 7) pathology limiting upper-limb exercise (i.e., shoulder-joint osteoarthritis); and 8) any other medical condition deemed a significant risk to study participation.

Interventions

The interventions are outlined below; please refer to supplementary material for full reporting of the interventions, per Template for Intervention Description and Replication (TIDieR) criteria.

Hot-water immersion (Heat)

Participants were seated for 20 min with water approximately mid-sternal level in a temperature-controlled spa (~40 °C). At the end of hot-water immersion, participants exited the spa, dried themselves and performed light-intensity resistance exercise (calisthenics). Calisthenics consisted of 10 upper- and lower-body exercises with a resistance band, progressing to 12-20 reps of each[25].

To assess adaptive responses, participants completed three hot-water immersion sessions per week, for 12 weeks (or less if surgery scheduled prior), with bathing duration progressively increasing from 20 to 30 min within 2-3 weeks, as tolerable[26].

High-intensity interval exercise (HIIE)

Exercise was performed on either an elliptical cross-trainer (NordicTrack e12.2, Utah, USA) or arm ergometer (Schwinn Windjammer, Washington, USA) (modality choice dependent on participant tolerance/preference). Participants performed 6 x 60-s intervals, separated by 90-s active recovery (very-light intensity). Exercise intensity was individualized aiming to ensure a rating of perceived exertion of 7/10 (very hard[27]; but less than 90% heart rate reserve) was achieved and maintained across the session.

To assess adaptive responses, participants completed three HIIE sessions per week, for 12 weeks. The number of intervals increased to 8, and recovery duration decreased to 60 s; the duration of exercise intervals remained constant throughout the intervention.

Measures - Study one

Acute

To quantify any beneficial effect of acute exposure on joint pain, participants used the visual analogue pain scale[28] to rate the pain in their operative joint, using a 10-point scale (0 = no pain, 10 = worst pain). Joint pain was recorded pre-exposure, during exposure and immediately post-exposure. Cardiovascular indices (i.e., blood pressure, heart rate), core temperature and thermal perceptions were measured across each session and have been reported elsewhere[29].

Adaptive

Joint pain ratings were repeated during a regular scheduled session in the final week of the intervention to assess if there was an enhanced or diminished analgesic effect with regular repetition.

Accelerometers (activPAL3c, Glasgow, Scotland) were worn to characterize physical activity levels in the 24 h following an acute exposure to explore any relationship between pain reduction and increased physical activity. Further, all participants wore an accelerometer for seven days prior to and after the intervention, to provide an estimate of habitual daily physical activity.

Venous blood samples were collected prior to and at the end of the intervention to explore the relationship between pro- and anti-inflammatory alterations and adaptive changes in pain. Samples were obtained via venipuncture, which was performed by an experienced phlebotomist. Samples were centrifuged at 3000 rpm for 10 min at 4 °C and the plasma frozen (-80°C) and stored for batch analysis. Enzyme-linked immunosorbent assay kits (ELISA) were used to quantify levels of inflammatory cytokines in plasma (interleukin-1 beta (IL-1β; R&D Systems Human IL-1β/IL-1F2 Quantikine HS ELISA kit), interleukin-10 (IL-10; R&D Systems Human IL-10 Quantikine HS ELISA kit) and tumor necrosis factor-alpha (TNF-α; &D Systems Human TNF-alpha Quantikine HS ELISA kit)). C-reactive protein (CRP) was measured using a particle-enhanced immunoturbidimetric assay (Roche CRP4 Tina-quant C-Reactive Protein IV).

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[30] questionnaires were completed to quantify any adaptive effect of the intervention on osteoarthritis impact. Perceptions of the intervention were assessed using a custom-designed questionnaire, using a five-point Likert scale (1 – strongly disagree, 5 – strongly agree; Supplementary material). Participants were also invited to document "the most challenging part of the training" and "best part of the training" on the form using free text. Throughout the intervention participants provided unprompted anecdotes about the effect of their therapy; these were transcribed verbatim and later analyzed using thematic analysis.

Measures - Study two

A subset of participants (Heat *n*=18; HIIE *n*=13) completed an additional session in week one and three to assess the durability of any acute analgesic effect. Joint pain was rated during an exposure (as above), then every hour for the first three hours post-exposure and three-hourly thereafter, plus immediately prior to overnight sleep, upon waking and for one-hour post-waking. Pain ratings were also collected in this subset during a separate session (no Heat or HIIE exposure) prior to entering the intervention study.

Statistical analyses

Statistical analysis was performed using SPSS (v27, IBM, New York, USA) and graphed using Prism (v8.0, GraphPad, San Diego, USA). Descriptive data were expressed as raw mean (± SD), median (IQR) or number (proportion). Ordinal data were analyzed using Kruskal-Wallis and Friedman Tests, with Wilcoxon signed rank tests used to isolate differences for the latter. A mixed model analysis of covariance (ANCOVA) using number of intervention sessions as the covariate was used to test for significant between-group differences in accelerometry, blood and WOMAC data. A Bonferroni adjustment was performed to account for multiple comparisons. A significance level of 0.05 was used for all tests. All qualitative data were independently coded, analyzed and categorized using agreed theme labels using a six-step process outlined by Braun et al.[31].

Results

Study one

Participant characteristics

Twenty-seven (Heat) and twenty-five (HIIE) participants (Table 1) completed study one, including acute assessment sessions (week one & final week) and the adaptive investigation (intervention). Heat and HIIE participants completed a similar number of sessions (36 ± 11 and, 33 ± 11, respectively). Of the HIIE participants, 9 completed training on the cross-trainer and 16 on the arm ergometer.

Acute effects

Joint Pain

Immediately upon sitting in the pool, joint pain consistently resolved in 24 of the 27 participants. In week one, pain decreased by 3 arbitrary units (AU) at 10 min during hot-water immersion and remained lower than pre-session throughout the session ($p < 0.001$; **Error! Reference source not found.**). Similarly, during HIIE, pain decreased by 2 AU across a session, and immediately post-exposure was lower than pre-session levels ($p = 0.035$;Figure 3).

Adaptive effects

Joint Pain

Acute analgesic responses persisted during the final week of the Heat and HIIE interventions ($p \leq 0.002$; Figure 2 & Figure 3). The magnitude of acute reductions in pain were not different at any measured time points for Heat ($p \geq 0.215$) or HIIE ($p \geq 0.285$). Neither the overall score ($p = 0.915$) or the pain sub-scale ($p = 0.684$) on the WOMAC questionnaire changed between pre-intervention and post-intervention assessment, for any group (Table 2).

Table 1. Descriptive statistics of participants.

Variable	**Heat (*n*=27)**	**HIIE (*n*=25)**
Age (y)	66 (7)	71 (9)
Male/female	13 (48%) / 14 (52%)	13 (52%) / 12 (48%)
BMI (kg·m^{-2})	31.6 (6.6)	32.2 (5.3)
Ethnicity		
NZ European / European	26 (96%)	24 (96%)
Māori	0	2 (8%)
Cook Island Māori	1 (4%)	0
Arthroplasty site		
Hip	11 (41%)	11 (44%)
Knee	16 (59%)	14 (56%)
Comorbidity		
Asthma / COPD	7 (26%)	5 (20%)
CVD		
Previous myocardial infarct	5 (19%)	3 (12%)
Atrial arrhythmia	0	1 (4%)
Previous stroke	3 (11%)	1 (4%)
Dyslipidaemia	13 (48%)	11 (44%)
Hypertension	18 (67%)	17 (68%)
Obesity	15 (56%)	12 (48%)
Diabetes mellitus / pre-diabetes	8 (30%)	4 (16%)
Pain medications		
NSAID	13 (48%)	14 (56%)
Paracetamol	19 (70%)	19 (76%)
Tramadol	4 (15%)	3 (12%)
Codeine	3 (11%)	7 (28%)
Paracetamol + codeine	2 (7%)	3 (12%)
Morphine	2 (7%)	0
Fentanyl patch	0	1 (4%)
Amitriptyline	0	5 (20%)
Gabapentin	0	1 (4%)
Reported PA status		
No physical activity	11 (41%)	10 (40%)
Active, but not meeting PA guidelines	5 (19%)	5 (20%)
Meeting PA guidelines	11 (41%)	10 (40%)

Data are mean (SD), median (IQR) or as an absolute number with the percentage (%) of the whole. ASA = American Society of Anesthesiologists; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; NSAID = non-steroidal anti-inflammatory; PA = physical activity.

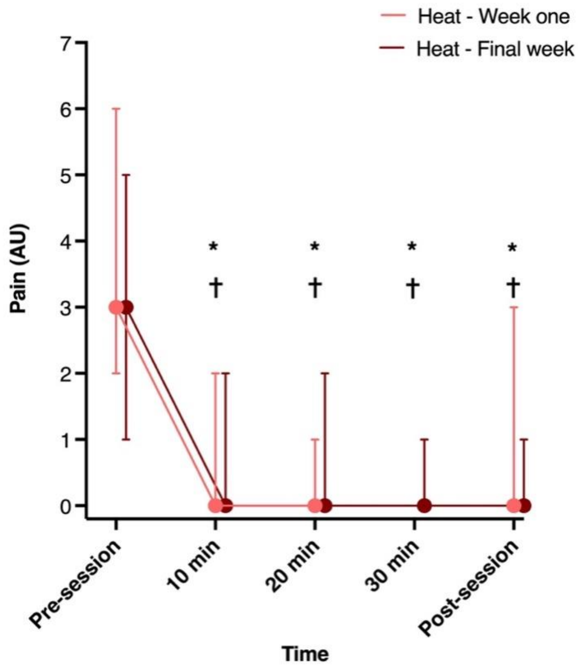

Figure 2. Pre-session, during and post-session pain scores during week one (20 min exposure) and final week of the Heat intervention (30 min exposure). Data are median (error bars indicate IQR) and were analyzed using Friedman tests. 0 = no pain, 10 = worst pain. * = p < 0.05 vs. baseline (week one); † = p < 0.05 vs. baseline (final week of intervention); *n*=27.

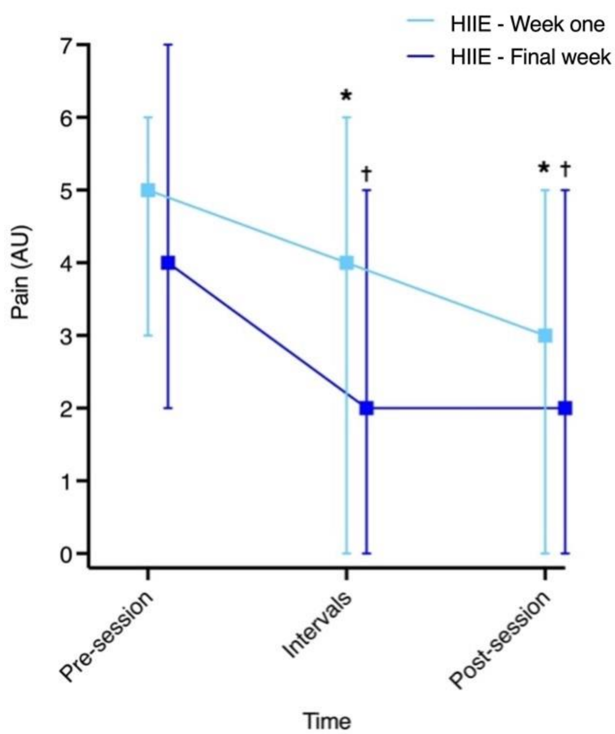

Figure 3. Pre-session, during and post-session pain scores during week one (6 intervals) and the final week (8 intervals) of the HIIE intervention. Data are median (error bars indicate IQR) and were analyzed using Friedman tests. 0 = no pain, 10 = worst pain. * = p < 0.05 vs. baseline (week one); † = p < 0.05 vs. baseline (final week of intervention); *n*=25.

Table 2. Osteoarthritis impact pre- and post-intervention for Heat and HIIE groups.

Variable	Heat (*n*=27)		HIIE (*n*=25)		Statistical significance		
	PRE	POST	PRE	POST	Group	Time	Interaction
WOMAC							
Overall score	54 (14)	52 (22)	58 (16)	60 (16)	0.421	0.710	0.915
Pain	11 (3)	11 (5)	11 (3)	12 (3)	0.906	0.455	0.684
Stiffness	5 (1)	5 (2)	5 (2)	5 (2)	0.276	0.654	0.432
Physical function	38 (10)	37 (16)	41 (12)	42 (12)	0.219	0.981	0.436

Data presented as mean (SD) and analyzed with a mixed-model ANCOVA. * $p < 0.05$ vs. PRE. PRE = pre-intervention; POST = post-intervention; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index (0 best – 94 worst).

Physical activity

There were no differences in any physical activity measures across the intervention (Table 3).

Inflammatory factors

No interaction effects were observed for any pro- or anti-inflammatory blood marker ($p \geq 0.250$; Table 4. An exploratory sub-analysis of HIIE participants, based on ergometer modality (i.e., arm ergometer vs. cross trainer) also showed no differences across the intervention ($p \geq 0.383$).

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Table 3. Pre-intervention and post-intervention daily physical activity data in Heat and HIIE groups.

Variable	Heat (n=27)		HIIE (n=25)		Statistical significance		
	PRE	POST	PRE	POST	Group	Time	Interaction
Total steps (n)	6436 (3135)	6303 (3246)	5299 (2031)	5466 (2265)	0.178	0.953	0.601
Time spent upright (min)	317 (124)	308 (130)	314 (118)	311 (117)	0.998	0.635	0.824
Time spent stepping (min)	86 (37)	86 (39)	73 (26)	77 (30)	0.211	0.655	0.536
Time spent sitting (min)	612 (190)	607 (118)	579 (113)	592 (136)	0.523	0.766	0.548
Sit-to-stand transitions (reps)	38 (10)	37 (10)	36 (10)	37 (10)	0.740	0.852	0.612
Sitting bouts >30 min (reps)	6 (4)	5 (2)	5 (2)	5 (2)	0.250	0.589	0.230
Sitting bouts >60 min (reps)	2 (1)	2 (1)	2 (1)	2 (1)	0.679	0.786	0.786
Time spent in sitting bouts > 30 min (min)	358 (185)	345 (120)	328 (133)	341 (150)	0.665	0.994	0.428

Data collected over a 7-d period and presented as daily mean (SD) and analyzed with a mixed-model ANCOVA. PRE = pre-intervention; POST = post-intervention.

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Table 4. Plasma pro-inflammatory and anti-inflammatory factors pre- and post-intervention in Heat and HIIE groups.

Variable	Heat (n=27)		HIIE (n=25)		Statistical significance		
	PRE	POST	PRE	POST	Group	Time	Interaction
CRP (mg/L)	2.7 (1.9)	2.6 (2.6)	3.6 (4.8)	3.6 (3.1)	0.332	0.066	0.714
IL-1β (pg/mL)	0.3 (0.2)	0.3 (0.2)	0.3 (0.2)	0.2 (0.2)	0.577	0.937	0.410
IL-10 (pg/mL)	0.3 (0.2)	0.2 (0.2)	0.2 (0.2)	0.2 (0.1)	0.360	0.081	0.849
TNF-α (pg/mL)	1.2 (0.6)	1.2 (0.6)	1.4 (0.6)	1.4 (0.6)	0.177	0.179	0.798

Data are presented as daily mean (SD) and analyzed with a mixed model ANCOVA. CRP = C-reactive protein; IL-1β = interleukin-1 beta; IL-10 = interleukin-10; PRE = pre-intervention; POST = post-intervention; TNF-α = tumor necrosis factor-alpha.

Study two

Eighteen (Heat) and thirteen (HIIE) participants volunteered for study two, completing the post-exposure pain diary and 24-h accelerometry, pre-intervention (baseline), week one and week three.

Joint pain

Acute analgesic responses persisted during the third week of the Heat and HIIE interventions ($p \leq 0.002$; Figure 4 and **Error! Reference source not found.**). However, pain was not significantly different from pre-session at 1-h post-session (Heat: $p = 0.248$; HIIE: $p = 0.452$) or thereafter ($p \geq 0.285$) for either intervention.

Physical activity

Physical activity in the 24 h following an acute Heat or HIIE session in week one and week three was not different to baseline (**Error! Reference source not found.**).

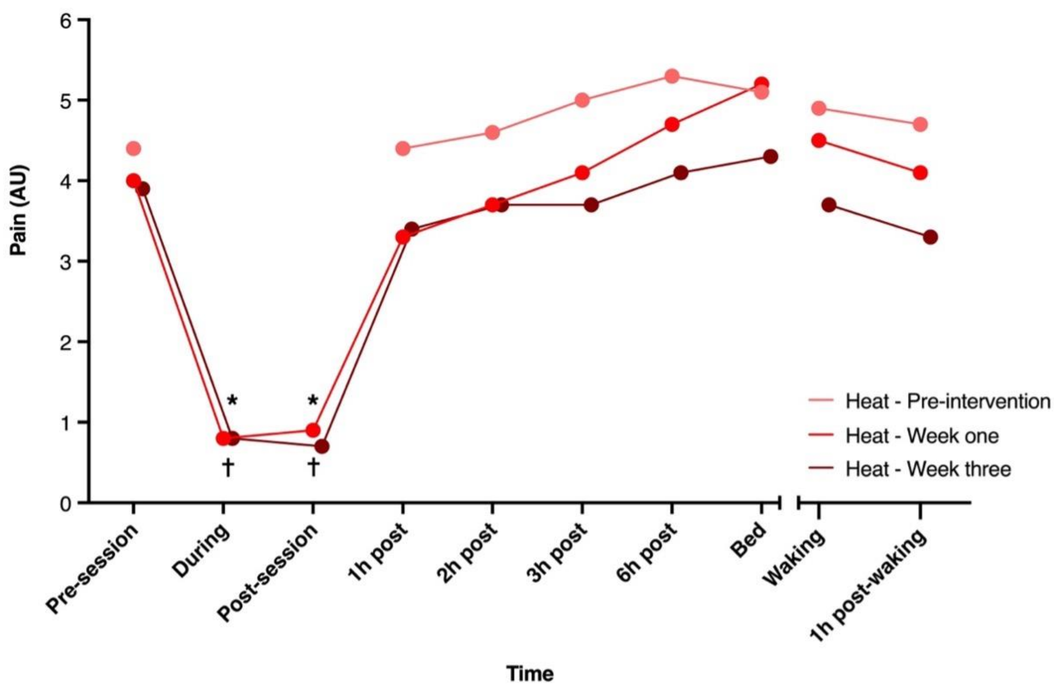

Figure 4. Joint pain during and following an acute session of hot-water immersion at pre-intervention, week one and week three. Data are presented as mean for illustrative purposes but were analyzed as median using Friedman and Kruskal Wallis tests. 0 = no pain, 10 = worst pain. * $p < 0.05$ vs. baseline in week one; † $p < 0.05$ vs. baseline in week three; n=18.

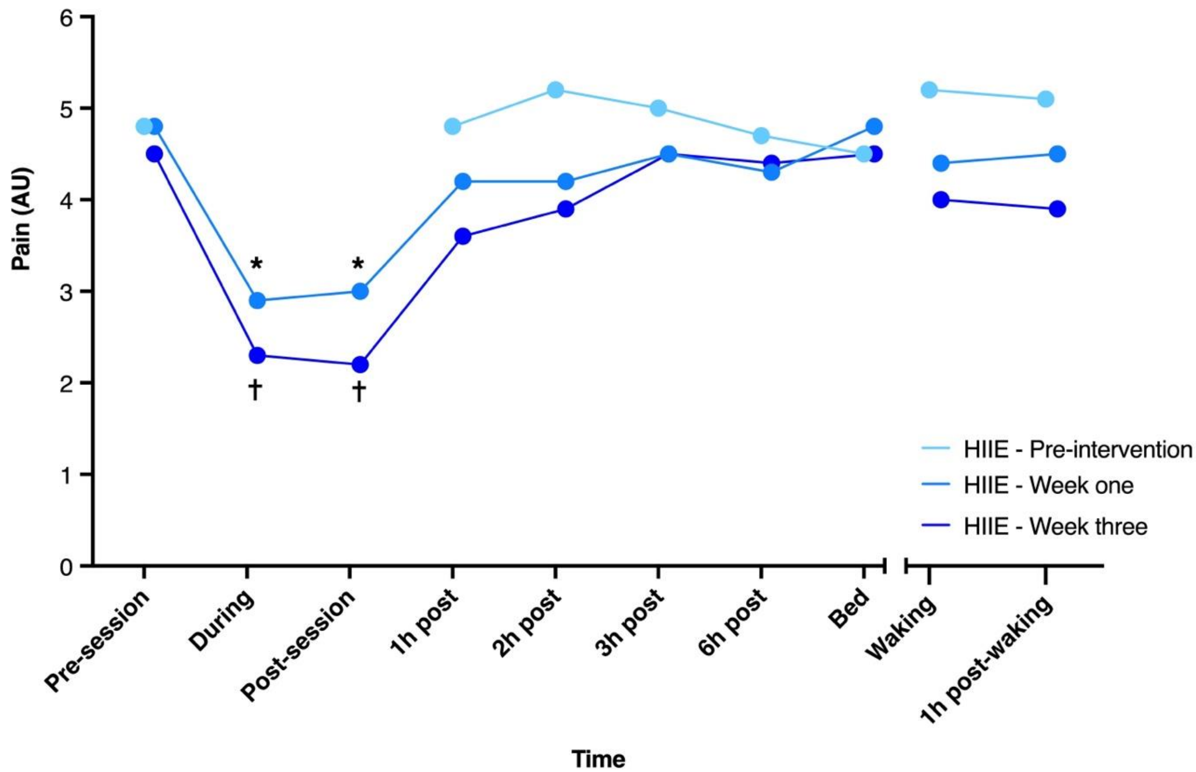

Figure 5. Joint pain during and following an acute session of high-intensity interval exercise at pre-intervention, week one and week three. Data are presented as mean for illustrative purposes but were analyzed as median using Friedman and Kruskal Wallis tests. 0 = no pain, 10 = worst pain. * = $p < 0.05$ vs. baseline in week one; † = $p < 0.05$ vs. baseline in week three; n=13.

Table 5. Baseline and week one and week three post-exposure 24-h physical activity data in a sub-group of Heat and HIIE participants.

Variable	Heat (n=18)			HIIE (n=13)			Statistical significance		
	Baseline	Week 1	Week 3	Baseline	Week 1	Week 3	Group	Time	Interaction
Total steps (n)	6349 (3019)	6327 (2642)	6130 (3471)	4898 (1765)	4439 (1939)	4401 (2115)	0.062	0.744	0.855
Time spent upright (min)	293 (92)	313 (115)	312 (138)	281 (85)	286 (110)	247 (122)	0.347	0.550	0.936
Time spent stepping (min)	85 (36)	87 (37)	85 (45)	68 (21)	61 (25)	61 (28)	0.058	0.763	0.655
Time spent sitting (min)‡	614 (128)	617 (135)	597 (94)	588 (82)	631 (107)	596 (147)	0.934	0.619	0.833
Sit-to-stand transitions (reps)	37 (10)	39 (13)	41 (10)	35 (11)	34 (11)	29 (12)*	0.81	0.700	**0.037**
Time spent in sitting bouts > 30 min (min)‡	367 (130)	365 (159)	300 (82)	328 (95)	377 (101)	381 (140)	0.480	0.650	0.303

Data collected over a 24-h period and presented as mean (SD) and analyzed with a mixed-model ACNOVA. ‡ = analyzed using log transformed data. * p < 0.05 vs. Heat - Week 3.

Participants' experiences of participating

There were no differences between groups for any perceptions (Table 6). Heat and HIIE participants on average "strongly agreed" that the intervention improved their fitness, was enjoyable and they would perform the intervention again. Heat participants on average "agreed" that it reduced joint pain, improved joint mobility, energy levels and mood. Participants who performed HIIE on average "agreed" that everyday activity was increased, and mood and energy levels were improved; on average, they "strongly disagreed" that the intervention was a significant time burden, and the physical strain associated with HIIE interfered with other aspects of life.

Results from anecdotal experiences and written feedback are presented as one overarching theme (joint pain), with five related sub-themes. The sub-themes relating to the effect of Heat or HIIE were becoming pain-free upon exposure, improved sleep, analgesia lasting after the session, requiring less medication and noticing effects when they missed a session.

Becoming pain free immediately upon entry to the hot water was a common finding across Heat participants. *"The pain disappears immediately, [as] soon as I sit down in the water, I can't feel a thing in my knee. When I'm in the pool, it's the only part of my day where I am pain free" (P3, Heat, Anecdote); "It's great being able to spend 3 hours a week with no pain, or very low pain during the spa and doing the exercises" (P4, Heat, Anecdote).* Participants in the HIIE group also commented on their pain relief. *"I needed a crutch because of the pain to walk in from the car, but I can walk out without it after a session. Sometimes I leave and [I] have forgotten my crutch!" (P14, HIIE, Anecdote).* "*The most painful part of the training is the walk from the car to the gym to start the session. The exercise itself and when I am done is fine, no pain at all" (P15, HIIE, Anecdote).*

Several participants reported that they noticed a difference when they missed a session or they went a few days without the heat (i.e., over a weekend). *"It makes such a difference; you know when you don't do it" (P4, Heat, Anecdote); "I didn't go last week and the day after my session should have been, my hip was really sore. I thought to myself, this [Heat] must be really doing something" (P5, Heat, Anecdote)*. One participant who had completed the intervention but was still awaiting surgery commented in their feedback form *"I purchased a spa and it's being delivered today. I didn't realise how much the heat helped with the pain until I stopped" (P6, Heat, Feedback questionnaire).*

Improved sleep was another benefit reported by many of the participants. *"I am definitely sleeping better. Last night I slept for at least 4 hours before waking, it used to be only 1-to-2 hrs. I also don't need to sleep with a pillow between my knees anymore" (P3, Heat, Anecdote); "The day after the first spa was the best my joint had felt in years. I*

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had a great sleep too" (P7, Heat, Anecdote); "I used to wake up in the middle of the night with pain, but that rarely happens now" (P17, HIIE, Anecdote).

Being able to do more in everyday life and improved function was another common theme, particularly among Heat participants. *"People at work are noticing how fitter and more able I am; I'm able to do a lot more. I can now walk up the stairs at work; before starting this I didn't use to be able to do that" (P8, Heat, Anecdote); "Monday was the first time in months I have been able to fully straighten my leg"; "The day after a spa I find it a lot easier to get out of bed"; "My joint feels a lot freer and I don't have to move it to try get it going for the day" (P7, Heat, Anecdote); "People ask me have I had my surgery as I am walking and moving so much better" (P9, Heat, Anecdote); "I am moving a lot better and others have noticed this too. I am able to get a lot more done and do more with the day" (P10, Heat, Anecdote).*

A reduced need for analgesic medication was reported by several Heat participants. *"Thursday, Friday and Saturday last week were the first days in a long time where I haven't needed painkillers" (P7, Heat, Anecdote); "Usually I'd take morphine at 1030am, but I didn't need it till 230pm in the afternoon after the first session" (P8, Heat, Anecdote).*

Table 6: Intervention perceptions in Heat and HIIE groups, as rated on a 1-5 Likert scale.

Question	Heat (n=27)	HIIE (n=25)	p-value
This has been an enjoyable experience	5 (5, 5)*	5 (4, 5)*	0.761
This has decreased my joint pain	4 (3, 5)*	3 (2, 4)	0.078
This has increased my joint mobility	4 (3, 4)*	3 (2, 4)	0.162
This has been a significant time burden	2 (1, 4)	1 (1, 3)	0.948
I would recommend this to my friends	5 (5, 5)*	5 (4, 5)	0.377
I would perform the same regimen again	5 (5, 5)	5 (4, 5)	0.699
I believe it has improved my fitness	5 (4, 5)*	5 (4, 5)*	0.556
This study has interfered with other aspects of my life:			
Due to the time commitment	1.5 (1, 2)	1 (1, 3)	0.563
Due to the physical strain	1 (1, 2)	1 (1, 3)	0.604
This has increased my mood	4 (3, 5)*	4 (3, 5)	0.690
I increased my everyday activity after this	3 (3, 5)*	4 (3, 4)*	0.859
I spent less time sitting after this	3 (2, 4)	3 (3, 5)	0.983
This has been more physically demanding than I expected	2 (1, 3)	3 (1, 4)	0.420
This has improved my sleep	3 (1, 4)	3 (2, 4)*	0.833
This has improved my energy levels	4 (2, 4)*	4 (3, 4)*	0.790

Data presented as median (IQR) and analyzed using Mann-Whitney U tests.; 1 – strongly disagree; 5 – strongly agree.

Discussion

An acute exposure of heat therapy or HIIE decreased joint pain in patients with severe hip or knee osteoarthritis for the duration of the session. Although this effect was generally lost within one hour of exposure, the *acute* analgesic effect of a single session of heat therapy or HIIE was still evident in the final week of the intervention period. Unfortunately, any analgesic effects did not translate to improved physical activity levels in the 24-h following acute exposure or across the intervention. Qualitative analysis revealed that heat therapy had a positive effect on joint pain, with participants describing the pain disappearing during immersion, and improved physical function and sleep. The findings from this study highlight the analgesic effects of acute hot-water immersion and HIIE, and that patients with severe lower-limb osteoarthritis can participate in high-intensity exercise utilizing the upper limbs, relatively pain free.

Joint pain

The almost-universal acute analgesic effect (resolution of pain whilst in the hot water) upon exposure was still evident in the final week of the intervention, but on average was lost within 1 h post-immersion. Similarly, HIIE had an acute analgesic effect during exposure, and this persisted across the intervention; however, within 1 h post-exercise joint pain was not different from pre-exercise levels. Despite these consistent improvements in joint pain during an acute exposure, joint pain was not different between pre- and post-intervention assessments for either group (i.e., no adaptive effect).

A lack of previous data on heat therapy and hot-water immersion in osteoarthritis cohorts makes it difficult to put the current findings in context. Matsumoto et al.[8] showed reduced pain in a fibromyalgia cohort following 12 weeks of combined sauna and underwater exercise. Pain assessed using the visual analogue scale reduced from 7.5 ± 1.3 to 3.1 ± 1.1 ($p < 0.001$) and remained so 6 months after the intervention (3.7 ± 0.9, $p < 0.001$). Four weeks of sauna reduced pain by 40% and 60% in patients with rheumatoid arthritis and ankylosing spondylosis, whilst not exacerbating the disease[9]. It is likely that the severity of the osteoarthritis in the current cohort contributed to this lack of change across the intervention. Participants in the current study on average were categorized as having "severe" osteoarthritis (i.e., WOMAC score ≥39)[32]. With respect to exercise, large improvements (~-12 AU and ~-15 AU) in WOMAC score with HIIE interventions in patients with knee osteoarthritis have been reported, albeit in participants less affected by osteoarthritis at baseline (WOMAC score ~32-36)[33, 34]. Interventions delivered earlier in the disease process may have had more favorable long-term pain outcomes.

The lack of change in chronic pain is supported by there being no consistent improvement in any of the analyzed pro- or anti-inflammatory cytokines. Acute passive heat exposure triggers an increase in IL-6 in sedentary and overweight adults, not dissimilar to acute exercise[13]. The post-exercise elevation in IL-6 mediates an anti-inflammatory response that may also facilitate pain modulation[14]. We did not assess inflammatory markers during or immediately post-exposure (when join pain was decreased). It is plausible any inflammatory effects are the product of an acute exposure (rather than cumulative following repeated exposures) and are lost within hours. Additionally, other mediators may be contributing than those measured in this study. For example, acute heat stress increases beta-endorphins, potentially accounting for some of the pleasure and analgesic effect of sauna[10-12]. A direct link between these mechanisms and pain modulation is yet to be shown, however future work should assess inflammatory and other humoral markers during or immediately following exposure in patients with osteoarthritis. Improvements in acute pain were eroded within 1 h of exposure and did not translate to improved activity in week one and three. In fact, in week three, there was a trend for HIIE participants to spend more time sitting, and compared to Heat participants they performed 12 fewer sit-to-stand transitions in the 24 h succeeding an acute session. Behavior change initiatives are likely necessary to increase physical activity, despite improvements in joint pain[35].

Acceptability questionnaire

The validated questionnaire (WOMAC) in this study has been used extensively in research; however, its feasibility for detecting changes in pain and other subjective aspects of health and life may not be appropriate in this research setting or cohort of patients with severe disease. Although unvalidated, the acceptability questionnaire provided more specific insight on subjective outcomes. Participants in the Heat group experienced reduced joint pain and increased joint mobility, felt fitter and had improved mood. A commonly reported benefit of participating in regular exercise is increased positive-activated affect, or the feeling of having more energy[36]; participants from the HIIE intervention reported an increase in perceived energy levels across the intervention, as did the Heat group. Whilst physiological alterations likely contribute to this positive-activated affect[37], many HIIE and Heat participants anecdotally commented that they were able to sleep better and for longer at night, without waking due to pain and this may have also influenced perceived mood and energy levels.

Thematic analysis

In contrast to the quantitative analysis, many participants reported an analgesic effect persisting after exposure to Heat or HIIE; this also contrasts with traditional forms of exercise that generally exacerbate joint pain[38]. Moreover, Heat participants noticed the effects when they missed a scheduled session. Although the severity of the osteoarthritis likely contributed to the lack of improvement in joint pain across the intervention, some participants reported they didn’t require any or as much pharmaceutical analgesia in the hours after a session; this was even reported in participants with severe disease requiring opioid analgesics such as morphine.

Decreased joint pain appeared to translate to other aspects of participants’ everyday life, although this finding wasn't supported by the quantitative measures presented here. For example, participants had noticed improvements in their ability to do their daily work, with some commenting that others (i.e., colleagues) had noticed improvements. Participants also reported they often didn't require their walking aid for the rest of the day following a Heat or HIIE session.

Insomnia is reported in more than 80% of patients with osteoarthritis[39]. Reassuringly, improved sleep was another commonly reported benefit for both Heat and HIIE participants. The mechanisms contributing to improved sleep are likely multi-factorial; although improved joint pain possibly contributed. Previous exercise studies have reported improved central nervous system activity, cardiac and autonomic function and mood as contributors[40]. The improvement in sleep likely confers other positive health benefits, not least improved clinical outcomes when patients eventually undergo arthroplasty[41].

Limitations

Due to the non-structured collection of participant anecdotes, it is likely that recall bias is present. It also relied on participants being forthcoming with their experiences, which may not be representative of all participants nor the study population. Furthermore, the data only captures the views of those who participated; data may not represent those who declined study participation or did not meet the eligibility criteria. It should also be acknowledged that some of the qualitative findings were not supported by quantitative findings (e.g., some participants reporting the analgesic effect lasting for hours after exposure, despite the data from participants joint pain diaries not supporting this statistically). Although Heat participants spent most of each session performing hot-water immersion, and the analgesic effect occurred during immersion, participants also performed light calisthenics, and this may have influenced post-session and adaptive responses. Study two was conceived as an exploratory add-on study, therefore sample size was less than study one and likely underpowered. Additionally, the post-exposure joint pain diary was performed at home therefore we cannot guarantee each rating was performed at the specified time point. In the rare instance where a participant missed a response, a researcher immediately prompted the participant to recall the activity at that time point and to rate their pain; this likely introduced recall bias, but due to the rarity of occurrence, unlikely influenced overall results.

Conclusion

An acute exposure of heat therapy or HIIE incorporating the upper limbs was effective for reducing joint pain during the exposure in patients with severe lower-limb osteoarthritis; this acute analgesic effect during exposure persisted across the 12-week intervention. Furthermore, patients with severe lower-limb osteoarthritis were able to participate in high-intensity exercise, relatively pain free; and importantly, pain decreased across an acute exposure. Future research is needed to identify potential mediators contributing to this acute analgesia. Unfortunately, acute reductions in joint pain were short lived (lost within 1 h of exposure) and no adaptive effect on chronic pain or changes in physical activity were observed with either intervention.

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Author contributions
Study conception and design: BR, DGJ, JC & KT. *Data collection, analysis and interpretation*: BR, HC, RG, JC & KT. *Drafting of original manuscript*: BR & KT. *Critical revisions of the work for important intellectual content*: BR, JC, HC, UR, DGJ, RG & KT. *Final approval*: BR, JC, HC, UR, DGJ, RG & KT.

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References

1. Martel-Pelletier J. Pathophysiology of osteoarthritis. *Osteoarthritis and Cartilage* 1999; 7: 371-373.
2. Murphy LB, Schwartz TA, Helmick CG, Renner JB, Tudor G, Koch G, et al. Lifetime risk of symptomatic knee osteoarthritis. *Arthritis Care and Research* 2008; 59: 1207-1213.
3. Murphy LB, Helmick CG, Schwartz TA, Renner JB, Tudor G, Koch GG, et al. One in four people may develop symptomatic hip osteoarthritis in his or her lifetime. *Osteoarthritis and Cartilage* 2010; 18: 1372-1379.
4. Kanavaki AM, Rushton A, Efstathiou N, Alrushud A, Klocke R, Abhishek A, et al. Barriers and facilitators of physical activity in knee and hip osteoarthritis: a systematic review of qualitative evidence. *BMJ Open* 2017; 7: e017042.
5. Wilcox S, Der Ananian C, Abbott J, Vrazel J, Ramsey C, Sharpe PA, et al. Perceived exercise barriers, enablers, and benefits among exercising and nonexercising adults with arthritis: results from a qualitative study. *Arthritis Care and Research* 2006; 55: 616-627.
6. Philbin EF, Groff GD, Ries MD, Miller TE. Cardiovascular fitness and health in patients with end-stage osteoarthritis. *Arthritis and Rheumatology* 1995; 38: 799-805.
7. Bailey TG, Cable NT, Miller G, Sprung V, Low D, Jones H. Repeated warm water immersion induces similar cerebrovascular adaptations to 8 weeks of moderate-intensity exercise training in females. *International Journal of Sports Medicine* 2016; 37: 757-765.
8. Matsumoto S, Shimodozono M, Etoh S, Miyata R, Kawahira K. Effects of thermal therapy combining sauna therapy and underwater exercise in patients with fibromyalgia. *Complementary Therapies in Clinical Practice* 2011; 17: 162-166.
9. Oosterveld FG, Rasker JJ, Floors M, Landkroon R, van Rennes B, Zwijnenberg J, et al. Infrared sauna in patients with rheumatoid arthritis and ankylosing spondylitis. *Clinical Rheumatology* 2009; 28: 29.
10. Kukkonen-Harjula K, Oja P, Laustiola K, Vuori I, Jolkkonen J, Siitonen S, et al. Haemodynamic and hormonal responses to heat exposure in a Finnish sauna bath. *Eur J Appl Physiol Occup Physiol* 1989; 58: 543-550.
11. Ježova D, Kvetňanský R, Vigaš M. Sex differences in endocrine response to hyperthermia in sauna. *Acta Physiologica Scandinavica* 1994; 150: 293-298.
12. Vescovi P, Gerra G, Pioli G, Pedrazzoni M, Maninetti L, Passeri M. Circulating opioid peptides during thermal stress. *Hormone and Metabolic Research* 1990; 22: 44-46.
13. Hoekstra SP, Bishop NC, Faulkner SH, Bailey SJ, Leicht CA. Acute and chronic effects of hot water immersion on inflammation and metabolism in sedentary, overweight adults. *J Appl Physiol (1985)* 2018; 125: 2008-2018.
14. Petersen AM, Pedersen BK. The anti-inflammatory effect of exercise. *J Appl Physiol (1985)* 2005; 98: 1154-1162.
15. Roddy E, Zhang W, Doherty M. Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. *Annals of the Rheumatic Diseases* 2005; 64: 544-548.

16. Koltyn KF, Umeda M. Exercise, hypoalgesia and blood pressure. *Sports Medicine* 2006; 36: 207-214.
17. de Meirleir K, Naaktgeboren N, Van Steirteghem A, Gorus F, Olbrecht J, Block P. Beta-endorphin and ACTH levels in peripheral blood during and after aerobic and anaerobic exercise. *European Journal of Applied Physiology and Occupational Physiology* 1986; 55: 5-8.
18. Schwarz L, Kindermann W. Changes in β-endorphin levels in response to aerobic and anaerobic exercise. *Sports Medicine* 1992; 13: 25-36.
19. Kelso TB, Herbert WG, Gwazdauskas FC, Goss FL, Hess JL. Exercise-thermoregulatory stress and increased plasma beta-endorphin/beta-lipotropin in humans. *J Appl Physiol Respir Environ Exerc Physiol* 1984; 57: 444-449.
20. Sprouse-Blum AS, Smith G, Sugai D, Parsa FD. Understanding endorphins and their importance in pain management. *Hawaii Medical Journal* 2010; 69: 70-71.
21. Wonders KY, Drury DG. Exercise intensity as a determinant of exercise induced hypoalgesia. *Journal of Exercise Physiology* 2011; 14: 134-144.
22. Naugle KM, Naugle KE, Fillingim RB, Samuels B, Riley III JL. Intensity thresholds for aerobic exercise–induced hypoalgesia. *Medicine and Science in Sports and Exercise* 2014; 46: 817-825.
23. Roxburgh BH, Campbell HA, Cotter JD, Reymann U, Williams MJA, Gwynne-Jones D, et al. Upper-limb high-intensity interval training or passive heat therapy to optimise cardiorespiratory fitness prior to total hip or knee arthroplasty: a randomised controlled trial. *Arthritis Care & Research* 2024; 76: 393-402.
24. Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GJ, Bittner VA, et al. Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation* 2013; 128: 873-934.
25. Pescastello L, Arena R, Riebe D, Thompson PD. *ACSM's guidelines for exercise testing and prescription*. 9th edn Edition. Philadelphia, Lippincott Williams & Wilkins 2013.
26. Akerman AP, Thomas KN, van Rij AM, Body ED, Alfadhel M, Cotter JD. Heat therapy vs. supervised exercise therapy for peripheral arterial disease: a 12-wk randomized, controlled trial. *American Journal of Physiology-Heart and Circulatory Physiology* 2019; 316: 1495-1506.
27. Borg G. Psychophysical bases of perceived exertion. *Medicine and Science in Sports and Exercise* 1982; 14: 377-381.
28. Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. *Academic Emergency Medicine* 2001; 8: 1153-1157.
29. Roxburgh BH, Campbell HA, Cotter JD, Reymann U, Williams MJA, Gwynne-Jones D, et al. Acute and adaptive cardiovascular and metabolic effects of passive heat therapy or high-intensity interval training in patients with severe lower-limb osteoarthritis. *Physiol Rep* 2023; 11: e15699.
30. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *Journal of Rheumatology* 1988; 15: 1833-1840.
31. Braun V, Clarke V, Weate P. Using thematic analysis in sport and exercise research. *Routledge handbook of qualitative research in sport and exercise* 2016; 1: 191-205.
32. Hawker GA, Wright JG, Coyte PC, Williams JI, Harvey B, Glazier R, et al. Differences between men and women in the rate of use of hip and knee arthroplasty. *New England Journal of Medicine* 2000; 342: 1016-1022.
33. Golightly YM, Smith-Ryan AE, Blue MN, Alvarez C, Allen KD, Nelson AE. High-Intensity Interval Training for Knee Osteoarthritis: A Pilot Study. *ACR Open Rheumatology* 2021; 3: 723-732.
34. Keogh JW, Grigg J, Vertullo CJ. Is high-intensity interval cycling feasible and more beneficial than continuous cycling for knee osteoarthritic patients? Results of a randomised control feasibility trial. *PeerJ* 2018; 6: e4738.
35. Castro O, Ng K, Novoradovskaya E, Bosselut G, Hassandra M. A scoping review on interventions to promote physical activity among adults with disabilities. *Disability and Health Journal* 2018; 11: 174-183.
36. Reed J, Buck S. The effect of regular aerobic exercise on positive-activated affect: A meta-analysis. *Psychology of Sport and Exercise* 2009; 10: 581-594.
37. Portugal EMM, Cevada T, Monteiro RS, Guimaraes TT, Rubini ED, Lattari E, et al. Neuroscience of Exercise: From Neurobiology Mechanisms to Mental Health. *Neuropsychobiology* 2013; 68: 1-14.
38. Roxburgh BH, Campbell HA, Cotter JD, Reymann U, Williams MJA, Gwynne-Jones D, et al. Cardiopulmonary exercise testing in severe osteoarthritis: a crossover comparison of four exercise modalities. *Anaesthesia* 2021; 76: 72-81.
39. De Baets L, Runge N, Labie C, Mairesse O, Malfliet A, Verschueren S, et al. The interplay between symptoms of insomnia and pain in people with osteoarthritis: a narrative review of the current evidence. *Sleep Medicine Reviews* 2023: 101793.
40. Uchida S, Shioda K, Morita Y, Kubota C, Ganeko M, Takeda N. Exercise effects on sleep physiology. *Front Neurol* 2012; 3: 48.
41. Luo Z-Y, Li L-L, Wang D, Wang H-Y, Pei F-X, Zhou Z-K. Preoperative sleep quality affects postoperative pain and function after total joint arthroplasty: a prospective cohort study. *Journal of Orthopaedic Surgery and Research* 2019; 14: 1-10.