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Pain-Free Versus Pain-Threshold Rehabilitation Following Acute Hamstring Strain Injury: A Randomized Controlled Trial

OBJECTIVE: The primary aim was to compare time from acute hamstring strain injury (HSI) to return-to-play (RTP) clearance following a standardized rehabilitation protocol performed within either pain-free or pain-threshold limits. Secondary aims were to compare isometric knee flexor strength, biceps femoris long head (BFLH) fascicle length, fear of movement, and reinjury occurrence at the 6-month follow-up between pain-free and pain-threshold groups.

DESIGN: Randomized controlled trial.

METHODS: Forty-three men with acute HSIs were randomly allocated to a pain-free (n = 22) or pain-threshold (n = 21) rehabilitation group. Days from HSI to RTP clearance, isometric knee flexor strength, BFLH fascicle length, fear of movement, and reinjury occurrence at the 6-month follow-up were reported.

RESULTS: Median time from HSI to RTP clearance was 15 days (95% confidence interval [CI]: 13, 17) in the pain-free group and 17 days (95% CI: 11, 24) in the pain-threshold group, which was not significantly different ($P = .37$). Isometric knee flexor strength recovery at 90° of hip and 90° of knee flexion was greater in the pain-threshold group at RTP clearance by 15% (95% CI: 1%, 28%) and by 15% (95% CI: 1%, 29%) at 2-month follow-up, respectively. Improvement in BFLH fascicle length from baseline was 0.91 cm (95% CI: 0.34, 1.48) greater at 2-month follow-up in the pain-threshold group. Two reinjuries occurred in both the pain-free and pain-threshold groups between RTP clearance and the 6-month follow-up.

CONCLUSION: Pain-threshold rehabilitation did not accelerate RTP clearance, but resulted in greater recovery of isometric knee flexor strength and better maintenance of BFLH fascicle length, compared to pain-free rehabilitation. *J Orthop Sports Phys Ther 2020;50(2):91-103. Epub 28 Jun 2019. doi:10.2519/jospt.2020.8895*

KEY WORDS: *hamstring strain injury, muscle, pain, rehabilitation, return to play*

Hamstring strain injuries (HSIs) remain the most prevalent cause of time lost from competition in a range of sports,[14,17,18,53] with associated performance[23] and financial consequences.[28] Deficits in function, such as reduced isometric knee flexor strength, exist acutely following HSI[4,44,58] and may increase reinjury risk if persistent at return-to-play (RTP) clearance.[16] Rehabilitation should aim to restore these deficits as quickly as possible following acute HSI and to return the injured athlete to his or her sport with minimal risk of reinjury.[26] However, even after completion of rehabilitation and RTP clearance, previously injured hamstrings may display eccentric strength[42,49,51,74] and biceps femoris long head (BFLH) fascicle length deficits,[73] which are both modifiable HSI risk factors.[11,52,71,79] Fyfe et al[22] hypothesized that a lack of eccentric loading and long-length exercise during early rehabilitation may contribute to residual deficits and the elevated risk of reinjury seen in previously injured hamstrings.[20,22,50]

SUPPLEMENTAL VIDEO ONLINE

Eccentric loading and long-length exercises reduce HSI risk,[3,77,80] increase knee flexor strength and BFLH fascicle length in uninjured individuals,[1,10,54,55,72] and accelerate RTP time when emphasized during rehabilitation.[5,6] However, the introduction and progression of eccentric loading and long-length exercises may be delayed by the consistently implemented guideline to only perform and progress exercise in the absence of pain.[30] Delaying the start of exercise rehabilitation by 9

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days, compared to 2 days, after acute muscle injury prolongs time to return to play.[9] Therefore, delaying exposure to exercise rehabilitation due to pain may limit the ability to achieve beneficial adaptations and may prolong RTP clearance following acute HSI.

Pain avoidance during HSI rehabilitation is consistent with conventional guidelines for the treatment of acute muscle injuries.[37] However, these guidelines state that "the current treatment principles of injured skeletal muscle lack firm scientific basis,"[37] which were largely based on clinical experience or laboratory-based animal studies.[32-35,48] In chronic or postoperative musculoskeletal conditions, allowing exercise to be performed up to a pain threshold is safe[7,21,46,64,69,70] and may improve outcomes compared to remaining pain free.[65,67] Mild pain or discomfort is permitted during HSI rehabilitation[27,40,45]; however, the pain-threshold approach has never been directly compared to the conventional practice of pain avoidance while performing the same rehabilitation protocol.

Therefore, the primary aim of this study was to compare the number of days from acute HSI to RTP clearance following a standardized rehabilitation protocol performed within either pain-free or pain-threshold limits. The secondary aims were to investigate the impact of pain-free and pain-threshold rehabilitation protocols on isometric knee flexor strength, BFLH fascicle length, fear of movement, and reinjury occurrence at a 6-month follow-up. We hypothesized that pain-threshold rehabilitation would accelerate the time needed to achieve RTP clearance compared to pain-free rehabilitation.

METHODS

Study Design

This study was a single-center, efficacy, double-blind randomized controlled trial, designed and conducted at the Australian Catholic University in Melbourne, Australia in accordance with the Consolidated Standards of Reporting Trials guidelines. The Australian Catholic University Human Research Committee granted ethical approval (2015-307H), and the trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12616000307404).

Participant Recruitment and Eligibility

Between February 2016 and May 2017, men and women aged 18 to 40 years and with a suspected HSI were invited to undergo an initial clinical assessment within 7 days of suffering acute-onset posterior thigh pain. Potential participants were recruited via advertisement of recruitment posters, and contact was made with sporting clubs and sports injury clinics around Melbourne, Australia. Informed written consent was provided by potential participants prior to undergoing a subjective interview and a series of clinical assessments to confirm the presence of acute HSI. Potential participants had to meet all predetermined eligibility criteria (**TABLE 1**)[45,81] to be included in the study.

Potential participants were excluded if they presented with signs and symptoms of other causes of posterior thigh pain (hamstring tendinopathy, referred lower back pain, etc), or warranted the opinion of a surgeon when complete muscle rupture was suspected. An independent physical therapist (E.R.) with 15 years of experience in sports injury clinical practice and research verified participant eligibility. Injuries were not confirmed via magnetic resonance imaging (MRI) or graded using subjective categorical systems; rather, variables collected during the initial clinical assessment were reported to indicate severity of injury on a more continuous and objective scale. This approach was taken because combinations of clinical assessments, such as between-leg deficits in strength, range of motion, and pain, correlate well with rehabilitation progression[83] and explain more of the variance in RTP clearance time following HSI than do MRI findings.[31,81]

Randomization and Blinding

Eligible participants were randomly allocated to either a pain-free or pain-threshold rehabilitation group after stratification for previous HSI and sex using a 4-block randomization approach. This was done by marking 4 separate folders: (1) male/previous HSI, (2) male/first-time HSI, (3) female/previous HSI, and (4) female/first-time HSI. Each of these folders contained 4 sealed and unmarked envelopes, which contained allocation to either the pain-free (2 envelopes) or pain-threshold (2 envelopes) group. The lead investigator (J.H.) randomly selected one of these sealed and unmarked envelopes and provided it to the participant to open, which revealed group allocation. These 4 envelopes were only replaced in their respective folders once the previous 4 had all been selected.

Participants allocated to the pain-free group were only permitted to perform and progress rehabilitation when, during exercise, they reported a complete absence of pain (0 on a 0-to-10 numeric rating scale [NRS]). In contrast, those in the pain-threshold group were permitted to perform and progress reha-

TABLE 1 Eligibility Criteria for Study Inclusion

- Men and women aged 18 to 40 years
- Acute-onset posterior thigh pain associated with clear injury mechanism (eg, high-speed running, kicking, etc) causing cessation of activity
- Present for initial clinical assessment within 7 days of suspected injury
- Pain on palpation of the injured muscle
- Pain localized to the site of injury during isometric knee flexor contraction

bilitation with a pain rating of 4 or less on the NRS during exercise. All participants were told how to report localized pain at the site of injury using the NRS, on which 0 represented "absolutely no pain" and 10 the "worst pain imaginable." Upon allocation, participants were informed only of the pain limits applicable to their respective group and then provided informed written consent prior to commencing rehabilitation. Participants were blinded to the presence of the alternative intervention to reduce the possibility of cross-group contamination. All objective outcome measures were collected by members of the research team (D.O., R.T., and N.M.) who were blinded to group allocation for the duration of the study.

Initial Subjective Interview

Injury details, demographic data, and relevant injury history were all ascertained from an initial subjective interview. The subjective interview was conducted by the lead investigator (J.H.), a health professional with 5 years' clinical experience in musculoskeletal injury assessment and rehabilitation. Upon completion of the subjective interview, participants completed the 17-item Tampa Scale of Kinesiophobia (TSK) to assess fear of movement.

Clinical Assessments

During each participant's initial visit to confirm acute HSI and prior to all subsequent rehabilitation sessions, a series of clinical assessments were conducted by members of the research team blinded to group allocation (D.O., R.T., and N.M.). First, ultrasound images were collected, and later analyzed offline by the same blinded and experienced investigator (R.T.), to ascertain BFLH architecture using previously described methodology with published reliability (intraclass correlation coefficient = 0.96-0.98; typical error, 2.1%-3.4%).[73]

The injured muscle was then palpated, with participants in a prone position, to determine injury location and pain. The assessor palpated along the length of the injured muscle to identify the location of peak palpation pain. Participants were asked to rate their pain on a 0-to-10 NRS, and the peak value was recorded. The distance from the ischial tuberosity to the site of peak palpation pain and the total craniocaudal length of palpable pain were also measured (centimeters).[4,83]

Hamstring range of motion was assessed via the passive straight leg raise[4,60] and active knee extension tests.[24,59] For both the passive straight leg raise and active knee extension, a digital inclinometer was placed on the anterior tibial border, just below the tibial tuberosity, to objectively measure the angle of hip flexion or knee extension, respectively, at the point of onset of localized pain or maximal tolerable stretch. Participants were asked to rate their pain on the 0-to-10 NRS if they experienced localized pain at the site of injury during either the passive straight leg raise or active knee extension. Three trials of the passive straight leg raise and active knee extension were performed on the uninjured (performed first) and injured legs, with the highest range-of-motion value and peak pain score recorded for each test.

Isometric knee flexor strength was assessed with the participant lying supine at 0°/0° and 90°/90° of hip/knee flexion, using an apparatus with published reliability (intraclass correlation coefficient = 0.87-0.91; typical error, 6.2%-8.1%).[29] In each position, the uninjured leg was tested prior to the injured leg, with 2 warm-up repetitions at 50%, then 75%, of perceived maximal effort followed by 3 maximal-effort isometric knee flexor contractions, with a minimum 30-second rest between trials. A standardized instruction, "Push your heel down into the strap, from complete rest without lifting up your heel, as fast and hard as you can, in 3, 2, 1, go," was given with strong verbal encouragement to ensure maximal effort. When performing contractions with the injured leg, the additional instruction of contracting "to an intensity that you feel comfortable with" was given. Participants were asked to report any pain localized to the site of injury on the NRS, with the peak pain score recorded in each position. For each day of testing, isometric knee flexor strength at both 0°/0° and 90°/90° was defined as the highest force output across 3 repetitions for each leg at each position. Isometric knee flexor strength of the injured leg was reported as a percentage relative to the strength of the participant's contralateral, uninjured leg at the initial clinical assessment,[83] to account for change with exposure to exercise performed by the uninjured leg during rehabilitation.

Rehabilitation Protocol

All participants performed a standardized rehabilitation protocol twice per week, consisting of hamstring-strengthening exercises and progressive running, with every session fully supervised by the lead investigator (J.H.). Participants were asked to rate pain at the site of injury on the NRS during each exercise or stage of progressive running. The only difference between the 2 groups was the amount of pain allowed during performance of the rehabilitation protocol, which determined whether an exercise would be performed and progressed on an individual basis. No pain-relieving strategies, such as ice, medication, or topical treatments, were provided to participants in either group during their supervised rehabilitation sessions. Pain-relieving strategies applied by participants outside of these sessions were not controlled. All participants were advised not to perform any additional rehabilitation exercises outside of their 2 supervised sessions per week. Participants were encouraged to gradually return to their regular team sports training throughout the rehabilitation period; however, they were advised to keep any running below the intensity that they had achieved during supervised progressive running at that time.

Hamstring-strengthening exercises involving either hip extension at moderate to long muscle lengths or knee flexion with eccentric bias were selected to target

BFLH fascicle length and eccentric knee flexor strength adaptations.[10,12] These exercises were bilateral and unilateral variations of a hamstring bridge, 45° hip extension, eccentric slider (**ONLINE VIDEOS**), and the Nordic hamstring exercise. During their first rehabilitation session, all participants attempted bilateral variations of the hamstring bridge, 45° hip extension, and eccentric slider. Participants were permitted to continue performing each exercise within their group's respective pain limits, with each exercise progressed on an individual basis using exercise-specific criteria (**FIGURE 1**).

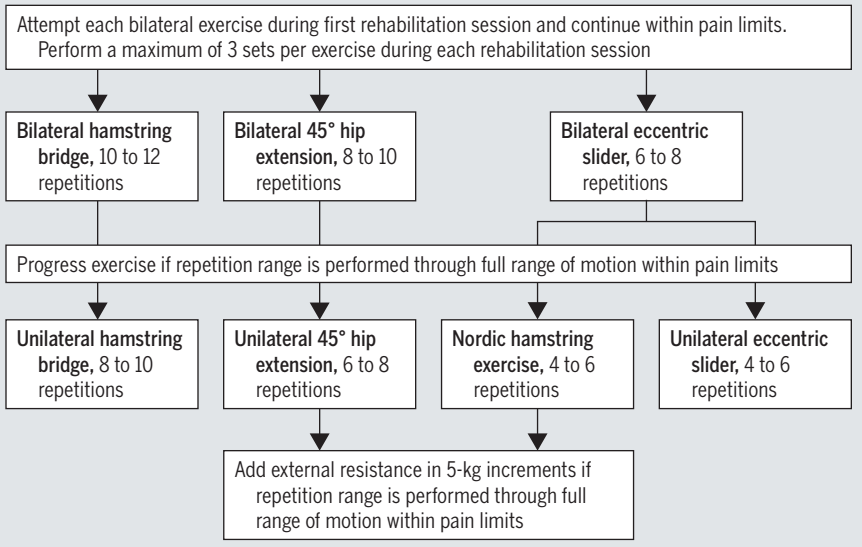

FIGURE 1. Exercise-specific progression criteria and prescribed repetition ranges for each exercise variation in the rehabilitation protocol.

TABLE 2 Intensity and Distance of the 9-Stage Progressive Running Protocol[a]

Stage	Acceleration Phase	Hold Phase	Deceleration Phase
1	Walk 20 m	Jog 10 m	Walk 20 m
2	Walk 15 m	Jog 20 m	Walk 15 m
3	Walk 10 m	Jog 30 m	Walk 10 m
4	Jog 20 m	Run 10 m	Jog 20 m
5	Jog 15 m	Run 20 m	Jog 15 m
6	Jog 10 m	Run 30 m	Jog 10 m
7	Run 20 m	Sprint 10 m	Run 20 m
8	Run 15 m	Sprint 20 m	Run 15 m
9	Run 10 m	Sprint 30 m	Run 10 m

[a]*Walk is defined as regular gait, jog as less than 50% of perceived maximal running speed, run as less than 70% of perceived maximal running speed, and sprint as greater than 90% of perceived maximal running speed.*

TABLE 3 Criteria for Return-to-Play Clearance

- No pain on palpation of the injured muscle
- No pain during the active knee extension or passive straight leg raise test, with range of motion at 90% or greater of that of the contralateral, uninjured leg
- No pain during maximal-effort isometric knee flexor contraction at 0°/0° and 90°/90° of hip/knee flexion
- No pain or apprehension during sprinting at 100% of perceived maximal running intensity

Progressive running was based on the work of Silder et al[66] and included 9 stages of increasing intensity and hold distance and decreasing acceleration and deceleration distances over a total distance of 50 m (**TABLE 2**). Participants commenced progressive running once they could walk with normal gait within their group's pain limits. Jog, run, and sprint intensities were explained to participants as being upper limits of, respectively, 50%, 70%, and 100% of their perceived maximal running speed. Progression from one stage to the next was achieved once participants could perform 3 repetitions at the relevant upper-limit intensity within their group's pain limits. No more than 9 repetitions were permitted during each rehabilitation session.[66]

Participants continued to perform this rehabilitation protocol twice per week until they met predetermined criteria for RTP clearance (**TABLE 3**), which were identical for all participants and based on the best available evidence.[2,78] Once RTP clearance criteria had been met, all participants were provided the same recommendation to complete at least 2 full training sessions prior to returning to competitive sport. However, the final decision to return to competition was left to the participant, coach, and medical/fitness staff at their respective sporting club to account for variation in sports, levels of competition, and the need for shared RTP decision making.[2,15,63] All participants were encouraged to continue with at least 1 hip extension and 1 eccentric knee flexion exercise once per week, although compliance was not enforced or monitored.

Follow-up

Participants were contacted at least once per month for a 6-month period follow-

ing RTP clearance to monitor for reinjury. If participants suspected reinjury, they were instructed to contact the lead investigator (J.H.), and attempts were made to confirm the presence of an acute HSI via clinical assessment by a blinded investigator, based on the previously described study inclusion criteria. However, if this was not possible, then reinjury was confirmed via telephone conversation with the participant and communication with relevant contacts at the participant's sporting club, such as a team physical therapist. All suspected reinjuries were verified by an independent physical therapist (E.R.) blinded to group allocation.

Two months following RTP clearance, participants attended a follow-up assessment, except for those who had already suffered a reinjury. This assessment was conducted entirely by the same blinded assessor as the one during rehabilitation (D.O., R.T., or N.M.), with BFLH muscle architecture, isometric knee flexor strength, and score on the TSK assessed as previously described.

Outcome Measures

The primary outcome measure, time to RTP clearance, was the number of days from acute HSI to meeting all RTP clearance criteria. Secondary outcome measures were BFLH fascicle length, isometric knee flexor strength, fear of movement at the initial clinical assessment, RTP clearance, and 2-month follow-up, and the number of reinjuries in the 6 months following RTP clearance.

Statistical Analysis

An a priori sample-size calculation determined that 29 participants were required to achieve 80% power, accounting for a dropout rate of 20%. The sample-size calculation was based on an effect size of 1.2, comparing RTP time between HSI rehabilitation emphasizing lengthening and rehabilitation emphasizing conventional exercises.[5,6]

Statistical analysis was performed in R Version 3.4.3,[56] using custom-written code. Intention-to-treat analysis was used to investigate the treatment's effect on the number of days from acute HSI to RTP clearance and the number of reinjuries during the 6-month follow-up, using a Cox proportional hazard model. Time-to-RTP clearance and survival-from-reinjury curves were fit via the Kaplan-Meier method, using the "survival" package.[68] Participants who ceased rehabilitation prior to achieving RTP clearance criteria were censored from analysis at the time of their last completed session. Participants who did not complete the 6-month reinjury follow-up were censored at the last time point they were contacted.

Linear mixed models were used to investigate the effect of pain-free and pain-threshold rehabilitation (group) on BFLH fascicle length, isometric knee flexor strength, and fear of movement at RTP clearance and 2-month follow-up (time). Linear mixed models were fit via restricted maximum likelihood using the "lme4" package.[8] Group, time, and their interaction were treated as fixed effects, with participant modeled as a random

TABLE 4 Baseline Participant Characteristics and Results of Initial Clinical Assessment[a]

Variable	Pain-Free Group (n = 22)	Pain-Threshold Group (n = 21)
Age, y	27.4 ± 5.2	24.9 ± 5.3
Height, cm	180.1 ± 7.5	182.2 ± 8.2
Mass, kg	86.5 ± 13.5	86.3 ± 9.2
Sport, d/wk	3 ± 1	3 ± 1
Sport, n		
Australian football	18	14
Other	4	7
Prior hamstring strain injury, n		
Yes	16	14
No	6	7
Initial clinical assessment/start of rehabilitation, d from injury	3 ± 2	3 ± 1
Activity at time of injury, n		
Competition	14	15
Training	8	6
Injury location, n		
Lateral	18	15
Medial	4	6
Pain at time of injury (0-10 NRS)	5.7 ± 2.0	5.8 ± 1.5
Peak palpation pain (0-10 NRS)	3.1 ± 1.7	3.6 ± 2.0
Peak palpation pain distance from ischium, cm	20.2 ± 6.7	19.6 ± 6.4
Total length of palpable pain, cm	5.5 ± 3.4	5.8 ± 4.4
Passive straight leg raise pain (0-10 NRS)	2.5 ± 2.2	2.3 ± 2.4
Active knee extension pain (0-10 NRS)	3.3 ± 2.5	2.9 ± 2.7
Passive straight leg raise deficit, %[b]	89.9 ± 14.8	84.6 ± 18.2
Active knee extension deficit, %[b]	84.3 ± 20.8	71.9 ± 27.3
Isometric knee flexor pain at 0°/0° (0-10 NRS)[c]	3.7 ± 2.8	3.1 ± 2.6
Isometric knee flexor pain at 90°/90° (0-10 NRS)[c]	4.5 ± 2.6	4.8 ± 2.1
Isometric knee flexor strength at 0°/0°, %[b,c]	70.1 ± 26.9	66.8 ± 26.8
Isometric knee flexor strength at 90°/90°, %[b,c]	60.1 ± 25.2	60.1 ± 26.4

Abbreviation: NRS, numeric rating scale.
[a]*Values are mean ± SD unless otherwise indicated.*
[b]*Relative to the uninjured leg.*
[c]*Degrees of hip and knee flexion, respectively.*

effect to account for individual variability. Residuals were plotted and checked for approximate normality, and statistical significance was assessed using 95% confidence intervals (CIs).

RESULTS

Participants

All 51 potential participants screened for eligibility were men, as no women presented to the investigators with suspected HSIs, despite being eligible for inclusion. Of these 52 potential participants, 43 met inclusion criteria and were randomized to the pain-free group (n = 22) and the pain-threshold group (n = 21) (**TABLE 4**). All participants were compliant with the rehabilitation protocol, performing supervised sessions twice per week, with no adverse events (reinjuries) occurring prior to RTP clearance. One rehabilitation session was ceased as a precaution when a participant in the pain-threshold group reported pain of 7/10 during sprinting. However, this was not considered an adverse event, as predetermined criteria for reinjury were not met immediately after cessation of this session or prior to the subsequent rehabilitation session 2 days later. This participant continued to be fully compliant with pain-threshold rehabilitation from 2 days after this session until achieving RTP clearance criteria.

One participant in the pain-free group ceased rehabilitation 24 days following acute HSI, without meeting RTP clearance criteria, and was censored from further analysis at this time point. Data for all secondary outcome measures at 2-month follow-up were missing from 4 participants in the pain-free group and 3 participants in the pain-threshold group (**FIGURE 2**).

RTP Clearance

Criteria for RTP clearance were met by 21 of the 22 participants in the pain-free group in a median time of 15 days (95% CI: 13, 17), and by all 21 participants in the pain-threshold group in a median time of 17 days (95% CI: 11, 24) (**FIGURE 3A**). The hazard ratio for time taken to achieve RTP clearance in the pain-threshold group was 0.75 (95% CI: 0.40, 1.40) relative to the pain-free group, which was not significantly different ($P = .37$; score test of treatment effect in the Cox proportional hazard model) (**FIGURE 3B**).

BFLH Fascicle Length

Data from the initial clinical assessment of the BFLH were missing for 1 participant in the pain-free group and 1 participant in the pain-threshold group, due to the assessor for this measure (R.T.) not being available at this time point. From initial clinical assessment to RTP clearance, BFLH fascicle length significantly improved by an average of 1.70 cm (95% CI: 1.33, 2.08) in the pain-free group (**FIGURE 4A**) and 1.95 cm (95% CI: 1.41, 2.48) in the pain-threshold group (**FIGURE 4B**), with no significant difference between the 2 groups (95% CI: −0.29, 0.78). Despite a slight reduction in the 2 months following RTP clearance, BFLH fascicle length was still significantly greater than at the initial clinical assessment, by an average of 0.56 cm (95% CI: 0.16, 0.97) in the pain-free group and 1.47 cm (95% CI: 0.90, 2.04) in the pain-threshold group. The difference in BFLH fascicle length from the initial clinical assessment to 2-month follow-up was significantly greater in the pain-threshold group than in the pain-free group, by an average of 0.91 cm (95% CI: 0.34, 1.48).

Isometric Knee Flexor Strength

From initial clinical assessment to RTP clearance, significant improvements in isometric knee flexor strength were observed at 0°/0°, by an average of 32% (95% CI: 22%, 41%) in the pain-free group (**FIGURE 5A**) and 39% (95% CI: 26%, 52%) in the

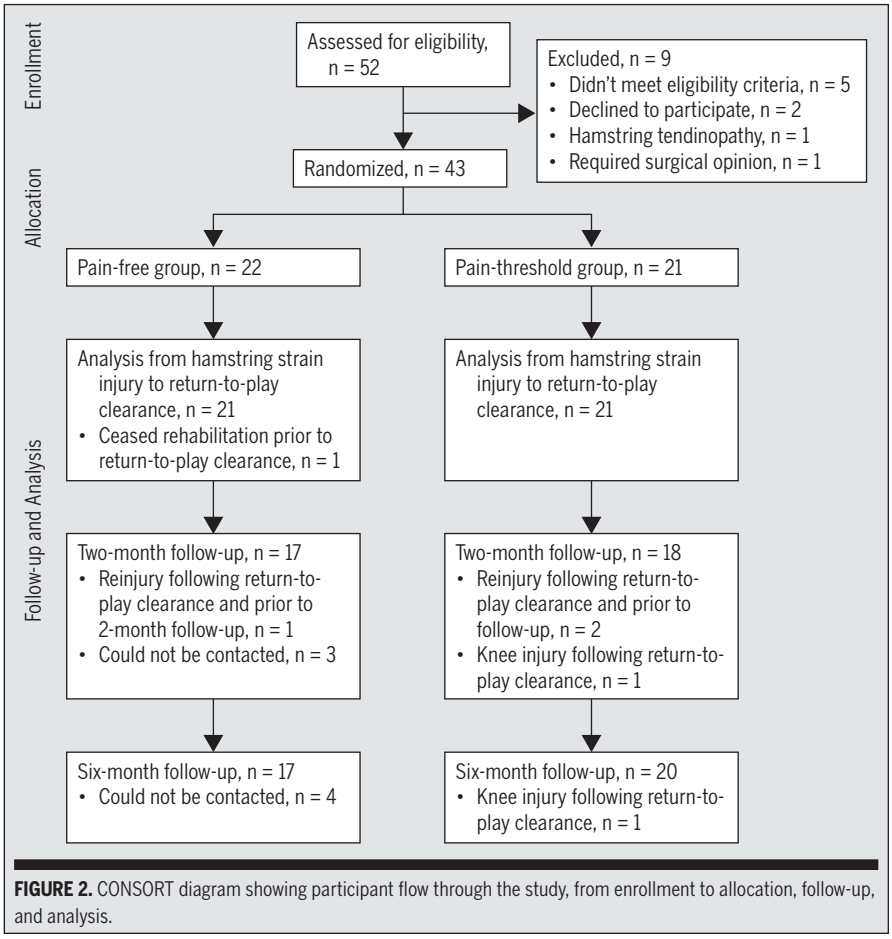

FIGURE 2. CONSORT diagram showing participant flow through the study, from enrollment to allocation, follow-up, and analysis.

pain-threshold group (**FIGURE 5B**), with no difference between groups (95% CI: −6%, 20%). Isometric knee flexor strength at 0°/0° remained significantly greater than at the initial clinical assessment in both groups 2 months following RTP clearance, with no significant difference between groups (95% CI: −6%, 22%).

Isometric knee flexor strength at 90°/90° improved significantly, by an average of 35% (95% CI: 26%, 44%) in the pain-free group (**FIGURE 5C**) and 49% (95% CI: 36%, 63%) in the pain-threshold group (**FIGURE 5D**), from initial clinical assessment to RTP clearance. This improvement was significantly greater, by an average of 15% (95% CI: 1%, 28%), in the pain-threshold group. Two months following RTP clearance, improvement in isometric knee flexor strength at 90°/90° from the initial clinical assessment remained significantly greater, by an average of 15% (95% CI: 1%, 29%), in the pain-threshold group.

Fear of Movement

Fear-of-movement data for 1 participant in the pain-threshold group at RTP clearance was missing, as the participant failed to complete the TSK at this time-point. According to the TSK, out of a maximum score of 68 points, fear of movement significantly reduced by an average of −7 points (95% CI: −5, −9) in the pain-free group (**FIGURE 6A**) and −8 points (95% CI: −5, −11) in the pain-threshold group (**FIGURE 6B**) from initial clinical assessment to RTP clearance. Between-group differences in reduction of fear of movement of −1 point (95% CI: −4, 2) at RTP clearance and −4 points (95% CI: −6, 0) at 2-month follow-up, compared to the initial clinical assessment, were nonsignificant.

Six-Month Reinjury Follow-up

All but 5 participants provided data at the 6-month follow-up assessment, 4 in the pain-free group who could not be contacted and 1 in the pain-threshold group who suffered an unrelated knee injury after RTP clearance. Two participants in the pain-free group suffered reinjuries 50 and 67 days after RTP clearance at 13 and 26 days, respectively, after the first HSI. Two participants in the pain-threshold group suffered reinjuries 8 and 17 days after RTP clearance at 6 and 11 days, respectively, after the first HSI (**FIGURE 7**). The hazard ratio for reinjury in the pain-threshold group was 1.05 (95% CI: 0.14, 7.47) relative to the pain-free group, which was not significantly different (P = 1.0; score test of treatment effect in the Cox proportional hazard model).

DISCUSSION

The main finding of this randomized controlled trial is that, following acute HSI, RTP clearance was not accelerated by performing and progressing a standardized rehabilitation protocol using a pain-threshold compared to a pain-free rehabilitation protocol. Regardless of the pain-threshold or pain-free group allocation, all participants showed large improvements in BFLH fascicle length and isometric knee flexor strength, along with reduced fear of movement. However, the pain-threshold rehabilitation protocol did result in greater recovery of isometric knee flexor strength at 90°/90° of hip/knee flexion for both RTP clearance and the 2-month follow-up time points and more sustained improvements in BFLH fascicle length 2 months after RTP clearance compared to pain-free rehabilitation.

This is the first randomized controlled trial with outcomes that did not support the long-held belief that pain-free rehabilitation is best clinical practice following acute muscle injury,[19,36-39,41,43] which is largely driven by fear of symptom exacerbation and/or reinjury.[37] In the current study, there was only a single rehabilitation session ceased, as a precaution due to pain exacerbation with sprinting; how-

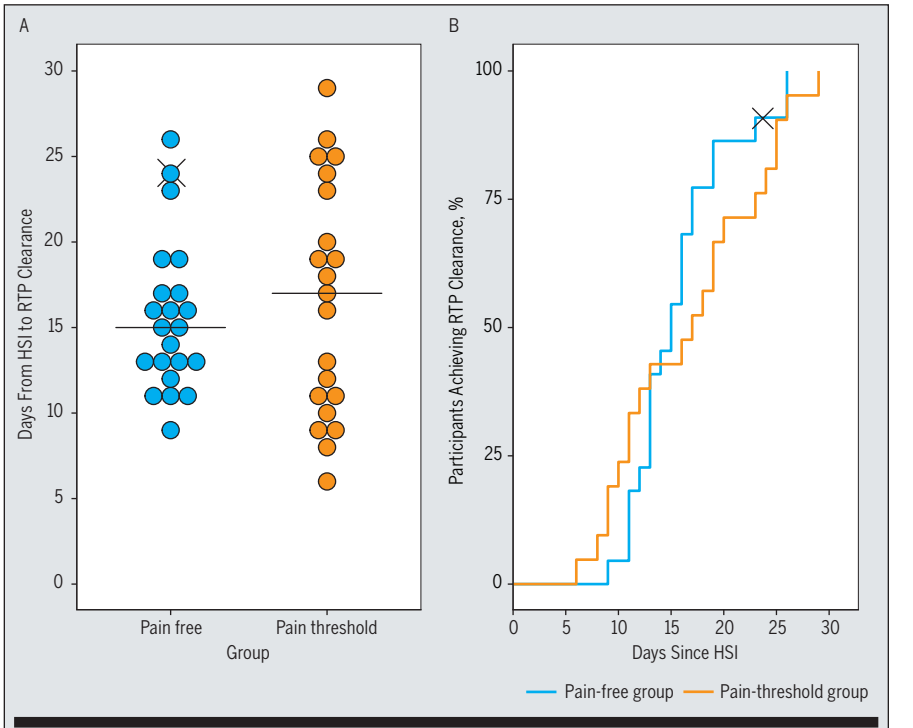

FIGURE 3. (A) Scatter plot of the number of days from HSI to RTP clearance for each individual participant within the pain-free and pain-threshold groups. The horizontal black lines represent the median RTP clearance time within each group. (B) Kaplan-Meier curves for the percentage of participants achieving RTP clearance within each group relative to the number of days since HSI. The "X" symbol in both (A) and (B) shows the amount of days from HSI to the last rehabilitation session completed by the 1 participant in the pain-free group who did not achieve RTP clearance. Abbreviations: HSI, hamstring strain injury; RTP, return to play.

ever, this was not a reinjury. Exposing participants to pain during rehabilitation did not induce fear, with both groups achieving significant reductions on the TSK from the initial clinical assessment to RTP clearance. Further, no adverse events occurred when exercise was permitted to continue and/or be progressed in the presence of pain rated up to 4/10 on the NRS in the pain-threshold group. The pain threshold of 4/10 or less was selected as a slightly more conservative version of the pain-monitoring model of 5/10 or less, previously implemented in patellofemoral joint pain and Achilles tendinopathy rehabilitation.[64,65,69] Selection of an appropriate pain threshold will always be somewhat of an arbitrary task, given the complex and subjective nature of pain perception.[47] Regardless of the specific pain threshold set, the current findings suggest that it is unnecessary to completely avoid pain during HSI rehabilitation.

Comparison of RTP clearance times in the current study to those previously reported in the HSI literature is difficult, due to inconsistent definitions of this outcome measure.[78] However, the RTP clearance times in the current study compare favorably to those in a previous study, which also reported time from HSI to meeting RTP clearance and reported a mean in excess of 21 days.[25] Perhaps of greater importance than RTP clearance time is that both groups achieved large improvements in isometric knee flexor strength and BFLH fascicle length within these relatively brief rehabilitation time frames.

Although both groups achieved large improvements in isometric knee flexor strength, recovery of between-leg deficits was greater in the pain-threshold group at 90°/90° of hip/knee flexion. Participants exposed to pain-threshold rehabilitation may have been more willing to contract to their maximal intensity if they saw pain as less of a barrier to exercise. However, between-group differences in isometric knee flexor strength were observed at RTP clearance and 2-month follow-up, at which all participants reported no pain. Therefore, allowing exercise to be performed and progressed up to a pain threshold appears to enhance recovery of isometric strength compared to avoiding pain during HSI rehabilitation.

The magnitudes of BFLH fascicle length improvement seen from the initial clinical assessment to RTP clearance in both groups were similar to those reported in uninjured males after 2 weeks of eccentric exercise.[55,72] In the current study, BFLH fascicle length improvements were relatively well maintained at 2-month follow-up, compared to the adaptation reversal seen after periods of detraining in uninjured males.[55,72] Lack of adaptation reversal may be explained by the advice given to all participants to continue with some form of eccentric loading at least once per week following RTP clearance. Although BFLH fascicle length improvements were better maintained at 2-month follow-up in the pain-threshold group, the mean ± SD increase from initial clinical assessment to RTP clearance of 1.82 ± 0.82 cm for all participants suggests adequate exposure to eccentric loading and long-length exercises in the current rehabilitation protocol, regardless of group allocation.

From the outset, eccentric loading and long-length exercises were introduced in the first rehabilitation session (average ± SD, 3 ± 2 days after HSI) and progressed individually, based on whether they could be performed through full range of motion for a prescribed repetition range within each group's pain limits. Askling et al[5,6] previously implemented similar exercise-specific progressions as part of the L-protocol, although rehabilitation did not commence until 5 days after HSI and progression was only allowed within strict pain-free limits. The L-protocol exercises recruit the hamstrings to a relatively low intensity[61] compared to the Nordic hamstring exercise[13] and eccentric sliding leg curl,[75] which were both implemented in the current rehabilitation protocol. It is typically recommended that progression to these exercises should be delayed during HSI rehabilitation until isometric knee flexor strength assessments are pain free[62] and/or within 10% of the uninjured leg.[45,76] However, we ob-

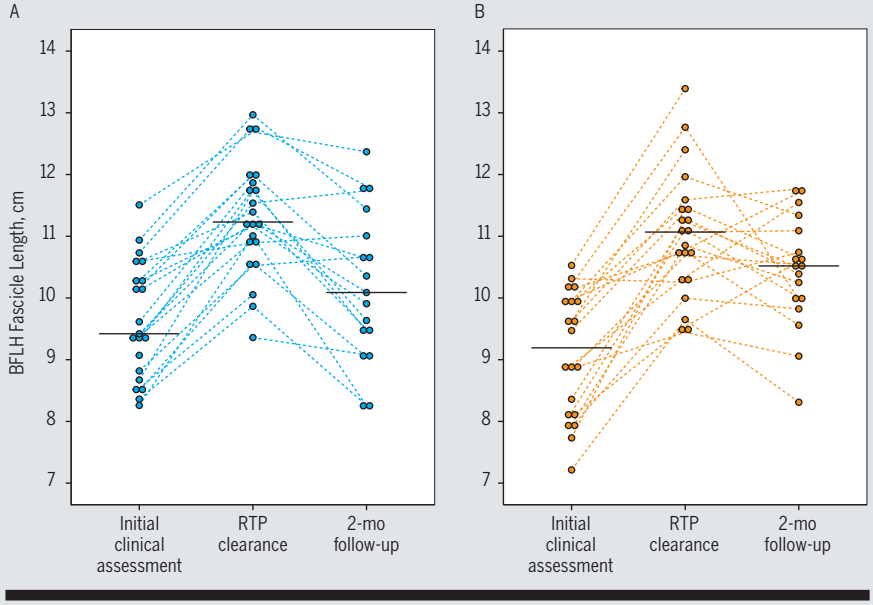

FIGURE 4. The BFLH fascicle length of the injured leg within (A) the pain-free group and (B) the pain-threshold group at the initial clinical assessment, RTP clearance, and 2-month follow-up. Each dot represents an individual participant, dotted lines indicate change over time, and the solid horizontal lines show the group medians. Abbreviations: BFLH, biceps femoris long head; RTP, return to play.

served that participants in the current study were often able to perform the Nordic hamstring exercise and the unilateral eccentric slider without pain, despite still reporting pain and/or demonstrating between-leg deficits greater than 10% during isometric knee flexor strength assessments. These findings suggest that eccentric loading can be progressed to a relatively high intensity by implementing exercise-specific criteria for progression, rather than delaying intervention by waiting for the alleviation of pain and/or between-leg deficits during isometric knee flexor strength assessments.

Interpretation of reinjury data is challenging due to the modest sample size and low number of reinjuries. Overall, the 4 reinjuries that occurred, as a percentage of the 37 participants compliant with 6-month follow-up, accounted for 11% of participants, which is comparable to recent HSI rehabilitation studies reporting rates of reinjury ranging from 4% to 30%.[25,45,58] Three of the 4 reinjuries in the current study occurred within 2 months of RTP clearance, which is consistent with data showing greater susceptibility to recurrence during this period.[25,82] Further, all 3 participants met RTP clearance within 2 weeks of their initial HSI. The 2 participants in the pain-threshold group who suffered reinjuries 8 and 17 days after RTP clearance at 6 and 11 days, respectively, following their initial HSI. These findings suggest a relationship between accelerated RTP clearance and elevated reinjury risk, along with potential inadequacies in the current RTP clearance criteria, which may need to better account for tissue healing time. Studies with larger numbers of participants and reinjuries are needed to shed more light on risk factors for HSI recurrence to better refine RTP criteria moving forward.

Our study used the revised Cochrane risk-of-bias tool for randomized trials to reduce risk of bias. Due to a concealed random-allocation sequence and blinding participants to the interventions, the risk of bias arising from the randomization process and deviations from the intended interventions was low. There may be bias related to the outcome of reinjury, as 20 of the 21 participants in the pain-threshold group completed 6-month follow-up, compared to 17 of the 22 participants in the pain-free group. However, risk of bias due to missing data and measurement of all other outcome measures was low, as the presence of missing data was reported and investigators were blinded to group allocation.

The current study is not without limitations. Confirmation of acute HSI was restricted to clinical assessment, as diagnostic tools such as MRI were not available. It is possible that although participants met inclusion criteria based on clinical assessment, some may have had a negative MRI result, which is associated with reduced RTP time.[57] However, many clinicians working with sports injuries are limited to confirming the presence

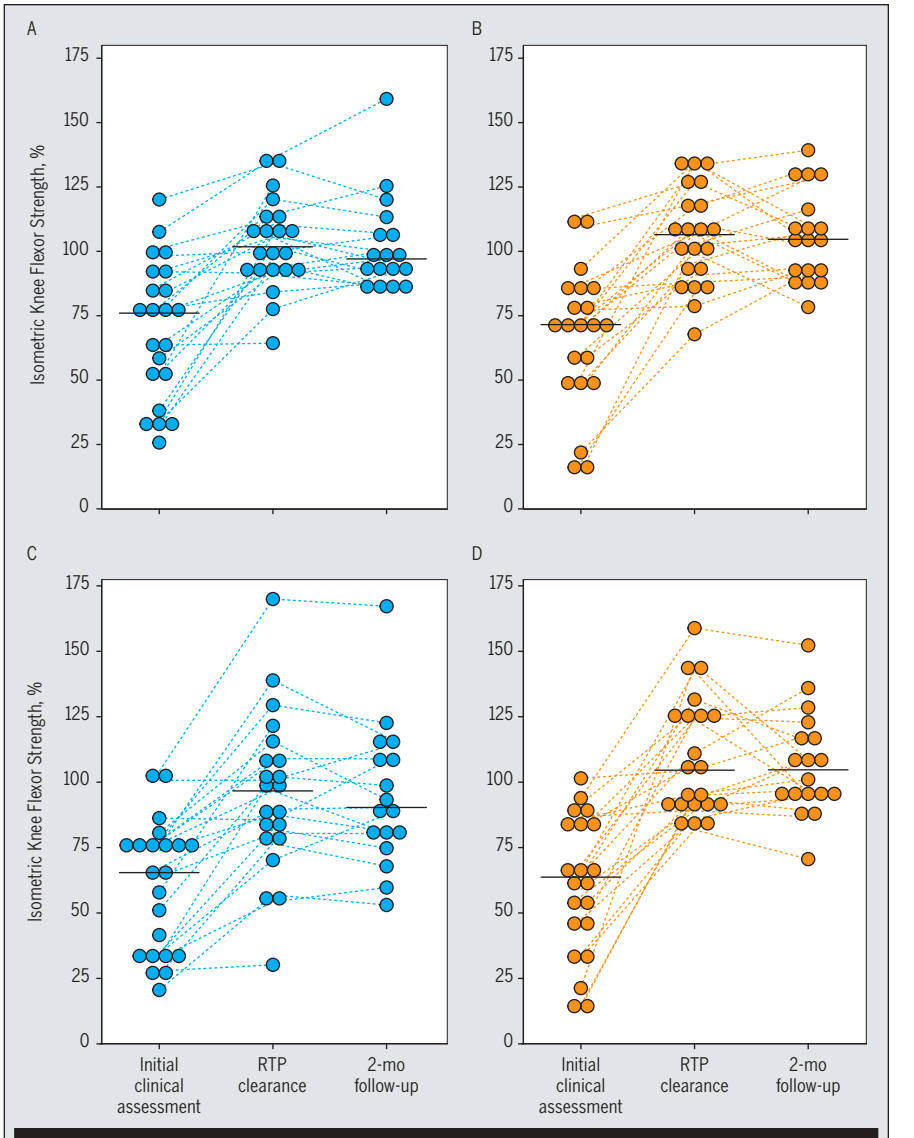

FIGURE 5. Isometric knee flexor strength of the injured leg at (A and B) 0°/0° and (C and D) 90°/90° of hip/knee flexion relative to the contralateral, uninjured leg (percent) within (A and C) the pain-free group and (B and D) the pain-threshold group at the initial clinical assessment, RTP clearance, and 2-month follow-up. Each dot represents an individual participant, dotted lines indicate change over time, and the solid horizontal lines show the group medians. Abbreviation: RTP, return to play.

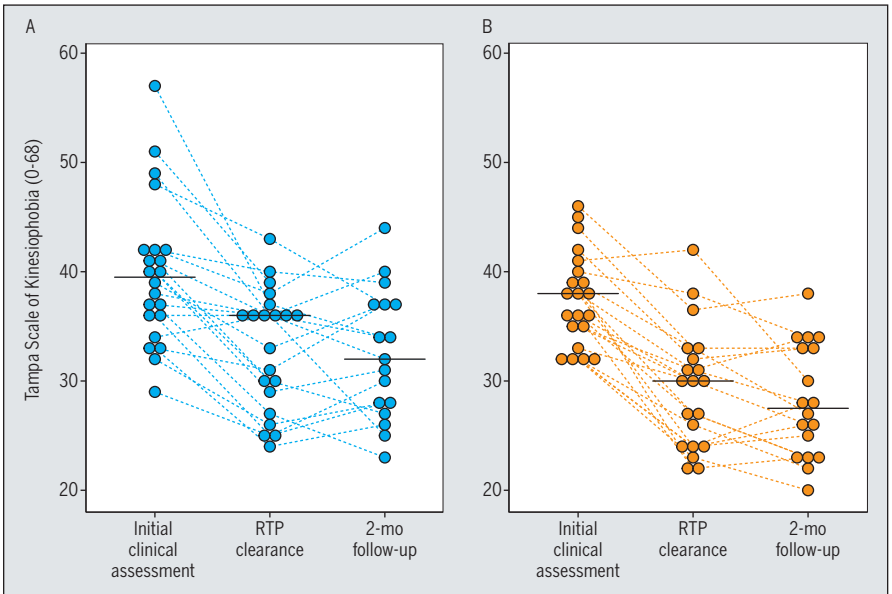

FIGURE 6. Fear of movement on the Tampa Scale of Kinesiophobia within (A) the pain-free group and (B) the pain-threshold group at the initial clinical assessment, RTP clearance, and 2-month follow-up. Each dot represents an individual participant, dotted lines indicate change over time, and the solid horizontal lines show the group medians. Abbreviation: RTP, return to play.

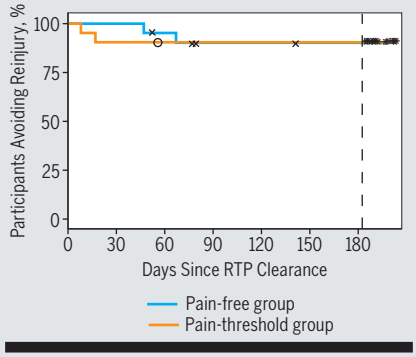

FIGURE 7. The percentage of participants avoiding reinjury in the 6 months following RTP clearance. The vertical dotted line indicates 182.5 days (6 months) from RTP clearance. The "X" symbol indicates the 4 participants in the pain-free group who were lost to follow-up and the last time point they were contactable. The "O" symbol represents the 1 participant in the pain-threshold group who suffered a knee injury during the 6-month follow-up period. The * symbols indicate the 15 participants in the pain-free group and the 18 participants in the pain-threshold group who completed 6-month follow-up without reinjury. Abbreviation: RTP, return to play.

of acute HSI using solely clinical assessments as described in this study, which enhances the ecological validity of the current findings. Return to full sporting activity was not reported, and it could be argued that the impact of pain-free and pain-threshold rehabilitation on complete recovery time is unclear. Time to RTP clearance using evidence-based criteria was chosen to reduce the influence of external factors on the primary outcome measure, such as pressure to return to different levels of sport participation, time of sports season, and team selection decisions from different coaches. Consequently, the primary outcome measure of time taken to achieve RTP clearance is more internally than externally valid.

CONCLUSION

Performing and progressing a standardized rehabilitation protocol up to a pain threshold did not accelerate RTP clearance compared to adhering to pain-free limits following acute HSI. However, pain-threshold rehabilitation did not cause any adverse events and resulted in greater recovery of isometric knee flexor strength and better maintenance of BFLH fascicle length improvements. Therefore, the conventional clinical practice of pain avoidance during HSI rehabilitation may not be necessary. ◉

KEY POINTS

FINDINGS: Pain-threshold rehabilitation did not accelerate return-to-play clearance compared to pain-free rehabilitation following acute hamstring strain injury, but did result in greater recovery of isometric knee flexor strength at 90°/90° of hip/knee flexion and better maintenance of biceps femoris long head fascicle length improvements.

IMPLICATIONS: The conventional practice of pain avoidance during hamstring strain injury rehabilitation may not be necessary, and emphasizing early progression of eccentric loading and long-length exercises appears to adequately address deficits in knee flexor strength and biceps femoris long head fascicle length.

CAUTION: The relatively small sample size and low number of reinjuries make it difficult to determine the impact of pain-free and pain-threshold rehabilitation on this outcome.

STUDY DETAILS

TRIAL REGISTRATION: Australian New Zealand Clinical Trials Registry (ACTRN12616000307404).

AUTHOR CONTRIBUTIONS: All authors met criteria for authorship based on the International Committee of Medical Journal Editors.

DATA SHARING: Deidentified data for outcomes reported in this manuscript are available on request from the corresponding author for research purposes.

PATIENT AND PUBLIC INVOLVEMENT: Participants and the public were not involved in the study design, conduct, interpretation, or translation of the research.

REFERENCES

1. Alonso-Fernandez D, Docampo-Blanco P, Martinez-Fernandez J. Changes in muscle architecture of biceps femoris induced by eccentric strength training with nordic hamstring exercise. *Scand J Med Sci Sports*. 2018;28:88-94. https://

doi.org/10.1111/sms.12877
2. Ardern CL, Glasgow P, Schneiders A, et al. 2016 consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med*. 2016;50:853-864. https://doi.org/10.1136/bjsports-2016-096278
3. Askling C, Karlsson J, Thorstensson A. Hamstring injury occurrence in elite soccer players after preseason strength training with eccentric overload. *Scand J Med Sci Sports*. 2003;13:244-250. https://doi.org/10.1034/j.1600-0838.2003.00312.x
4. Askling C, Saartok T, Thorstensson A. Type of acute hamstring strain affects flexibility, strength, and time to return to pre-injury level. *Br J Sports Med*. 2006;40:40-44. https://doi.org/10.1136/bjsm.2005.018879
5. Askling CM, Tengvar M, Tarassova O, Thorstensson A. Acute hamstring injuries in Swedish elite sprinters and jumpers: a prospective randomised controlled clinical trial comparing two rehabilitation protocols. *Br J Sports Med*. 2014;48:532-539. https://doi.org/10.1136/bjsports-2013-093214
6. Askling CM, Tengvar M, Thorstensson A. Acute hamstring injuries in Swedish elite football: a prospective randomised controlled clinical trial comparing two rehabilitation protocols. *Br J Sports Med*. 2013;47:953-959. https://doi.org/10.1136/bjsports-2013-092165
7. Bandholm T, Thorborg K, Lunn TH, Kehlet H, Jakobsen TL. Knee pain during strength training shortly following fast-track total knee arthroplasty: a cross-sectional study. *PLoS One*. 2014;9:e91107. https://doi.org/10.1371/journal.pone.0091107
8. Bates D, Mächler M, Bolker B, Walker S. Fitting linear mixed-effects models using lme4. *J Stat Softw*. 2015;67:i01. https://doi.org/10.18637/jss.v067.i01
9. Bayer ML, Magnusson SP, Kjaer M. Early versus delayed rehabilitation after acute muscle injury [letter]. *N Engl J Med*. 2017;377:1300-1301. https://doi.org/10.1056/NEJMc1708134
10. Bourne MN, Duhig SJ, Timmins RG, et al. Impact of the Nordic hamstring and hip extension exercises on hamstring architecture and morphology: implications for injury prevention. *Br J Sports Med*. 2017;51:469-477. https://doi.org/10.1136/bjsports-2016-096130
11. Bourne MN, Opar DA, Williams MD, Shield AJ. Eccentric knee flexor strength and risk of hamstring injuries in rugby union: a prospective study. *Am J Sports Med*. 2015;43:2663-2670. https://doi.org/10.1177/0363546515599633
12. Bourne MN, Timmins RG, Opar DA, et al. An evidence-based framework for strengthening exercises to prevent hamstring injury. *Sports Med*. 2018;48:251-267. https://doi.org/10.1007/s40279-017-0796-x
13. Bourne MN, Williams MD, Opar DA, Al Najjar A, Kerr GK, Shield AJ. Impact of exercise selection on hamstring muscle activation. *Br J Sports Med*. 2017;51:1021-1028. https://doi.org/10.1136/bjsports-2015-095739
14. Brooks JH, Fuller CW, Kemp SP, Reddin DB. Incidence, risk, and prevention of hamstring muscle injuries in professional rugby union. *Am J Sports Med*. 2006;34:1297-1306. https://doi.org/10.1177/0363546505286022
15. Creighton DW, Shrier I, Shultz R, Meeuwisse WH, Matheson GO. Return-to-play in sport: a decision-based model. *Clin J Sport Med*. 2010;20:379-385. https://doi.org/10.1097/JSM.0b013e3181f3c0fe
16. De Vos RJ, Reurink G, Goudswaard GJ, Moen MH, Weir A, Tol JL. Clinical findings just after return to play predict hamstring re-injury, but baseline MRI findings do not. *Br J Sports Med*. 2014;48:1377-1384. https://doi.org/10.1136/bjsports-2014-093737
17. Ekstrand J, Hägglund M, Waldén M. Injury incidence and injury patterns in professional football: the UEFA injury study. *Br J Sports Med*. 2011;45:553-558. https://doi.org/10.1136/bjsm.2009.060582
18. Elliott MC, Zarins B, Powell JW, Kenyon CD. Hamstring muscle strains in professional football players: a 10-year review. *Am J Sports Med*. 2011;39:843-850. https://doi.org/10.1177/0363546510394647
19. Fernandes TL, Pedrinelli A, Hernandez AJ. Muscle injury – physiopathology, diagnosis, treatment and clinical presentation. *Rev Bras Ortop*. 2011;46:247-255. https://doi.org/10.1016/S2255-4971(15)30190-7
20. Freckleton G, Pizzari T. Risk factors for hamstring muscle strain injury in sport: a systematic review and meta-analysis. *Br J Sports Med*. 2013;47:351-358. https://doi.org/10.1136/bjsports-2011-090664
21. Frohm A, Saartok T, Halvorsen K, Renström P. Eccentric treatment for patellar tendinopathy: a prospective randomised short-term pilot study of two rehabilitation protocols. *Br J Sports Med*. 2007;41:e7. https://doi.org/10.1136/bjsm.2006.032599
22. Fyfe JJ, Opar DA, Williams MD, Shield AJ. The role of neuromuscular inhibition in hamstring strain injury recurrence. *J Electromyogr Kinesiol*. 2013;23:523-530. https://doi.org/10.1016/j.jelekin.2012.12.006
23. Hägglund M, Waldén M, Magnusson H, Kristenson K, Bengtsson H, Ekstrand J. Injuries affect team performance negatively in professional football: an 11-year follow-up of the UEFA Champions League injury study. *Br J Sports Med*. 2013;47:738-742. https://doi.org/10.1136/bjsports-2013-092215
24. Hamid MS, Ali MR, Yusof A. Interrater and intrarater reliability of the active knee extension (AKE) test among healthy adults. *J Phys Ther Sci*. 2013;25:957-961. https://doi.org/10.1589/jpts.25.957
25. Hamilton B, Tol JL, Almusa E, et al. Platelet-rich plasma does not enhance return to play in hamstring injuries: a randomised controlled trial. *Br J Sports Med*. 2015;49:943-950. https://doi.org/10.1136/bjsports-2015-094603
26. Heiderscheit BC, Sherry MA, Silder A, Chumanov ES, Thelen DG. Hamstring strain injuries: recommendations for diagnosis, rehabilitation, and injury prevention. *J Orthop Sports Phys Ther*. 2010;40:67-81. https://doi.org/10.2519/jospt.2010.3047
27. Herrington L. Patients with hamstring muscle strains returning to sport in less than 14 days: a case report of treatment used. *Phys Ther Sport*. 2000;1:137-138. https://doi.org/10.1054/ptsp.2000.0021
28. Hickey J, Shield AJ, Williams MD, Opar DA. The financial cost of hamstring strain injuries in the Australian Football League. *Br J Sports Med*. 2014;48:729-730. https://doi.org/10.1136/bjsports-2013-092884
29. Hickey JT, Hickey PF, Maniar N, et al. A novel apparatus to measure knee flexor strength during various hamstring exercises: a reliability and retrospective injury study. *J Orthop Sports Phys Ther*. 2018;48:72-80. https://doi.org/10.2519/jospt.2018.7634
30. Hickey JT, Timmins RG, Maniar N, Williams MD, Opar DA. Criteria for progressing rehabilitation and determining return-to-play clearance following hamstring strain injury: a systematic review. *Sports Med*. 2017;47:1375-1387. https://doi.org/10.1007/s40279-016-0667-x
31. Jacobsen P, Witvrouw E, Muxart P, Tol JL, Whiteley R. A combination of initial and follow-up physiotherapist examination predicts physician-determined time to return to play after hamstring injury, with no added value of MRI. *Br J Sports Med*. 2016;50:431-439. https://doi.org/10.1136/bjsports-2015-095073
32. Järvinen M. Healing of a crush injury in rat striated muscle. 2. A histological study of the effect of early mobilization and immobilization on the repair processes. *Acta Pathol Microbiol Scand A*. 1975;83:269-282. https://doi.org/10.1111/j.1699-0463.1975.tb01874.x
33. Järvinen M. Healing of a crush injury in rat striated muscle. 3. A micro-angiographical study of the effect of early mobilization and immobilization on capillary ingrowth. *Acta Pathol Microbiol Scand A*. 1976;84:85-94. https://doi.org/10.1111/j.1699-0463.1976.tb00114.x
34. Järvinen M. Healing of a crush injury in rat striated muscle. 4. Effect of early mobilization and immobilization on the tensile properties of gastrocnemius muscle. *Acta Chir Scand*. 1976;142:47-56.
35. Järvinen M, Sorvari T. Healing of a crush injury in rat striated muscle. 1. Description and testing of a new method of inducing a standard injury to the calf muscles. *Acta Pathol Microbiol Scand A*. 1975;83:259-265. https://doi.org/10.1111/j.1699-0463.1975.tb01383.x
36. Järvinen TA, Järvinen TL, Kääriäinen M, et al. Muscle injuries: optimising recovery. *Best Pract Res Clin Rheumatol*. 2007;21:317-331. https://doi.org/10.1016/j.berh.2006.12.004
37. Järvinen TA, Järvinen TL, Kääriäinen M, Kalimo H, Järvinen M. Muscle injuries: biology and

treatment. *Am J Sports Med*. 2005;33:745-764. https://doi.org/10.1177/0363546505274714
38. Järvinen TA, Kääriäinen M, Järvinen M, Kalimo H. Muscle strain injuries. *Curr Opin Rheumatol*. 2000;12:155-161. https://doi.org/10.1097/00002281-200003000-00010
39. Kannus P. Immobilization or early mobilization after an acute soft-tissue injury? *Phys Sportsmed*. 2000;28:55-63. https://doi.org/10.3810/psm.2000.03.775
40. Kilcoyne KG, Dickens JF, Keblish D, Rue JP, Chronister R. Outcome of grade I and II hamstring injuries in intercollegiate athletes: a novel rehabilitation protocol. *Sports Health*. 2011;3:528-533. https://doi.org/10.1177/1941738111422044
41. Kujala UM, Orava S, Järvinen M. Hamstring injuries. Current trends in treatment and prevention. *Sports Med*. 1997;23:397-404. https://doi.org/10.2165/00007256-199723060-00005
42. Lee MJ, Reid SL, Elliott BC, Lloyd DG. Running biomechanics and lower limb strength associated with prior hamstring injury. *Med Sci Sports Exerc*. 2009;41:1942-1951. https://doi.org/10.1249/MSS.0b013e3181a55200
43. Maffulli N, Oliva F, Frizziero A, et al. ISMuLT guidelines for muscle injuries. *Muscles Ligaments Tendons J*. 2013;3:241-249.
44. Maniar N, Shield AJ, Williams MD, Timmins RG, Opar DA. Hamstring strength and flexibility after hamstring strain injury: a systematic review and meta-analysis. *Br J Sports Med*. 2016;50:909-920. https://doi.org/10.1136/bjsports-2015-095311
45. Mendiguchia J, Martinez-Ruiz E, Edouard P, et al. A multifactorial, criteria-based progressive algorithm for hamstring injury treatment. *Med Sci Sports Exerc*. 2017;49:1482-1492. https://doi.org/10.1249/MSS.0000000000001241
46. Mikkelsen LR, Petersen AK, Mechlenburg I, Mikkelsen S, Søballe K, Bandholm T. Description of load progression and pain response during progressive resistance training early after total hip arthroplasty: secondary analyses from a randomized controlled trial. *Clin Rehabil*. 2017;31:11-22. https://doi.org/10.1177/0269215516628305
47. Moseley GL. Reconceptualising pain according to modern pain science. *Phys Ther Rev*. 2007;12:169-178. https://doi.org/10.1179/108331907X223010
48. Nikolaou PK, Macdonald BL, Glisson RR, Seaber AV, Garrett WE, Jr. Biomechanical and histological evaluation of muscle after controlled strain injury. *Am J Sports Med*. 1987;15:9-14. https://doi.org/10.1177/036354658701500102
49. Opar DA, Piatkowski T, Williams MD, Shield AJ. A novel device using the Nordic hamstring exercise to assess eccentric knee flexor strength: a reliability and retrospective injury study. *J Orthop Sports Phys Ther*. 2013;43:636-640. https://doi.org/10.2519/jospt.2013.4837
50. Opar DA, Williams MD, Shield AJ. Hamstring strain injuries: factors that lead to injury and reinjury. *Sports Med*. 2012;42:209-226. https://doi.org/10.2165/11594800-000000000-00000
51. Opar DA, Williams MD, Timmins RG, Dear NM, Shield AJ. Knee flexor strength and bicep femoris electromyographical activity is lower in previously strained hamstrings. *J Electromyogr Kinesiol*. 2013;23:696-703. https://doi.org/10.1016/j.jelekin.2012.11.004
52. Opar DA, Williams MD, Timmins RG, Hickey J, Duhig SJ, Shield AJ. Eccentric hamstring strength and hamstring injury risk in Australian footballers. *Med Sci Sports Exerc*. 2015;47:857-865. https://doi.org/10.1249/MSS.0000000000000465
53. Orchard JW, Seward H, Orchard JJ. Results of 2 decades of injury surveillance and public release of data in the Australian Football League. *Am J Sports Med*. 2013;41:734-741. https://doi.org/10.1177/0363546513476270
54. Pollard CW, Opar DA, Williams MD, Bourne MN, Timmins RG. Razor hamstring curl and Nordic hamstring exercise architectural adaptations: impact of exercise selection and intensity. *Scand J Med Sci Sports*. 2019;29:706-715. https://doi.org/10.1111/sms.13381
55. Presland JD, Timmins RG, Bourne MN, Williams MD, Opar DA. The effect of Nordic hamstring exercise training volume on biceps femoris long head architectural adaptation. *Scand J Med Sci Sports*. 2018;28:1775-1783. https://doi.org/10.1111/sms.13085
56. R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2014.
57. Reurink G, Brilman EG, de Vos RJ, et al. Magnetic resonance imaging in acute hamstring injury: can we provide a return to play prognosis? *Sports Med*. 2015;45:133-146. https://doi.org/10.1007/s40279-014-0243-1
58. Reurink G, Goudswaard GJ, Moen MH, et al. Rationale, secondary outcome scores and 1-year follow-up of a randomised trial of platelet-rich plasma injections in acute hamstring muscle injury: the Dutch Hamstring Injection Therapy study. *Br J Sports Med*. 2015;49:1206-1212. https://doi.org/10.1136/bjsports-2014-094250
59. Reurink G, Goudswaard GJ, Oomen HG, et al. Reliability of the active and passive knee extension test in acute hamstring injuries. *Am J Sports Med*. 2013;41:1757-1761. https://doi.org/10.1177/0363546513490650
60. Schneider-Kolsky ME, Hoving JL, Warren P, Connell DA. A comparison between clinical assessment and magnetic resonance imaging of acute hamstring injuries. *Am J Sports Med*. 2006;34:1008-1015. https://doi.org/10.1177/0363546505283835
61. Severini G, Holland D, Drumgoole A, Delahunt E, Ditroilo M. Kinematic and electromyographic analysis of the Askling L-Protocol for hamstring training. *Scand J Med Sci Sports*. 2018;28:2536-2546. https://doi.org/10.1111/sms.13288
62. Sherry MA, Johnston TS, Heiderscheit BC. Rehabilitation of acute hamstring strain injuries. *Clin Sports Med*. 2015;34:263-284. https://doi.org/10.1016/j.csm.2014.12.009
63. Shrier I. Strategic Assessment of Risk and Risk Tolerance (StARRT) framework for return-to-play decision-making. *Br J Sports Med*. 2015;49:1311-1315. https://doi.org/10.1136/bjsports-2014-094569
64. Silbernagel KG, Thomeé R, Eriksson BI, Karlsson J. Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with Achilles tendinopathy: a randomized controlled study. *Am J Sports Med*. 2007;35:897-906. https://doi.org/10.1177/0363546506298279
65. Silbernagel KG, Thomeé R, Thomeé P, Karlsson J. Eccentric overload training for patients with chronic Achilles tendon pain – a randomised controlled study with reliability testing of the evaluation methods. *Scand J Med Sci Sports*. 2001;11:197-206. https://doi.org/10.1034/j.1600-0838.2001.110402.x
66. Silder A, Sherry MA, Sanfilippo J, Tuite MJ, Hetzel SJ, Heiderscheit BC. Clinical and morphological changes following 2 rehabilitation programs for acute hamstring strain injuries: a randomized clinical trial. *J Orthop Sports Phys Ther*. 2013;43:284-299. https://doi.org/10.2519/jospt.2013.4452
67. Smith BE, Hendrick P, Smith TO, et al. Should exercises be painful in the management of chronic musculoskeletal pain? A systematic review and meta-analysis. *Br J Sports Med*. 2017;51:1679-1687. https://doi.org/10.1136/bjsports-2016-097383
68. Therneau TM. survival: Survival Analysis. Available at: https://cran.r-project.org/web/packages/survival/index.html. Accessed January 2, 2020.
69. Thomeé R. A comprehensive treatment approach for patellofemoral pain syndrome in young women. *Phys Ther*. 1997;77:1690-1703. https://doi.org/10.1093/ptj/77.12.1690
70. Thorstensson CA, Roos EM, Petersson IF, Ekdahl C. Six-week high-intensity exercise program for middle-aged patients with knee osteoarthritis: a randomized controlled trial [ISRCTN20244858]. *BMC Musculoskelet Disord*. 2005;6:27. https://doi.org/10.1186/1471-2474-6-27
71. Timmins RG, Bourne MN, Shield AJ, Williams MD, Lorenzen C, Opar DA. Short biceps femoris fascicles and eccentric knee flexor weakness increase the risk of hamstring injury in elite football (soccer): a prospective cohort study. *Br J Sports Med*. 2016;50:1524-1535. https://doi.org/10.1136/bjsports-2015-095362
72. Timmins RG, Ruddy JD, Presland J, et al. Architectural changes of the biceps femoris long head after concentric or eccentric training. *Med Sci Sports Exerc*. 2016;48:499-508. https://doi.org/10.1249/MSS.0000000000000795
73. Timmins RG, Shield AJ, Williams MD, Lorenzen C, Opar DA. Biceps femoris long head architecture: a reliability and retrospective injury study. *Med Sci Sports Exerc*. 2015;47:905-913. https://doi.org/10.1249/MSS.0000000000000507
74. Tol JL, Hamilton B, Eirale C, Muxart P, Jacobsen P, Whiteley R. At return to play following hamstring injury the majority of professional football players have residual isokinetic deficits. *Br J Sports Med*. 2014;48:1364-1369. https://doi.org/10.1136/

bjsports-2013-093016
75. Tsaklis P, Malliaropoulos N, Mendiguchia J, et al. Muscle and intensity based hamstring exercise classification in elite female track and field athletes: implications for exercise selection during rehabilitation. *Open Access J Sports Med*. 2015;6:209-217. https://doi.org/10.2147/OAJSM.S79189
76. Valle X, Tol JL, Hamilton B, et al. Hamstring muscle injuries, a rehabilitation protocol purpose. *Asian J Sports Med*. 2015;6:e25411.
77. van der Horst N, Smits DW, Petersen J, Goedhart EA, Backx FJ. The preventive effect of the Nordic hamstring exercise on hamstring injuries in amateur soccer players: study protocol for a randomised controlled trial. *Inj Prev*. 2014;20:e8. https://doi.org/10.1136/injuryprev-2013-041092
78. van der Horst N, van de Hoef S, Reurink G, Huisstede B, Backx F. Return to play after hamstring injuries: a qualitative systematic review of definitions and criteria. *Sports Med*. 2016;46:899-912. https://doi.org/10.1007/s40279-015-0468-7
79. van Dyk N, Bahr R, Whiteley R, et al. Hamstring and quadriceps isokinetic strength deficits are weak risk factors for hamstring strain injuries: a 4-year cohort study. *Am J Sports Med*. 2016;44:1789-1795. https://doi.org/10.1177/0363546516632526
80. van Dyk N, Behan FP, Whiteley R. Including the Nordic hamstring exercise in injury prevention programmes halves the rate of hamstring injuries: a systematic review and meta-analysis of 8459 athletes. *Br J Sports Med*. 2019;53:1362-1370. https://doi.org/10.1136/bjsports-2018-100045
81. Wangensteen A, Almusa E, Boukarroum S, et al. MRI does not add value over and above patient history and clinical examination in predicting time to return to sport after acute hamstring injuries: a prospective cohort of 180 male athletes. *Br J Sports Med*. 2015;49:1579-1587. https://doi.org/10.1136/bjsports-2015-094892
82. Wangensteen A, Tol JL, Witvrouw E, et al. Hamstring reinjuries occur at the same location and early after return to sport: a descriptive study of MRI-confirmed reinjuries. *Am J Sports Med*. 2016;44:2112-2121. https://doi.org/10.1177/0363546516646086
83. Whiteley R, van Dyk N, Wangensteen A, Hansen C. Clinical implications from daily physiotherapy examination of 131 acute hamstring injuries and their association with running speed and rehabilitation progression. *Br J Sports Med*. 2018;52:303-310. https://doi.org/10.1136/bjsports-2017-097616