Appendix B

Proximal hamstring tendon avulsions: comparable clinical outcomes of operative and non-operative treatment at one-year follow-up using a shared decision-making model.

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Surgical technique

Operative reattachment of the proximal hamstrings tendons was jointly performed by a senior orthopaedic and trauma surgeon (GK and RP) under general anaesthesia in prone position with padding under the chest, pelvis, knees, and ankles. A horizontal incision was made in the gluteal crease and extended vertically, followed by a vertical incision through subcuticular tissue and fascia. Upon opening the hematoma, the sciatic nerve was identified and protected. The proximal hamstring tendons were identified and any scar tissue hindering free motion of the proximal hamstrings was removed. The ischial tuberosity was identified and debrided, removing any scar tissue and tendon remnants. Three titanium suture anchors (Mitek G2, Raynham, MA) were inserted into the ischial tuberosity and the proximal hamstring tendons were secured to the bone in knee flexion. By varying the degree of knee flexion after reattachment, the surgeons assessed tension on the proximal hamstring attachment. Based on this assessment, a cast was applied in the operation room. Post-operatively, cast immobilization was used for two weeks followed by a hinged knee brace for four weeks that limited full knee extension but allowed knee flexion. The brace was set at 30 degrees knee flexion and gradually (10 degrees per week) progressed towards full knee extension. Post-operatively, a criteria-based rehabilitation programme was initiated as soon as the knee brace was applied.

Rehabilitation protocol

Adapted from: Sherry & UW Health Sports Medicine physician group. Rehabilitation Guidelines Following Proximal Hamstring Primary Repair [1]

Phase I – Protective phase (only applicable post-operatively)

Appointments	Start 7-10 days after surgery, 2+ sessions/week
Rehabilitation goals	• Protection of the repaired tendon(s) • Pain control Week 1: Protective phase Week 2-6: Activation of affected hamstrings while protecting repair Week 6: Start weightbearing
Weight bearing	• Use of crutches as long as a brace/cast is used • Post-operative weeks 0-2: Cast immobilization • Post-operative weeks 3-6: Hinged knee brace • Post-operative weeks 6: Touch down weight bearing. Gradual increase in weightbearing up to weightbearing as tolerated
Immobilisation	• Cast immobilization for 2 weeks, followed by a hinged knee brace limiting knee extension. Knee extension limit is started at 30° knee flexion, which is reduced by 10°per week. In week 6, the knee brace is set at 0° for one week to avoid knee hyperextension
Precautions	• Avoid hip flexion coupled with knee extension • Avoid unsafe surfaces and environments
Suggested therapeutic exercises	• Quadriceps and gluteus isometric exercises • Ankle pumps • Abdominal isometrics • Passive knee range of motion (ROM) with no hip flexion during knee extension • Week 3: Start of electrical muscle stimulation of the hamstrings • Hip abduction, hip extension, and balance exercises • Scar mobilization
Cardiovascular exercise	Upper body circuit training or upper body ergometer (UBE)
Progression criteria	6 weeks post-operative

Phase II

Appointments	2+ sessions/week
Rehabilitation goals	• Normalize gait • Good control and no pain with functional movements, including step up/down, squat, partial lunge (do not exceed 60° of knee flexion)
Precautions	• Avoid dynamic stretching • Avoid loading the hip at deep flexion angles • No impact or running
Suggested therapeutic exercises	• Non-impact balance and proprioceptive drills, beginning with double leg and gradually progressing to single leg • Stationary bike • Gait training using an AlterG anti-gravity treadmill • Electrical muscle stimulation of the hamstrings • Hamstring strengthening – start by avoidance of lengthened hamstring position (hip flexion combined with knee extension) by working hip extension and knee flexion moments separately; begin with isometric and concentric strengthening with hamstring sets, heel slides, double leg bridge, standing leg extensions, and physioball curls • Hip and core strengthening
Cardiovascular exercise	• Upper body circuit training or UBE
Progression criteria	• Normal gait on all surfaces • Ability to carry out functional movements without unloading the affected leg or pain while demonstrating good control

Phase III

Appointments	2+ sessions/week
Rehabilitation goals	Good control and no pain with sport- and work-specific movements, including impact
Precautions	• No pain during strength training • Post-activity soreness should resolve within 24 hours
Suggested therapeutic exercises	• Continue hamstring strengthening. Progress toward strengthening in lengthened hamstring positions; begin to incorporate eccentric strengthening with single leg forward leans, single leg bridge lowering, prone foot catches, and assisted Nordic curls • Hip and core strengthening • Impact control exercises beginning 2 feet to 2 feet, progressing from 1 foot to the other and then 1 foot to same foot • Movement control exercise beginning with low velocity, single-plane activities and progressing to higher velocity, multi-plane activities • Initiate running drills, but no sprinting until Phase IV
Cardiovascular exercise	Biking, elliptical machine, Stairmaster, swimming, and running using AlterG anti-gravity treadmill and ultimately at bodyweight.
Progression criteria	• Dynamic neuromuscular control with multi-plane activities at low to medium velocity without pain or swelling

Phase IV

Appointments	2+ sessions/week
Rehabilitation goals	Good control and no pain with sport- and work-specific movements, including impact
Precautions	• No pain during strength training • Post-activity soreness should resolve within 24 hours
Suggested therapeutic exercises	• Continue hamstring strengthening. Progress toward higher velocity strengthening and reaction in lengthened positions, including eccentric strengthening with single leg forward leans with medicine ball, single leg dead lifts with dumbbells, single leg bridge curls on physioball, resisted running foot catches, and Nordic curls • Running and sprinting mechanics and drills • Hip and core strengthening • Impact control exercises beginning 2 feet to 2 feet, progressing from 1 foot to other and then 1 foot to same foot • Movement control exercise beginning with low velocity, single plane activities and progressing to higher velocity, multi-plane activities • Sport/work specific balance and proprioceptive drills • Stretching for patient specific muscle imbalances
Cardiovascular exercise	Replicate sport- or work-specific energy demands
Progression criteria	• Dynamic neuromuscular control with multi-plane activities at high velocity without pain or swelling • Pain-free and unrestricted participation in work- or sport-specific activities

Questionnaires

Questionnaires included the Perth Hamstring Assessment Tool (PHAT)[2], Proximal Hamstring Injury Questionnaire (PHIQ)[3], EQ-5D-3L, and Tegner Activity Scale (TAS)[4]. The PHAT (0-100, a higher score corresponds with better outcome) consists of four questions on symptoms of pain/discomfort and level of activity specific for proximal hamstring tendon injury. It has been validated and has high reproducibility (ICC: 0.84). The minimal detectable change was determined at 16.4 points[2]. The PHIQ is a hamstring avulsion-specific questionnaire that surveys proximal hamstring tendon-specific symptoms, functional restrictions, subjective rate of recovery, and sports participation. It consists of 11 predominantly nominal questions. The EQ-5D-3L is a quality-of-life questionnaire consisting of five nominal questions surveying different domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), and one question to rate quality of life on a visual analogue scale (0-100, a higher score corresponds with better outcome). The TAS expresses the level of activity as a number (0-10, a higher score indicates a higher level of activity).

Clinical tests

Hamstring flexibility

Tests to evaluate hamstring flexibility and strength were carried out by five male testers. All received training and practiced until they were familiar with the tests and able to carry out the testing independently. Hamstring flexibility was measured using the Goniometer app for iOS [5] in two supine positions: the passive straight leg raise (PSLR) and active knee extension test (AKET). Inter-rater reliability for the PSLR and AKET are moderate and good with intraclass correlation coefficients (ICCs) of 0.74 [6] and 0.89 [7]. The PSLR was performed by passively lifting the leg while ensuring full knee extension with the goniometer mid-shin on the anterior tibial margin. We recorded range of motion (i.e. hip flexion) between starting position and the position where the patient reported onset of pain, maximal tolerable stretch, or when the examiner noted start of pelvic rotation. The AKET was performed by positioning the examined leg in 90 degrees hip and knee flexion. The patient was asked to hold the thigh in this position with both hands just proximal to the knee and to actively extend the knee. Range of motion (i.e. knee extension) from starting position to the point of onset of pain or maximal tolerable stretch was recorded.

Isometric knee flexor strength assessment

Isometric knee flexor strength was assessed with a Hoggan MicroFET2 hand-held dynamometer (Hoggan Scientific, LLC, Salt Lake City, UT, USA). We measured strength in three positions: prone 0/90 (°hip flexion/°knee flexion), prone 0/15, and supine 90/90 [8,9]. Previously reported inter-rater reliability for these positions is good with ICCs of 0.76-0.84 [8,9]. Patients were verbally encouraged to perform a maximal voluntary contraction for 3 seconds while the tester held the dynamometer in place. We recorded the best of three efforts per position per leg in Newtons. If a patient reported onset of pain (pain score ≥3/10), that specific measurement was terminated.

MRI protocol

Images were acquired using a Philips 3.0T Ingenia system and an anterior body coil. The MRI protocol in our center included coronal T2 mDixon (repetition time [TR]/echo time [TE] 2000-6000/60 ms, field of view [FOV] 450x450 mm, slice thickness 4 mm, and matrix 820x651) and axial T2 TSE (proximal and distal, TR/TE 2500-6000/70 ms, FOV 450x250 mm, slice thickness 2.5 mm, and matrix 900x360) and PD mDixon drive (TR/TE 2000-3500/'shortest' ms, FOV 400x450 mm, slice thickness 3.5 mm, and matrix 800x699) images. A range in TR/TE indicates that actual repetition time will be calculated based on the number of slices. 'Shortest' TR/TE indicates that the shortest possible TE will be used.

Statistical analysis

Covariates included in post-hoc analysis

Age, level of participation, days from injury to start of treatment, hamstring flexibility, isometric hamstring strength, side of injury, tendon(s) with proximal full-thickness free tendon discontinuity, tendon retraction, sciatic nerve aspect, Tegner Activity Scale score (before injury).

Post-hoc analysis: Time variables as covariates

As between-group differences at baseline could potentially be attributed to timing of the initial visit, we repeated this sensitivity analysis with 'time between injury and initial visit' as covariate instead of 'time between injury and start of treatment', as well as the combination of both, to explore whether our choice of included time variable impacted outcome.

Using 'time between injury and initial visit' as covariate instead of 'time between injury and start of treatment': The adjusted increase in mean PHAT score after one year in the operative group was 44 (95%CI: 37-51, p<0.001) and 40 (95%CI: 32-47, p<0.001) in the non-operative group.

Using both time variables as covariates: The adjusted increase in mean PHAT score after one year in the operative group was 45 (95%CI: 36-54, p<0.001) and 39 (95%CI: 30-48, p<0.001) in the non-operative group.

Post-hoc analysis: Best- & worst-case scenario analyses

For patients lost to follow-up, data from the last observation were carried forward. Additional best-/worst-case scenario analyses were performed in which highest and lowest values were entered for missing PHAT values.

In the operative group, three of 26 (12%) patients were lost to follow-up after 6 months. In the non-operative group, one of 33 (3%) was lost to follow-up after start of treatment, one (3%) at 2 months, and one (3%) at 6 months.

In the best-case scenario analysis, unadjusted increase in PHAT score was 52 (95%CI: 44-60) for operative and 38 (95%CI: 31-45) for non-operative treatment.

In the worst-case scenario analysis, unadjusted increase in PHAT score was 40 (95%CI:28-53) for operative and 29 (95%CI: 18-40) for non-operative treatment.

In both scenarios the within-group increase was statistically significant ($p<0.001$), but there were no significant between-group differences in PHAT score at 1-year follow-up.

Estimated sample sizes for future (randomised) trials

The data from the current study may assist in sample size/power calculations for future (randomised) trials. We present estimations for sample size for superiority and non-inferiority designs below. Note that these are simple examples that may be different based on methodological and statistical considerations in future studies. Calculations were performed using nQuery (Statsols, Cork, Ireland). In these examples the significance level is set at 5% and power at 80%. For relevant between-group difference in PHAT increase we have used both 10.0, which is 10% on the PHAT scale, and 16.4, which is the MDC (minimal detectable change) [2] and thus the minimum change required to be 95% confident that real clinical change has occurred. The standard deviation for PHAT increase is 21.4, 17.7 in the operative and 22.5 in the non-operative group.

Superiority trial

In a hypothetical study with the aim of evaluating whether operative treatment is superior to non-operative treatment in terms of increase in mean PHAT score, the following sample size calculations may be used:

-In a (two-sided) Z-test for two means, a study group with 65 patients in the operative and 65 patients in the non-operative group achieves 80.4% power at the 5% significance level when the difference in PHAT increase under the alternative hypothesis is 10.0, with standard deviations in the

operative and non-operative group of 17.7 and 22.5, respectively. Assuming a dropout rate of 15%, the preferred sample size would be 154 patients.

-In a (two-sided) Z-test for two means, a study group with 24 patients in the operative and 24 patients in the non-operative group achieves 80.1% power at the 5% significance level when the difference in PHAT increase under the alternative hypothesis is 16.4, with standard deviations in the operative and non-operative group of 17.7 and 22.5, respectively. Assuming a dropout rate of 15%, the preferred sample size would be 56 patients.

Non-inferiority trial

In a hypothetical study with the aim of evaluating whether non-operative treatment is not inferior to operative treatment in terms of increase in mean PHAT score, the following sample size calculations may be used:

-A two-group (one-sided) t-test with 58 patients in the operative and 58 patients in the non-operative group achieves 80% power at the 5% significance level to reject the null hypothesis that non-operative and operative treatment are not non-inferior (the difference in means is -10.0 or farther from zero in the same direction) in favour of the alternative hypothesis that the means of the two groups are non-inferior, assuming that the expected difference in means is 0 and the common standard deviation is 21.4. Assuming a dropout rate of 15%, the preferred sample size would be 138 patients.

-A two-group (one-sided) t-test with 22 patients in the operative and 22 patients in the non-operative group achieves 80% power at the 5% significance level to reject the null hypothesis that non-operative and operative treatment are not non-inferior (the difference in means is -16.4 or farther from zero in the same direction) in favour of the alternative hypothesis that the means of the two groups are non-inferior, assuming that the expected difference in means is 0 and the common standard deviation is 21.4. Assuming a dropout rate of 15%, the preferred sample size would be 58 patients.

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