Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Breda SJ, *et al. Br J Sports Med* 2020;0:1–9. doi: 10.1136/bjsports-2020-103403

Supplementary Appendix

SUPPLEMENTAL METHODS

INFORMATION BROCHURE FOR PARTICIPANTS ALLOCATED TO PROGRESSIVE TENDON-LOADING EXERCISES (PTLE) CONSISTING OF 4 STAGES

Why exercise therapy?

Exercise therapy is an effective treatment for pain reduction and considered as the first treatment of choice for patellar tendinopathy. Conservative treatment approaches are directed at effecting changes in patellar tendon structure. Accordingly, the patellar tendon adapts to this specific loading. Inherent to the slow metabolic rate of tendons, the response to exercise therapy is usually slow, both in improving load capacity and in resolving pain.

Why progressive loading exercise therapy?

The rehabilitation process of patellar tendinopathy is designed in 4 subsequent stages – the isometric stage, isotonic stage, energy-storage stage and sport-specific exercises. These stages involve slowly progressive loading, in order to develop load tolerance of the patellar tendon before returning to sports. The duration of each stage is flexible, and determined by individual response to the isometric, isotonic or energy-storage exercises. The pain response is evaluated after 24 hours of exercise therapy using the single-leg squat pain provocation test.

Single-leg squat pain provocation test

The level of pain 24 hours after exercise is monitored using this pain provocation test. This test is administered daily, at the same time of the day, throughout the entire duration of the exercise therapy. The eccentric (downward) phase of the single-leg squat is performed by squatting down while keeping the elevated leg off the floor and a straight back. Then slowly flex the symptomatic knee to 90° or maximum angle allowed by pain. The concentric (upward) phase is performed by using both legs. The pain level that is considered acceptable is a pain rating of 3/10 or less (a score of 0 points is no pain and 10 points is the worst pain imaginable).

Pain during the exercise programme?

The exercises may induce muscle soreness, however, there should only be mild discomfort during the exercises. The level of pain that is accepted during exercise therapy and 24 hours after exercise is 3/10 or less. If the exercises provoke more pain and the symptoms persist after the performance of the exercises, the intensity of the exercises should be reduced by performing fewer repetitions and/or by reducing additional weight. If this does not resolve symptoms to the previous level, the specific exercises should be ceased temporarily. We advise continuing the exercises that can be performed without pain.

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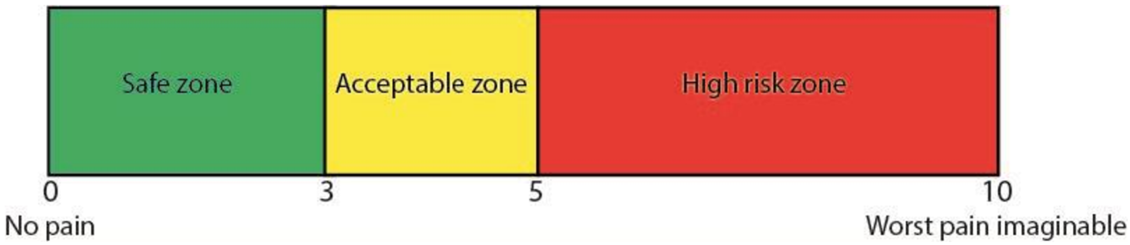

Training and competition during the exercise programme?

Modification of athletic activity (intensity, duration, frequency and type of load) will be necessary for activities that result in considerable patellar tendon pain throughout the 4 stages of the exercise programme. This means that sports activities with high patellar tendon loading or repetitive energy storage and release, such as jumping/landing, acceleration/deceleration and cutting should be significantly reduced or even avoided if this results in knee pain. These provoking sports activities should be stopped or adapted for at least 4 weeks.

Stages of the exercise programme and progression criteria

Participants will perform a 4-stage criteria-based exercise protocol within the limits of pain. This means that a maximum pain level (3/10 or less) will be maintained during all stages of the exercise programme. Each of the stages has specific goals, from reducing patellar tendon pain to increasing strength and introducing energy-storage loads. Individualized progression criteria will define the duration of each subsequent stage.

Stage 1 – Isometric stage

In the first stage, isometric loading of the patellar tendon will be applied with the aim to reduce and manage patellar tendon pain. In this stage, reduction of provoking athletic activity is advised and symptoms should resolve within 24 hours after exercise. Typically, this stage takes 1-2 weeks but may last longer in athletes with a high level of pain.

Exercises and dosage:

- Daily single-leg isometric exercises using a leg extension (preferentially) or leg press machine in mid-range knee flexion (around 60° of knee flexion), 5 repetitions of 45 seconds (with 2 minutes rest); progress to 70% maximum voluntary contraction (MVC).
- An alternative exercise that can be performed, only when no leg extension or leg press machine is available, is the isometric wall sit exercise (eventually increase the intensity of the exercise by adding external weights).
- Start with the exercises targeting risk factors for 3 times/week (Supplement 1c).

Progression criteria – Stage 2 can be initiated when:

- Stage 1 exercises can be performed within the acceptable levels of pain (3/10 or less) during 1 week
- The provocation test can be performed within the acceptable levels of pain (3/10 or less)

STAGE 1: ISOMETRIC LEG PRESS

Steps:

1. Start off sitting on a leg press machine or leg extension machine with both feet shoulder width apart against the footplate (or position both legs under the padded bar for the leg extension). Grasp the handle grips and keep your entire back firmly set against the seat for stability during the exercise.
2. Push the weight until your knees make a flexion angle of 60°. Then hold the weight for 45 seconds with only one leg, and leave the contralateral leg resting during the exercise.
3. After 45 seconds, place the contralateral leg on the footplate again and return back to the starting position using both legs.
4. Progress the weight in 5 repetitions of 45 seconds to 70% of the maximum voluntary contraction load (MVC) and rest for 2 minutes between the repetitions. Make sure to train both legs separately.

Tip: The 70% MVC load is approximately the maximum weight that can be held for 45 seconds. The MVC can be estimated using standard tables based on the maximum number of repetitions using a specific weight: https://krachttraining.info/1-rm-calculator/.

STAGE 1: ISOMETRIC WALL SIT

This exercise is an alternative for the isometric leg press or leg extension exercises.

Steps:

1. Start off sitting with your back flat against the wall. The feet are shoulder width apart and the knees are above the ankles.
2. Slide your back down the wall, until the knees are flexed in 90°.
3. Extend one leg and hold this position for 45 seconds, repeat this 5 times.
4. Rest standing upright for 2 minutes between the repetitions. Make sure to train both legs.

Tip: To increase the intensity of the exercise, you can hold a weight in different positions (guided by the maximum load that can be held for 45 seconds).

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Stage 2 – Isotonic stage

In this second stage, isotonic loading will be applied to restore lower extremity strength through functional ranges of movement. Initially, isotonic exercises should be performed within 10-60° of knee flexion and can be progressed with increased loading and finally, towards 90° of knee flexion within the limits of pain.

Exercises and dosage:

- Every second day, single-leg isotonic exercises using a leg press (preferentially) or leg extension machine.
- Initiate with loading that can be performed in 4 sets of 15 repetitions (with 2 minutes rest) within 10-60° of knee flexion, and progress to heavier loading (6 repetition maximum; RM) if the exercises can be performed within the limits of pain.
- Then increase the range of motion towards 90° of flexion and fully extended leg (without locking or hyperextending the knee) as pain permits in 4 sets of 15 repetitions (15RM) and progress again to heavier loading (6RM).
- Alternative exercises that can be performed when no leg extension or leg press machine is available, are the walking lunge and step up exercises.
- Continue the exercises targeting risk factors for 3 times/week (Supplement 1c).

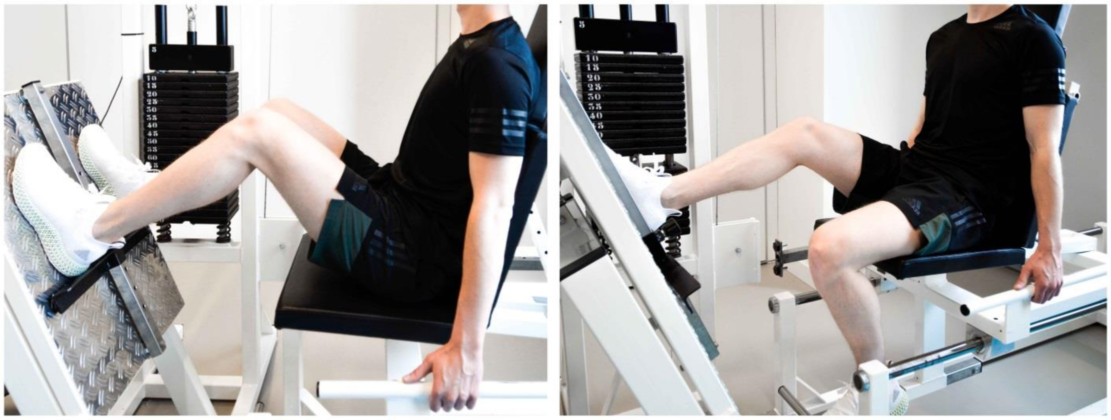
Maintenance exercises:

- Stage 1 exercises (isometric leg extension or leg press) are continued on the days when stage 2 exercises are not performed.

Progression criteria – Stage 3 can be initiated when:

- Stage 2 exercises can be performed within the acceptable levels of pain (3/10 or less) during 1 week
- The provocation test can be performed within the acceptable levels of pain (3/10 or less)
- The strength in both legs is similar, as measured by the weight that can be pushed away during the isotonic exercises. If there are bilateral symptoms, another guideline can help. In these cases. approximately 100-150% of the body weight can be accepted as sufficient external weight during the single-leg isotonic exercises. Multiply the body weight by 1.0 to 1.5 and set this weight on the leg press at the end of this stage. It should be possible to push this weight on the leg press machine in a series of 4x6 repetitions within the acceptable levels of pain (3/10 or less).

STAGE 2: ISOTONIC LEG PRESS



Steps:

1. Start off sitting on a leg press machine (or leg extension machine) with both feet shoulder width apart against the footplate (or position both legs under the padded bar for the leg extension). Grasp the handle grips on the machine and keep your entire back firmly set against the seat for stability during the exercise.
2. Push the weight with one leg to a flexion angle of 60°. Then briefly pause and slowly bring the weight back to the starting position, approximately 10° of knee flexion. Add enough weight that you can do maximum 15 repetitions (15RM). Leave the contralateral leg resting during the exercise.
3. Initiate with loading that can be performed in 4 sets of 15 repetitions. Progress the weight in 4 sets of 6 repetitions when the exercises can be performed within the acceptable limits of pain. Make sure to train both legs separately.
4. Increase the intensity of the exercise by first increasing the weight to 6RM. When heavy weights (similar to the asymptomatic leg or approximately the body weight) can be used within the limits of pain, lower the weights to the amount used with the 4 x 15 repetitions. Then increase the range of motion, by performing the exercise with a flexion angle of 90° to fully extended leg, without locking or hyperextending the knee.

Tip: First increase the load within 10-60° of knee flexion angles and then decrease the load again before starting exercises towards 90° of knee flexion and full knee extension within the limits of pain. Within this wide range, weights can be further progressed to values similar to the asymptomatic leg or to approximately the body weight.

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STAGE 2: WALKING LUNGE & STEP UPS

These exercises are an alternative for the isotonic leg press or leg extension exercises.

WALKING LUNGE

Steps:

1. Start standing upright with your feet shoulder-width apart.
2. Step forward with one leg and lower down until the front knee is flexed to 90°.
3. Without moving the front leg, step forward with the contralateral leg and repeat the lunge.
4. Increase the intensity of the exercise by adding weight in a backpack or use dumbbells.

STEP UPS

Steps:

1. Approach the box and step up by placing one foot on the box.
2. Then stretch the standing leg on the box and lift the contralateral leg up in the air to a hip flexion angle of 90°.
3. Step off the box on the same side.
4. Increase the intensity of the exercise by increasing the box height (if possible) or by adding weight in a backpack or dumbbells.

Stage 3 – Energy-storage stage

In this third stage, energy-storage loads are introduced when lower extremity muscle strength is restored using the isotonic exercises. The goal is to further increase the load tolerance of the patellar tendon and to improve power. The type of energy-storage loading exercises will be individualized to the sports performed by the athlete. For example, basketball players and volleyball players will focus more on jumping and landing, whereas football players or field hockey players will focus more on acceleration/deceleration and cutting abilities. We advise to initiate with jump squats and split jump squats for all athletes.

Exercises and dosage:

- Every third day: jump squats, split jump squats, box jumps, interval runs or zig-zag runs.
- Initiate with loading that can be performed in 3 sets of 10 repetitions (with 2 minutes rest) and progress to landing on 1 instead of 2 legs for the jumping exercises and from interval runs to zig-zag runs.
- Then increase the loading by increasing the jump height for the jumping exercises and to higher speeds for the running exercises.
- Finally, increase the load by slowly progressing to 6 sets of 10 repetitions or remove the approach run for the running exercises so that the explosive running is initiated from a standstill.
- Continue exercises targeting risk factors for 3 times/week (Supplement 1c).

Maintenance exercises:

- Stage 1 exercises (isometric exercises) are continued on each first day after stage 3 exercises are performed.
- Stage 2 exercises (isotonic exercises) are continued on each second day after stage 3 exercises are performed.

Progression criteria – Stage 4 can be initiated when:

- Stage 3 exercises can be performed within the acceptable levels of pain (3/10 or less) during 1 week
- The provocation test can be performed within the acceptable levels of pain (3/10 or less)

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STAGE 3: ENERGY-STORAGE EXERCISES

JUMP SQUAT

Steps:

1. Start standing upright with your feet shoulder-width apart.
2. Squat down while keeping your chest upright, and your head facing forward.
3. Initiate an explosive jump upwards and jump as high as you can.
4. Use your arms to add extra momentum into the jump (try to touch the ceiling!)
5. To increase the intensity of the exercise, adapt the exercise by first landing using only one leg and then increase your jump height.

Tip: Inhale as you descend into the squat and exhale as you jump.
Always keep your lower back straight and your hip in flexion during the landing phase!

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SPLIT JUMP SQUAT

Steps:

1. Start standing upright with your feet standing shoulder-width apart.
2. Initiate an explosive jump and land in a split squat position (as illustrated).
3. Without pausing, jump again and reverse the position of your legs.
4. To increase the intensity of the exercise, first increase the amount of sets performed from 3 to 6 and then increase your jump height.

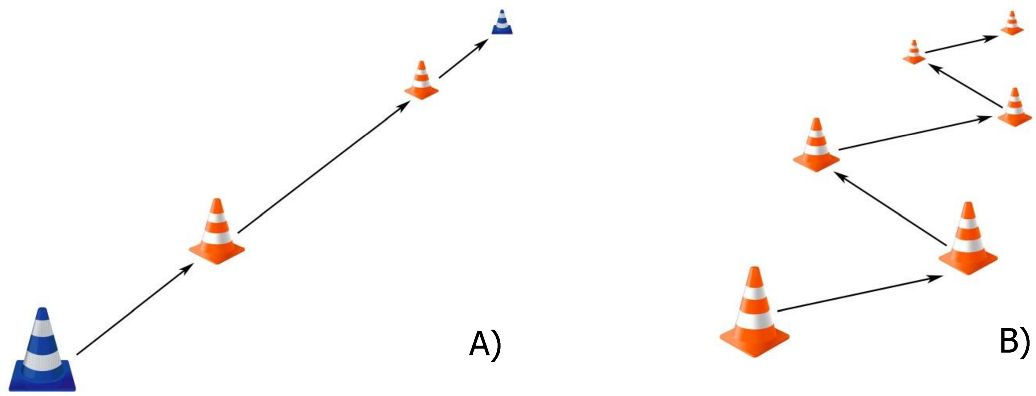
Tip: Try to land with the front leg in 90° flexion (3rd illustration).

BOX JUMPS

Steps:

1. Start standing upright with your feet standing shoulder-width apart, at a comfortable distance from the box.
2. Initiate an explosive jump and land softly on the box in a squat position (as illustrated).
3. The knee flexion angle should be minimal 60° (as illustrated) or greater (towards 90° knee flexion).
4. Without pausing, jump again and land in a squat position, in front of the box.
5. Use your arms to add extra momentum into the jump.
6. To increase the intensity of the exercise, first adapt the exercise by using only one leg and then increase the jump height.

Tip: Try to land softly on the box, don't let your feet make a lot of noise on landing.



RUNNING EXERCISES

Steps:

A) INTERVAL RUNS

1. Approach the first cone (blue) and start jogging to the first orange cone (5 meters).
2. When approaching the orange cone, start to increase running speed until the second orange cone (30 meters). Begin with 60% of your maximum sprint speed.
3. Jog to the last (blue) cone and rest for 2 minutes before repeating the exercise.
4. Increase the intensity of the exercise by increasing your sprint speed gradually to 100%.

B) ZIG-ZAG RUNS

1. Approach the first cone and sprint from cone to cone.
2. Before approaching the first cone, start jogging for 5 meters as in exercise A).
3. Increase the intensity of the exercise by increasing your sprint speed and by removing the blue cones (start sprinting from a standstill).

Tip: Don't forget to warm up for 10 minutes at an easy jog and cool down for 5 minutes.

Stage 4 – Sport-specific exercises

Athletes can gradually return to sport-specific training when all the relevant energy-storage exercises of stage 3 can be performed without provocation of knee symptoms during exercise and 24 hours after performing stage 1-2-3 exercises. The sport-specific exercises are ideally performed every 2-3 days, to allow for recovery from high tendon loading exercises. The type of sport-specific exercises will be individualized to the sports performed by the athlete. For example, basketball players could focus more on dribbling, jumping and cutting with the ball. Football players will focus more on shooting and passing exercises. If these individual exercises are not provoking pain, players could initiate group training (start 30 minutes of low intensity group training and gradually increase training time and intensity). When a minimum of 3 full group trainings can be done within the acceptable limits of pain, return to match play is allowed.

Return to competition:

- Returning to competition is only advised when the provocation test 24 hours after a minimum of 3 full group trainings can be performed within the acceptable levels of pain (3/10 or less);

Maintenance exercises:

- Continue to perform the stage 2 exercises (isotonic leg press) for at least 2x/week.
- Continue to perform the exercises targeting risk factors (Supplement 1c).

INFORMATION BROCHURE FOR PARTICIPANTS ALLOCATED TO PAIN PROVOKING ECCENTRIC EXERCISE THERAPY (EET)

Why exercise therapy?

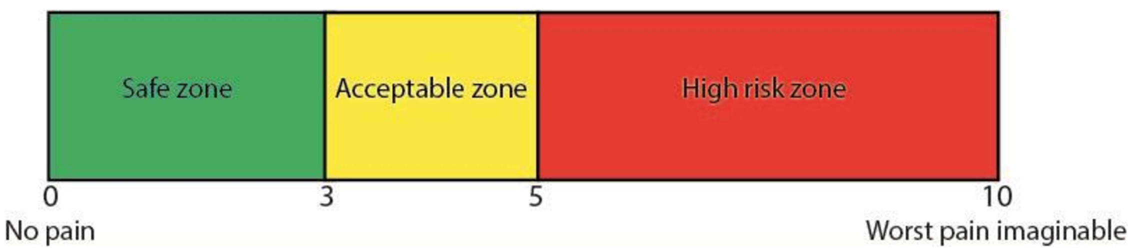
Exercise therapy is an effective treatment for pain reduction and considered as the first treatment of choice for patellar tendinopathy. Conservative treatment approaches are directed at effecting changes in patellar tendon structure. Accordingly, the patellar tendon adapts to this specific loading. Inherent to the slow metabolic rate of tendons, the response to exercise therapy is usually slow, both in improving load capacity and in resolving pain.

Why eccentric exercise therapy?

The single-leg decline squat exercise consists of a downward eccentric component performed on the symptomatic leg and an upward concentric component using mainly the contralateral leg. The exercise is typically performed on a 25° decline board to target the knee extensor mechanism more specifically than a regular squat. Studies using eccentric exercise protocols have shown positive effects. Therefore, these painful pain provoking exercises are currently considered as standard care.

Pain during the exercise programme?

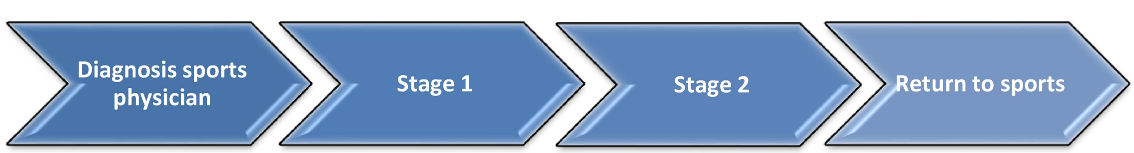
The single-leg decline squat should be performed with pain. A pain scale can be used for this purpose, with a score of 0 points reflecting no pain and 10 points as the worst pain imaginable. The minimum pain score should be 5 out of 10 during the eccentric exercises in order to be effective. If the exercises provoke persisting symptoms for more than 24 hours after the performance of the exercises and problems with normal daily functioning, the intensity of the exercises should be reduced by performing fewer repetitions and/or by reducing additional weight.



Training and competition during the exercise programme?

Modification of athletic activity (intensity, duration, frequency and type of load) will be necessary for activities that result in considerable patellar tendon pain. This means that activities with high patellar tendon loading or repetitive energy storage and release, such as jumping/landing, acceleration/deceleration and cutting abilities should be significantly reduced or even avoided if this results in knee pain. These provoking sports activities should be stopped or adapted for at least 4 weeks.

Stages of the exercise programme and progression criteria



Participants will perform a 2-stage criteria-based exercise protocol. In the first stage, pain provoking eccentric training will be applied for recovery from the knee pain. Then, sport-specific exercises will be applied in stage 2 before returning to sports.

Stage 1 – Eccentric exercises on a decline board

In this first stage, eccentric loading will be applied to restore the lower extremity strength through functional ranges of movement and with the aim to improve tendon structure. The eccentric exercises should be performed on a decline board and provoke pain during and shortly after performing the exercises.

Exercises and dosage:

- Twice-daily single-leg decline squat (around 90° of knee flexion), 3 sets of 15 repetitions per leg.
- Perform the exercises for at least 12 consecutive weeks.
- These exercises should be performed with pain (VAS ≥ 5/10). When the exercises are not painful to perform, increase the load by adding weights in a backpack or by using dumbbells.
- Start with the exercises targeting risk factors for 3 times/week (Supplement 1c).

Progression criteria – Stage 2 can be initiated when::

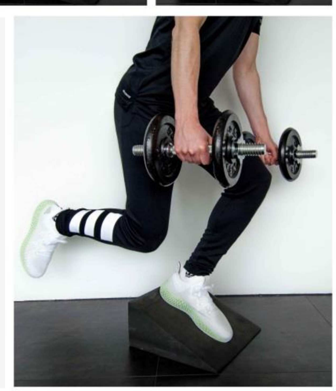
- The eccentric exercise therapy has been performed conscientiously for least 3 consecutive weeks.
- The single-leg decline squat can be performed with a maximum pain score of 3 out of 10 over 1 week using external weights.

SINGLE-LEG DECLINE SQUAT

Steps:

1. Start upright with both feet standing on the 25° decline board.
2. Remove one leg from the decline board and perform a single leg squat in 3 seconds until 60° of knee flexion.
3. Then place the contralateral leg again on the decline board and use mainly the contralateral leg to come back to an upright position.
4. To increase the load of the exercise, add weight in a backpack or use dumbbells. Start with 5 kg external weight.

Tip: This exercise should be performed with discomfort (VAS ≥ 5/10). No pain, no gain!



Stage 2 – Sport-specific exercises

Athletes can gradually return to sport-specific training when the single-leg decline squat exercises of stage 1 can be performed without provocation of knee symptoms during exercise and 24 hours after performing stage 1 exercises. The sport-specific exercises are ideally performed every 2-3 days to allow for recovery from high tendon loading exercises. The type of sport-specific exercises will be individualized to the sport performed by the athlete. For example, basketball players could focus more on dribbling, jumping and cutting with the ball. Football players will focus more on shooting and passing exercises. If these individual exercises do not provoke pain, players could initiate group training (start 30 minutes of low intensity group training and gradually increase training time and intensity). When a minimum of 3 full group trainings can be done within the acceptable limits of pain, return to match play is allowed.

Return to competition:

- Returning to competition is only advised when the single-leg decline squat 24 hours after a minimum of 3 full group trainings can be performed within the acceptable level of pain (3/10 or less);

Maintenance exercises:

- Continue to perform the single-leg decline squat exercises for 2x/week.
- Continue to perform the risk factor exercises for 3x/week (Supplement 1c).

INFORMATION BROCHURE FOR EXERCISES TARGETING RISK FACTORS, APPLICABLE TO BOTH STUDY ARMS

EXERCISES TARGETING RISK FACTORS

STRETCHING EXERCISES

Steps:

A) STANDING QUADRICEPS STRETCH EXERCISE – 3x/week, 3x 30 seconds

B) STANDING HAMSTRING STRETCH EXERCISE – 3x/week, 3x 30 seconds

C) CALF STRETCH (GASTROCNEMIUS) EXERCISE – 3x/week, 3x 30 seconds

D) CALF STRETCH (SOLEUS) EXERCISE – 3x/week, 3x 30 seconds

Tip: Don’t forget to warm up for 10 minutes before stretching and only stretch to the point of mild discomfort.

RESISTANCE BAND EXERCISES

A) HIP ABDUCTOR STRENGTHENING EXERCISE – 3x/week, 3x 15 repetitions

B) HIP EXTENSOR STRENGTHENING EXERCISE– 3x/week, 3x 15 repetitions

Tip: Hold the outer range position for one second before slowly returning to the starting position in 3 seconds. When the exercises are easy to perform, increase the resistance by changing the resistance band to one with a heavier tension level.

SINGLE LEG BRIDGE

A) STATIC EXERCISE – 3x/week, 3x 30 seconds

B) DYNAMIC EXERCISE – 3x/week, 3x 15 repetitions

Tip: Hold the body in a straight line with the static exercise and outer range position of the dynamic exercise. When the exercises are easy to perform, increase the resistance by holding an external weight in front of the pelvis.

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CALF STRENGTHENING EXERCISES

Steps:

A) STANDING CALF RAISE EXERCISE – 3x/week, 3x 15 repetitions

B) SEATED CALF RAISE EXERCISE – 3x/week, 3x 15 repetitions

Tip: Move through a complete range of motion of the ankle. When the exercises are easy to perform, increase the resistance by performing the exercises with single leg or add external weights.

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ADDITIONAL SECONDARY OUTCOMES

Registered training or match days

Participants were asked to register the number of training or match days in the weekly online questionnaire. The duration of the training or match (in minutes) and the intensity of the training/match was registered using the rated perceived exertion (RPE) scale (range 1: very light to 10: maximum effort activity). The questionnaire also included the reasons for not performing the tendon-specific exercises and exercises targeting risk factors (lack of time, pain, preferring sports activities, rest day and lack of motivation).

Pain scores

The visual analogue scale (VAS) was used for the assessment of pain related to the tendon-specific exercises, exercises targeting risk factors, most recent sport activity, activities of daily living, palpation of the patellar tendon, pain provocation test using the single-leg decline squat (**Figure S1,e**) and vertical jump test (**Figure S1,h+i**). The VAS score ranged from 0 to 10, with 0 indicating no pain and 10 indicating maximum pain. Palpation of the patellar tendon was performed manually by palpating its most tender locations.

Questionnaires

We used three questionnaires that were administered at baseline and after 24 weeks follow-up. First, the EuroQol 5 dimensions (EQ-5D) which is a frequently used questionnaire to measure health-related quality of life. [1] The score ranges from 0 (worst imaginable health state) to 100 (best imaginable health state). Second, the painDETECT questionnaire, which is a validated screening tool to aid in identifying neuropathic pain components. The score ranges from 0 to 38 and scores of ≥ 19 indicate a likelihood of more than 90% that a neuropathic pain component is present. Scores of ≤12 indicate that a neuropathic pain component is less likely than 15% to be present, and scores in between suggest an ambiguous result, however a neuropathic pain component could be present (e.g., in mixed pain). [2] Third, we used the Pain-Coping Inventory (PCI), which is a validated questionnaire to determine the levels of active (range, 0-100%) and passive coping mechanisms (range, 0-100%). [3] The participants rated 33 questions on a 4-point Likert scale ranging from 1 (hardly ever) to 4 (very often) in order to calculate the level of active and passive coping.

Functional tests

The functional tests that we performed are illustrated in **Figure S1**.

Advanced imaging methods

Ultrasound was performed using a LOGIQ E9 (GE Healthcare) machine, equipped with shear-wave elastography (SWE). A linear 5-15 MHz transducer (ML6-15, GE Healthcare) was used for greyscale ultrasound and power Doppler ultrasound and a linear 3.1-10 MHz transducer (9L, GE Healthcare) for SWE. Maximum thickness of the proximal patellar tendon was measured in the transverse plane. Tendon vascularity was assessed using power Doppler, which was assessed using the modified-Öhberg score. [4] This is a 5-point grading scale to score neovascularization in various types of tendinopathy; 0 indicates the absence of Doppler flow, 1+ indicates 1-2 blood vessels mostly in the posterior portion of the tendon, 2 indicates 1-2 intratendinous blood vessels, 3 indicates 3-4 intratendinous blood vessels and 4 indicates a network of intratendinous blood vessels. SWE was used as quantitative measure for patellar tendon stiffness in kilopascal (kPa). This is an ultrasound technique that measures tissue stiffness by measuring the velocity of directional propagating shear-waves that are generated by an acoustic radiation force. [5] The analysis of patellar tendon stiffness was performed using a previously described method, in which the stiffness of the proximal patellar tendon was quantified on elastograms. [6] These elastograms are color-coded maps overlying a normal greyscale ultrasound image, on which the quantitative analysis was performed by placing multiple regions-of-interest. Ultrasound gel (Sonogel Vertriebs GmbH) was used at room temperature (21°C).

Magnetic resonance imaging (MRI) was performed using a 3.0T clinical scanner (Discovery MR750, GE Healthcare). Quantitative T2* mapping was performed by using T2* relaxation times from an imaging sequence called 3D ultrashort echo time (UTE). This relatively new imaging sequence allows for detecting ultrashort T2* relaxation times from the patellar tendon, which can be used for voxel-wise quantification of patellar tendon hydration state. [7] This hydration state is influenced by the typical structural changes that are associated with patellar tendinopathy, and include increased proteoglycans and associated glycosaminoglycan side chains within the extracellular matrix of the patellar tendon. [8] Both have a strong potential for binding water and contribute to the increased hydration state. [9] The state in which water is present in the patellar tendon can be distinguished by investigating the specific T2* relaxation times, which reflects the macromolecular bound water compartment (short T2*) or loosely bound water (longer T2*). [10] The percentage of short T2* components was voxel-wisely calculated in three tissue compartments of the patellar tendon in tendinopathy: 1) collagen (mostly short T2*), 2) interface between collagen and degenerative tissue (mixed T2*) and 3) degenerative tissue (mostly long T2*). The full examination protocol was published elsewhere [11].

Outcomes

All additional secondary outcome measures performed are listed in **Table S1**. The single significant adjusted mean between-group difference after Bonferroni correction was VAS related to the tendon-specific exercises. The VAS related to tendon-specific exercises at 24 weeks was significantly lower in the PTLE group than in the EET group with an estimated mean of 1.8 vs 3.7 (adjusted mean between-group difference: 1.9 [95% CI, 0.7 to 3.0]; *P* = .006).

Additional statistical methodology

POST-HOC SENSITIVITY ANALYSIS OF MISSINGNESS

Nine of the 76 included participants (11.8%) were lost to follow-up for the primary outcome (VISA-P score). One was missing from the 4-stage progressive tendon-loading group and eight from the eccentric exercise group. To evaluate the impact of missingness on the primary outcome, sensitivity analysis was conducted using the following 3 approaches:

1. Worst case scenario for 4-stage progressive tendon-loading exercises: the single missing participant from the progressive tendon-loading group was assigned the worst outcome of this treatment group (VISA-P 43 points and 49 points at 12 weeks and 24 weeks, respectively) while all missing participants from the eccentric exercise group were assigned the best outcome of their treatment group (VISA-P 91 points and 100 points at 12 weeks and 24 weeks, respectively).

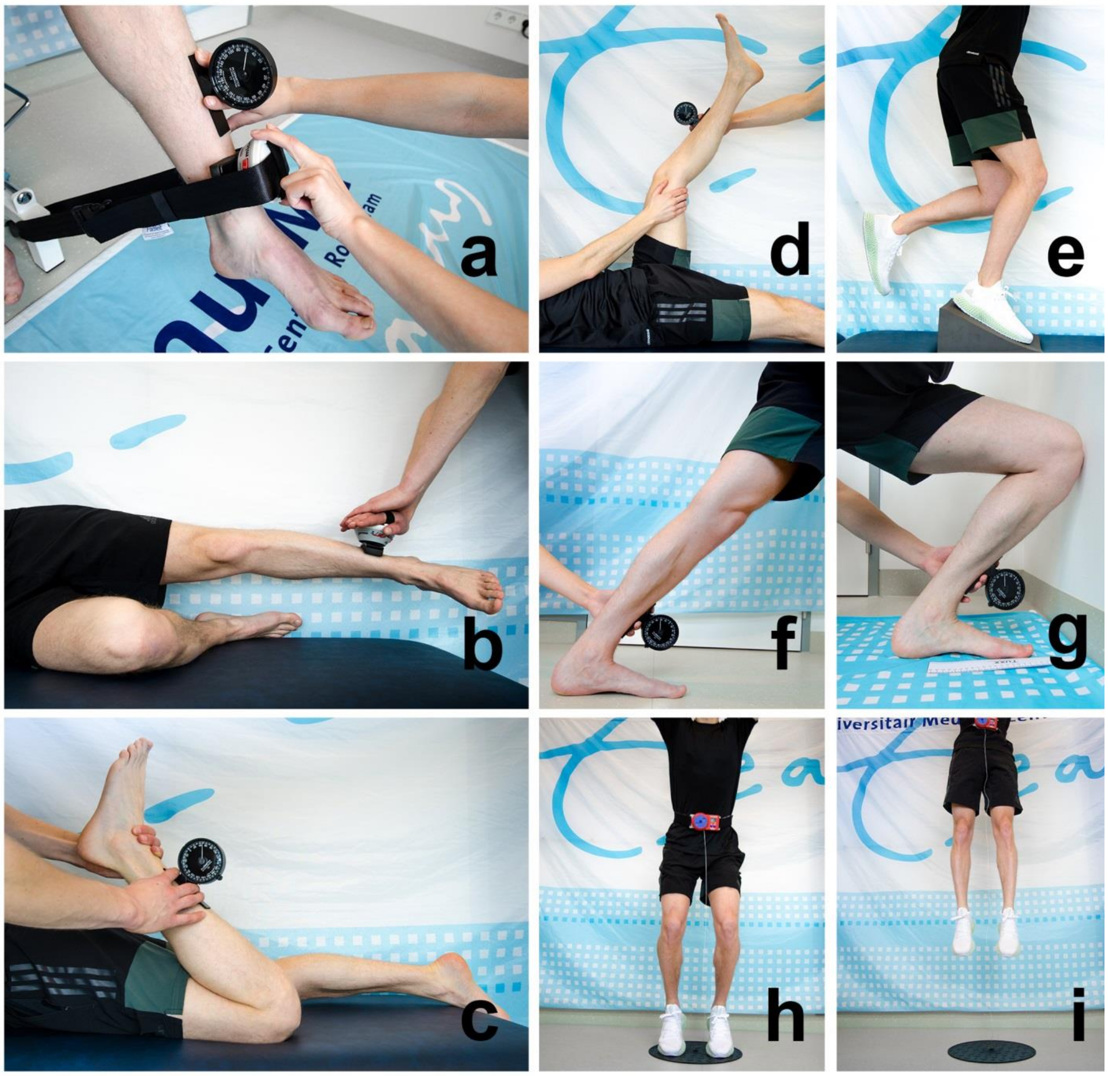
2. Best case scenario for 4-stage progressive tendon-loading exercises: the single missing participant from the progressive tendon-loading group was assigned the best outcome of this treatment group (VISA-P 100 points at 12 weeks and 24 weeks) while all missing participants from the eccentric exercise group were assigned the worst outcome of this treatment group (VISA-P 32 points at both 12 weeks and 24 weeks).

3. Most likely scenario for both treatment groups: last observation carried forward (LOCF) approach, by imputing the last observed score of the VISA-P for all missing follow up measurements.

Table S2 shows the results of these 3 scenarios.

Supplemental Figures

Figure S1. Functional Tests Performed as Additional Secondary Outcome Measures



[a]**Quadriceps strength measurement.** Maximal isometric voluntary contraction (MVC) of the quadriceps muscle was measured with a MicroFet 2 hand-held dynamometer (Hoggan Health Industries, USA), using an established method. [12] The quadriceps muscle strength was assessed in seated position of the participants, with a straight back and with both hands on their shoulders, so that holding on to the examination table was not possible. The flexion angle of the knee was fixed at 60° using a fixation belt (FixBelt) and a plurimeter (Dr. Rippstein, La Conversion, Switzerland). The participants were instructed to produce their maximal force in three seconds against the fixed dynamometer. Consequently, the isometric strength was tested (Newton). For each strength measurement, two maximal voluntary contraction trials were performed of which the highest score was used for analysis.

[b]**Hip abductor strength measurement.** Maximal isometric voluntary contraction (MVC) of the hip abductor muscles was measured with a MicroFet 2 hand-held dynamometer (Hoggan Health Industries, USA), using an established method. [13] The hip abductor muscle strength was assessed in side-lying position of the participants as a 'make test' (isometric contraction). The knee of the contralateral leg was in 90° flexion and the head of the patient was placed on his own hand with a flexed arm and the other hand was used for holding on to the examination table. The participants were instructed to produce their maximal force in three seconds against the resistance of the examiner. Consequently, the isometric strength was tested (Newton). For each strength measurement, two maximal voluntary contraction trials were performed of which the highest score was used for analysis.

[c]**Quadriceps flexibility measurement.** The passive flexibility of the quadriceps muscle was measured with the patient in prone position by measuring the maximum knee flexion angle after passive knee flexion. Eventual anterior pelvic tilt while performing the test was prevented by the investigator. [14] The fully extended leg defined the goniometric 0°.

[d]**Active knee extension test for hamstring flexibility.** The flexibility of the hamstrings was measured with the patient in supine position by measuring the maximum knee extension, dictated by the patient. The patients were instructed to hold their hands in the knee cavity and fixate the hip in 90° flexion (the goniometric 0°). The contralateral leg was fully extended. The maximum degree of knee extension was measured by placing a plurimeter (Dr. Rippstein, La Conversion, Switzerland) on the tibial shaft. This test has been shown to have an excellent reliability. [15]

[e]**Pain provocation test using the single-leg decline squat.** One single-leg squat was performed on a 25° decline board, in order to measure the provocation of pain in the patellar tendon. [16] The downward (eccentric) component was performed on the symptomatic leg and the upward (concentric) component using mainly the contralateral leg. Patients were asked to report the Visual Analogue Scale (VAS) for pain using the 0-10 scale.

[f+g]**Weight-bearing dorsiflexion lunge test.** The maximum ankle dorsiflexion range of motion was assessed using the weight-bearing dorsiflexion lunge test. [17] For this test, the patient was asked to lunge the knee towards the wall and where the foot was progressively moved away from the wall without lifting the heel. The angle of the tibial shaft was measured by placing a plurimeter (Dr. Rippstein, La Conversion, Switzerland) on the tibial shaft in the maximum range of ankle dorsiflexion by the investigator, which defined the soleus flexibility. The wall defined the goniometric 0°. Anterior pelvic tilt was avoided while performing the test. Subsequently, the patients were asked to move their foot as far from the wall as possible, while remaining the heel on the floor and the knee fully extended. The maximum range of ankle dorsiflexion was again tested which defined the gastrocnemius flexibility.

[h+i]**Vertical jump test.** The vertical jump test was performed by using a digital vertical jump meter (Takei 5406 Jump-MD, Takei Scientific Instruments Co., Japan). The rubber test mat was connected by a piece of rope to an adjustable belt which was fixated around the waist of the participant. After tightening the rope, the digital device was set to zero centimetres. Participants were asked to complete 3 maximal counter-movement jumps with arm swing on the jump mat (h). [18] The landing should be on the jump mat to qualify. The maximum jump height out of three attempts was registered. Patients were asked to report the VAS for the maximum pain during these vertical jumps using the 0-10 scale.

Supplemental Tables

Table S1. Additional Secondary Outcome Measures in the Progressive Tendon-loading Exercise (PTLE) and Pain provoking Eccentric Exercise Therapy (EET) Groups

	PTLE group (n = 38)	EET group (n = 38)	Adjusted mean between-group difference
Additional Secondary Outcome Measures (GEE model)			
Registered training or match days per week, estimated mean (95% CI)[1]			
0-12 weeks	1.5 (0.8 to 2.2)	1.3 (0.7 to 1.8)	0.2 (-0.6 to 1.0)
0-24 weeks	1.6 (1.0 to 2.2)	0.7 (0.2 to 1.2)	0.9 (0.2 to 1.6)
Duration of the training or match, minutes, estimated mean (95% CI) [1]			
0-12 weeks	80.7 (68.2 to 93.3)	67.3 (57.3 to 77.4)	13.4 (-1.1 to 27.9)
0-24 weeks	69.7 (56.9 to 82.6)	75.3 (52.1 to 98.4)	-5.6 (-33.8 to 22.7)
Rated Perceived Exertion (0-10 points), estimated mean (95% CI) [1]			
0-12 weeks	4.7 (3.9 to 5.5)	4.0 (3.2 to 4.8)	0.8 (-0.4 to 1.9)
0-24 weeks	3.9 (2.9 to 4.9)	4.8 (3.3 to 6.3)	-0.9 (-2.7 to 0.8)
VAS related to tendon-specific exercises, estimated mean (95% CI)[1]			
12 weeks	2.9 (2.0 to 3.8)	4.5 (3.8 to 5.3)	1.7 (0.4 to 2.9)
24 weeks	1.8 (1.1 to 2.6)	3.7 (2.9 to 4.5)	1.9 (0.7 to 3.0)*
VAS related to exercises targeting risk factors, estimated mean (95% CI)[1]			
12 weeks	2.7 (2.3 to 3.2)	3.3 (2.9 to 3.7)	0.6 (0.0 to 1.2)
24 weeks	3.0 (2.5 to 3.5)	3.0 (2.5 to 3.4)	0.0 (-0.6 to 0.7)
VAS related to most recent sport activity (0-10 points), estimated mean (95% CI)[1]			
Baseline	7.0 (6.5 to 7.5)	7.2 (6.6 to 7.7)	0.2 (-0.6 to 0.9)
12 weeks	4.2 (3.4 to 5.0)	5.2 (4.4 to 6.0)	1.1 (-0.1 to 2.2)
24 weeks	2.7 (2.1 to 3.3)	3.9 (3.0 to 4.8)	1.3 (0.2 to 2.3)
VAS related to activities of daily living (0-10 points), estimated mean (95% CI)[1]			
Baseline	4.3 (3.4 to 5.1)	4.8 (4.1 to 5.5)	0.5 (-0.5 to 1.6)
12 weeks	2.0 (1.2 to 2.8)	3.0 (2.2 to 3.8)	1.0 (-0.7 to 2.1)
24 weeks	1.3 (0.6 to 2.0)	1.7 (1.0 to 2.4)	0.4 (-0.5 to 1.2)
VAS related to palpation of the patellar tendon (0-10 points), estimated mean (95% CI)[1]			
Baseline	5.5 (4.5 to 6.4)	6.0 (4.9 to 7.1)	0.5 (-0.8 to 1.9)

12 weeks	2.8 (1.9 to 3.7)	3.6 (2.3 to 4.8)	0.8 (-0.6 to 2.1)
24 weeks	1.9 (1.2 to 2.7)	3.1 (2.0 to 4.3)	1.2 (-0.2 to 2.5)
VAS related to single-leg decline squat (0-10 points), estimated mean (95% CI)[1]			
Baseline	4.8 (4.1 to 5.5)	4.9 (4.2 to 5.7)	0.1 (-0.8 to 1.1)
12 weeks	2.6 (1.7 to 3.4)	3.4 (2.7 to 4.1)	0.8 (-0.3 to 1.9)
24 weeks	1.5 (0.9 to 2.2)	2.7 (1.8 to 3.5)	1.1 (0.1 to 2.1)
VAS related to vertical jump test (0-10 points), estimated mean (95% CI)[1]			
Baseline	2.9 (2.2 to 3.7)	2.5 (1.7 to 3.3)	-0.5 (-1.6 to 0.6)
12 weeks	1.4 (0.7 to 2.1)	1.4 (0.6 to 2.3)	0.0 (-1.0 to 1.0)
24 weeks	0.4 (-0.1 to 1.0)	1.4 (0.6 to 2.2)	1.0 (-0.0 to 2.0)
Vertical jump height, centimetres, estimated mean (95% CI)[1]			
Baseline	45.3 (42.7 to 48.0)	46.4 (44.0 to 48.8)	-1.1 (-4.4 to 2.2)
12 weeks	46.5 (44.0 to 49.1)	46.3 (43.9 to 48.7)	0.2 (-3.0 to 3.5)
24 weeks	46.5 (43.9 to 49.1)	46.2 (43.7 to 48.7)	0.3 (-3.0 to 3.6)
EQ-5D quality of life questionnaire (0-100 points), estimated mean (95% CI)[1]			
Baseline	81.8 (77.7 to 86.0)	81.3 (77.1 to 85.5)	0.6 (-5.2 to 6.3)
24 weeks	84.7 (80.0 to 89.4)	83.9 (80.0 to 87.8)	0.8 (-4.8 to 6.5)
painDETECT questionnaire (0-38 points), estimated mean (95% CI)[1]			
Baseline	8.7 (7.2 to 10.2)	9.8 (8.2 to 11.3)	1.1 (-1.0 to 3.1)
24 weeks	5.2 (3.9 to 6.5)	7.3 (5.8 to 8.8)	2.1 (0.3 to 4.0)
Pain coping inventory, % active coping (0-100%), estimated mean (95%) CI)[1]			
Baseline	35.0 (30.5 to 39.5)	31.8 (26.4 to 37.2)	4.2 (-3.6 to 12.1)
24 weeks	30.8 (25.1 to 36.5)	26.6 (20.5 to 32.8)	-5.2 (-10.9 to 0.5)
Pain coping inventory, % passive coping (0-100%), estimated mean (95%) CI)[1]			
Baseline	21.7 (17.8 to 25.6)	19.6 (15.5 to 23.7)	-4.3 (-10.6 to 2.0)
24 weeks	18.0 (13.9 to 22.1)	17.4 (12.0 to 22.8)	-0.6 (-7.0 to 5.8)
MVC strength hip abductors, Newton, estimated mean (95% CI)[1]			
Baseline	167 (156 to 178)	156 (145 to 167)	11 (-3 to 24)
12 weeks	177 (167 to 187)	171 (160 to 180)	7 (-6 to 20)
24 weeks	175 (165 to 185)	168 (159 to 178)	7 (-6 to 19)
MVC strength quadriceps, Newton, estimated mean (95% CI)[1]			
Baseline	357 (327 to 387)	351 (326 to 375)	6 (-30 to 42)
12 weeks	413 (389 to 436)	373 (349 to 396)	40 (8 to 72)

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24 weeks	416 (392 to 440)	390 (366 to 412)	27 (-5 to 59)
Flexibility quadriceps, degrees, estimated mean (95% CI)[1]			
Baseline	147 (143 to 151)	144 (139 to 149)	3 (-1 to 7)
12 weeks	148 (144 to 152)	146 (142 to 151)	2 (-2 to 6)
24 weeks	148 (144 to 153)	145 (138 to 152)	4 (-2 to 9)
Flexibility hamstrings, degrees, estimated mean (95% CI)[1]			
Baseline	63 (57 to 69)	61 (54 to 68)	2 (-4 to 8)
12 weeks	67 (61 to 73)	64 (56 to 72)	3 (-4 to 11)
24 weeks	66 (59 to 72)	65 (59 to 72)	0 (-6 to 7)
Flexibility gastrocnemius, degrees, estimated mean (95% CI)[1]			
Baseline	39 (36 to 42)	38 (35 to 40)	1 (-2 to 4)
12 weeks	40 (38 to 43)	39 (37 to 41)	1 (-2 to 5)
24 weeks	40 (38 to 43)	41 (38 to 44)	-1 (-4 to 2)
Flexibility soleus, degrees, estimated mean (95% CI)[1]			
Baseline	41 (38 to 43)	41 (39 to 44)	-1 (-4 to 2)
12 weeks	42 (40 to 45)	42 (40 to 45)	0 (-3 to 3)
24 weeks	43 (40 to 45)	43 (41 to 46)	-1 (-4 to 3)
Ultrasound: patellar tendon thickness, mm, estimated mean (95% CI)[1]			
Baseline	7.4 (6.5 to 8.3)	7.9 (7.2 to 8.6)	0.5 (-0.5 to 1.6)
12 weeks	7.3 (6.4 to 8.2)	8.0 (7.3 to 8.8)	0.7 (-0.4 to 1.8)
24 weeks	7.0 (6.1 to 7.9)	7.7 (6.9 to 8.5)	0.7 (-0.4 to 1.8)
Ultrasound: degree of Doppler flow, Öhberg score, estimated mean (95% CI)[1]			
Baseline	2.7 (2.2 to 3.2)	3.3 (2.7 to 3.8)	0.6 (-0.0 to 1.1)
12 weeks	2.3 (1.9 to 2.8)	2.7 (2.2 to 3.3)	0.4 (-0.2 to 1.0)
24 weeks	2.0 (1.4 to 2.6)	2.7 (2.1 to 3.2)	0.6 (-0.0 to 1.3)
Ultrasound: patellar tendon stiffness, kilopascal, estimated mean (95% CI)[1]			
Baseline	73.7 (62.2 to 85.2)	63.2 (55.1 to 71.2)	-10.5 (-22.4 to 1.4)
12 weeks	57.4 (46.9 to 67.8)	64.5 (54.6 to 74.4)	7.1 (-4.5 to 18.7)
24 weeks	57.7 (48.6 to 66.7)	61.2 (51.3 to 71.2)	3.6 (-8.6 to 15.7)
MRI: percentage of short T2* components in voxels with mostly short T2*, percentage, estimated mean (95% CI)[1]			
Baseline	84.1 (82.3 to 85.8)	83.0 (80.3 to 85.7)	1.1 (-2.1 to 4.3)
12 weeks	84.6 (82.8 to 86.3)	84.1 (82.2 to 86.1)	0.5 (-1.7 to 2.6)
24 weeks	83.6 (81.7 to 85.6)	85.1 (83.0 to 87.1)	-1.4 (-4 to 1.2)

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MRI: percentage of short T2* components in voxels with mixed T2*, percentage, estimated mean (95% CI)[1]			
Baseline	40.9 (37.3 to 44.4)	42.8 (38.3 to 47.4)	-2.0 (-7.1 to 3.1)
12 weeks	42.4 (38.7 to 46.1)	39.7 (36.4 to 43.1)	2.7 (-2.2 to 7.6)
24 weeks	44.3 (40.6 to 47.9)	45.1 (40.1 to 50.0)	-0.8 (-6.2 to 4.6)
MRI: percentage of short T2* components in voxels with mostly long T2*, percentage, estimated mean (95% CI)[1]			
Baseline	20.1 (19.2 to 21.0)	20.8 (19.5 to 22.0)	-0.7 (-2.1 to 0.8)
12 weeks	20.7 (19.6 to 21.9)	19.7 (18.3 to 21.0)	1.0 (-0.7 to 2.8)
24 weeks	22.5 (21.2 to 23.9)	20.9 (19.0 to 22.7)	1.6 (-0.6 to 3.9)
Additional Secondary Outcomes (Fisher exact test)			
Reasons for not performing tendon-specific exercises, n (%)[2]			
Lack of time	901 (37)	1072 (51)	
Pain	211 (9)	154 (7)	
Preferring sports activities	325 (13)	299 (14)	
Rest day	565 (23)	245 (12)	
Lack of motivation	417 (17)	339 (16)	
Reasons for not performing exercises targeting risk factors, n (%)[2]			
Lack of time	1097 (31)	1015 (33)	
Pain	149 (4)	105 (3)	
Preferring sports activities	521 (15)	253 (8)	
Rest day	1249 (35)	1284 (41)	
Lack of motivation	548 (15)	459 (15)	

Abbreviations: PTLE, progressive tendon-loading exercise therapy; EET, pain provoking eccentric exercise therapy; VAS, visual analogue scale; CI, confidence interval; MVC, maximum voluntary contraction; RPE, rated perceived exertion; SD, standard deviation.

[1]The mean estimated number of registered training or match days per week, duration of the training or match, rated perceived exertion of the training or match, VAS related to tendon-specific exercises, VAS related to exercises targeting risk factors, VAS related to most recent sport activity, VAS related to activities of daily living, VAS related to palpation of the patellar tendon, VAS related to single-leg decline squat, VAS related to vertical jump test (3 maximal jumps), vertical jump height (maximum of 3 attempts), EQ-5D questionnaire, painDETECT questionnaire, pain coping inventory questionnaire (active/passive coping), MVC strength hip adductors, MVC strength quadriceps, flexibility quadriceps, flexibility hamstrings, flexibility gastrocnemius, flexibility soleus, ultrasound-based patellar tendon thickness, ultrasound-based Doppler flow, ultrasound-based patellar tendon stiffness (measured with shear-wave elastography), MRI-based percentage of short T2* in voxels with mostly short T2*, MRI-based percentage of short T2* in voxels with intermediate T2* and MRI-based percentage of short T2* in voxels with mostly long T2* are denoted for the PTLE and EET group. The estimated means and adjusted mean between-group differences were calculated using Generalized Estimating Equations (GEE) with

adjustments for the following pre-defined baseline variables: age, sex, BMI, symptom duration and Cincinnati Sports Activity Scale. Positive adjusted mean between-group differences favour the PTLE-group.

The interaction term study arm*visit was significant for the following outcomes: VAS related to exercises targeting risk factors (P=.013), VAS related to vertical jump test (P=.039), MVC strength quadriceps (P=0.049) and ultrasound-based patellar tendon stiffness (P=.007). This means that the course of the VISA-P score over time was statistically different for the PTLE and EET group.

The interaction term study arm*visit was not statistically significant for the following outcomes: compliance to tendon-specific exercises (P=.84), compliance to exercises targeting risk factors (P=.94), number of registered training or match days per week (P=0.17), duration of the training or match (P=.22), rated perceived exertion (P=.11), VAS related to tendon-specific exercises (P=.68), VAS related to most recent sport activity (P=.23), VAS related to activities of daily living (P=.55), VAS related to palpation of the patellar tendon (P=.80), VAS related to single-leg decline squat (P=.21), vertical jump height (P=.35), EQ-5D questionnaire (P=.93), painDETECT questionnaire (P=.35), pain coping inventory questionnaire, active coping (P=.78) and passive coping (P=.66), MVC strength hip adductors (P=.73), flexibility quadriceps (P=.38), flexibility hamstrings (P=.35), flexibility gastrocnemius (P=.11), flexibility soleus (P=.60), ultrasound-based patellar tendon thickness (P=.63), ultrasound-based Doppler flow (P=.63), MRI-based percentage of short T2* in voxels with mostly short T2* (P=.37), MRI-based percentage of short T2* in voxels with intermediate T2* (P=.46) and MRI-based percentage of short T2* in voxels with mostly long T2* (P=.07). This means that the course of the VISA-P score over time did not differ between the PTLE and EET group for these outcome measures.

[2]The number and percentage of reasons registered for not performing the tendon-specific exercises are denoted for the PLTE and EET group. The reasons lack of time (P<.001), pain (P=0.045) and rest day (P<.001) were significantly different between the study arms and sports activities (P=.25) and lack of motivation (P=.16) were not.
The total number and percentage of reasons registered for not performing the exercises targeting risk-factors are denoted for the PLTE and EET group. The reasons pain (P=0.048), sports activities (P<.001) and rest day (P<.001) were significantly different between the study arms and lack of time (P=.06) and lack of motivation (P=.24) were not.

Table S2: Sensitivity Analysis of Missingness

Outcome Scenario	Absolute mean between-group difference		Adjusted mean between-group difference (95% CI)	
	12 weeks	**24 weeks**	**12 weeks**	**24 weeks**
1. Worst case	-4.5	2.7	-4.2 (-11.6 to 3.2)	3.0 (-4.7 to 10.7)
2. Best case	13.8	18.3	12.4 (4.6 to 20.1)*	16.7 (8.6 to 24.9)*
3. Most likely	1.8	10.8	1.7 (-5.1 to 8.6)	10.6 (3.4 to 17.8)*

*The mean between-group difference is significant at the .001 level.

Any positive mean difference indicates a favourable outcome for the progressive tendon-loading exercise (PTLE) group.

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