The Achilles tendon back on track. Feasibility of an early progressive strength exercise programme for acute Achilles tendon rupture.

Protocol version 1.0

29.Sept 2019

Protocol

Administrative information

1.Title

Feasibility of an early progressive strength exercise programme for acute Achilles tendon rupture.

2.Trial registration

2a The study will be registered at ClinicalTrials.gov: nr and date

2b WHO Trial Registration Data Set

Data category	Information
Primary registry and trial identifying number	Clinical Trials
Date of registration in primary registry	19.Sept 2019
Secondary identifying numbers	Ethics Committee N-20180072
Source(s) of monetary or material support	Physiotherapy and Occupational therapy, Aalborg University Hospital
Primary sponsor	Physiotherapy and Occupational therapy, Aalborg University Hospital
Secondary sponsor(s)	Orthopaedic department, Aalborg University Hospital
Contact for public queries	mc@rn.dk
Contact for scientific queries	mc@rn.dk
Public title	The Achilles tendon back on track. Feasibility of an early progressive strength exercise programme for acute Achilles tendon rupture.
Scientific title	Feasibility of an early progressive strength exercise programme for acute Achilles tendon rupture.
Countries of recruitment	Denmark
Health condition(s) or problem(s) studied	Achilles tendon rupture
Intervention(s)	Early progressive strength exercise programme
Key inclusion and exclusion criteria	Inclusion criteria: Patients with acute Achilles tendon rupture treated non-surgically. Diagnosed and treatment initiated within 3 days (of their injury). Age 18 - 65, able and willing to participate in the intervention. Able to speak and understand Danish Exclusion criteria: Insertional Achilles tendon rupture on calcaneus or rupture in the musculo-tendinous junction of the triceps surae. Previous Achilles tendon rupture or other conditions in either leg causing lower leg disability (pain, deficits in strength or range of movement). Treated with Fluorquinolons or Corticosteroids within the last 6 months. Diabetes. Severe medical illness: ASA score higher than or equal to 3
Study type	Interventional, feasibility
Date of first enrollment	October 2019
Target sample size	16
Recruitment status	Not yet recruiting
Primary outcome(s)	Feasibility: Acceptability and compliance
Key secondary outcomes	Fear of re-rupture, ATRS, IPAQ short form, ATRA, Achilles tendon properties, delay in start of exercises, adverse events, muscle endurance

3. Protocol version

Version 1.0

4. Funding

The Physiotherapy and Occupational therapy department and Orthopaedic Surgery department at Aalborg University Hospital has guaranteed for the funding of the PhD study. This work was also supported by the Danish Physiotherapist Research Foundation, North Denmark Region Research foundation and AP Møller Lægefonden.

5. Roles and responsibilities.

5a Names, affiliations, and roles of protocol contributors

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  - Orthopaedic Research Unit, Aalborg University Hospital, Aalborg, Denmark
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- Michael Skovdal Rathleff (MSR), Physiotherapy and Occupational Therapy, Aalborg University Hospital, Hobrovej 18-22, 9000 Aalborg, Denmark, misr@hst.aau.dk
- Inge Lunding Kjær (ILK), Orthopaedic Research Unit, Aalborg University Hospital, Hobrovej 18-22, 9000 Aalborg, Denmark. i.kjaer@rn.dk

The project will be conducted with MC as primary investigator as part of her Ph.D.-studies. MC and MSR wrote the first draft of the protocol. ILK and KGS both made valuable scientific additions to the draft. ILK is chief orthopaedic foot surgeon and has the clinical responsibility for the study. MSR and KGS provided contribution to the study design, contents of the intervention and the evaluation methods. All authors approved the study protocol.

5b Name and contact information for the trial sponsor

Physiotherapy and Occupational Therapy department, Orthopaedic department,
Clinic Head- and Orto,
Aalborg University Hospital
Hobrovej 18-22
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Denmark

5c Role of study sponsor and funders

Sponsor is a part of the study, but is not involved in design, planning and analysis of the study. Sponsor will collaborate to ensure the right conditions for planning and conduct of the study and the publication of the results. Sponsor is non-commercial and declares no conflict of interest.

The funding sources will have no influence in the design of this study and will not have any role during the study execution, interpretation of the data or dissemination of results.

5d Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)

N/A

Introduction

6. Background and rationale

6a Descriptions of research question

Acute Achilles tendon rupture is a common injury and in Denmark the incidence has increased in recent years from 18.2/100.000 in 1984 and up to 31.17/100.000 in 2013.[1,2] Achilles tendon rupture usually occurs at age 30-50 with a male to female ratio 3-5:1.[1-3] The Achilles tendon is the largest and strongest tendon in the human body and is crucial for normal gait and running.[4]
Regardless of choice of either surgical or non-surgical treatment, long-term muscular deficits and a decreased function after Achilles tendon rupture is found up to 7 and 10 years later.[5-7] The majority of the patients are of working age and a deficit in physical performance will have impact on returning to work and sports.[8-10] The risk of not being able to return to work or sport has potential influence on patients quality of life, risk of lifestyle diseases and healthcare economics.

Historically surgical treatment has been favoured mainly because the re-rupture rates are lower compared to non-surgical treatment (3 vs 13%, respectively).[11,12] However, there is a risk of wound infection in surgical treatment compared to non-surgical and the results after a deep infection are often devastating.[13,14]
There has been promising results in treatments using early functional rehabilitation (EFR) during the first eight weeks of treatment after both surgical and non-surgical treatment. The re-rupture rate after EFR is reported similar to those of surgery, which gives EFR an advantage to the former non-surgical treatment with immobilisation.[13,15-18] The early functional rehabilitation aims at minimizing the loss of muscle strength that is inevitable in the immobilizing period. Laboratory studies have also indicated that early loading of the ruptured tendon will improve the tendon healing in animals[19,20] and clinical studies have confirmed this[21].

Several studies have reported use of controlled ankle/foot exercises, but few studies examined the effect of the exercises on its own and primarily after surgery.[22-25] We recently conducted a systematic review investigating the EFR used in the first 8 weeks of treatment and it showed very heterogeneus intervention protocols. (Zellers et al, accepted)(Christensen et al, in review) The components used in the EFR ranges from early weight-bearing and controlled range of motion ankle/foot exercises to strength exercises. Also the type of immobilisation varies from using a rigid cast to specially designed shoes to mobile walker orthosis. The timing of initiating exercises, weight-bearing and changing foot position from equinus to neutral also varies. The majority of the published protocols mainly focused on mobilisation of the patient and not including exercises for the foot/ankle that would load the Achilles tendon.
The general descriptions of the exercise programs were lacking important information such as type, time of application, frequency, intensity and progression of the exercises. This emphasises the problem that exists with the heterogeneous EFR and lack of systematic reviews and clinical guidelines that translate result into reproducible exercise protocols.

It is time for optimizing the exercises to address the need for improvement of the muscle strength and function, and ensuring that the exercises are well described.
In the long term the optimal goal is to present a well described new exercise intervention and investigate the effect compared to the present treatment in a RCT. When developing a new treatment, essential questions about the feasibility of the intervention are not known. It is important to know this before embarking on a large scale trial. Even though the RCT has advantages, it often demands a lengthy time perspective to include sufficient number of participants and it will all be wasted if you in retrospect discover that there are feasibility issues of the intervention.[26,27]
Consequently it is reasonable to do a feasibility study of how the patients tolerate a new exercise program regarding adherence and willingness to the exercise program.

6b Explanation for choice of comparators

The purpose of this study is to test the feasibility of the exercise program and it is not the intention to replicate the future RCT with both intervention and a comparator. Therefore comparators will not be included in the feasibility study.

7. Objectives

The primary aim is to test the feasibility of an early progressive exercise program for patients with Achilles tendon rupture treated non-surgically. Feasibility in this study will be defined as successful patient acceptability and compliance of the exercise intervention. It will not include feasibility of physiotherapist prescription of the exercises or the feasibility in a health care system perspective. Definition of feasibility is described further in section 12. Outcome.

8. Trial design

This study is designed as a single group, interventional feasibility study. Follow-up after 9 and 13 weeks. The protocol will follow the SPIRIT statement and the reporting of the study will follow the CONSORT 2010 statement, extension to randomised pilot and feasibility trials.[28,29]

Week	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Emergency department																
Diagnostic and treatment																
Inclusion																
Outpatient Clinic																
Immobilisation in equinus																
Orthosis + wedges																
Exercise intervention																
Follow-up			F	F	F	F	F	F	F	F	F				F	
Risk assessment			!	!	!	!	!	!	!	!						
Data analysis																D

	Ordinary patient visits to hospital
	Treatment
	Feasibility study
F	Follow-up
!	Risk assessment
D	Data analysis

Methods: Participants, interventions, and outcomes

9. Study setting

Participants will be recruited from the emergency Department at Aalborg University Hospital Denmark and followed at the Orthopaedic Outpatient Clinic. The intervention will take place at the Physiotherapy and Occupational Therapy Department.

The primary investigator (MC) will be responsible for screening for eligibility, exercise intervention, data collection and prevention of adverse events. The primary investigator has more than 20 years of experience as a physiotherapist and currently holds a position with diagnostic responsibility at the Foot and ankle outpatient clinic. The chief orthopaedic foot surgeon (ILK) has the overall responsibility for the clinical treatment and safety. At the joint weekly meeting the progression of the study inclusion and treatment is evaluated.

10. Eligibility criteria

Inclusion criteria:

- Patients with acute total Achilles tendon rupture treated non-surgically
- Diagnosed and treatment initiated within 3 days (of their injury)

- Age 18 - 65, able and willing to participate in the intervention
- Able to speak and understand Danish

Exclusion criteria:

- Insertional Achilles tendon rupture on calcaneus or rupture in the musculo-tendinous junction of the triceps surae
- Previous Achilles tendon rupture or other conditions in either leg causing lower leg disability (pain, deficits in strength or range of movement)
- Treated with Fluorquinolons or Corticosteroids within the last 6 months
- Diabetes
- Severe medical illness: ASA score higher than or equal to 3.[30]

Excluded patients and patients not willing to participate will follow the usual program of rehabilitation for non-surgical treatment at Aalborg University Hospital.

11. Interventions

11a Intervention for each group with sufficient detail to allow replication, including how and when they will be administered.

The exercise intervention starts one week after diagnosis at the Emergency Department. There will be weekly exercise sessions and daily home program until removal of the walker after nine weeks. The exercise intervention aims at facilitating the muscle activity in the beginning of the immobilising period and subsequently progress the load to strengthen the muscles within the restrictions for the healing tendon. The strength exercises aims at loading the Achilles tendon-muscle complex as opposed to more general exercises that involves the whole leg.

To protect the tendon while doing range of motion of the foot, dorsiflexion is restricted beyond neutral (0 degrees of dorsiflexion). The load on the strength exercises will progress from isometric contraction without external load to strengthening exercises with 10-20 RM. Each strength exercise can progress with added weight or stronger elastic band. The Borg scale is used to guide the patient to progress or regress the load in each exercise. The recommended level being “easy” to “hard” (2-5/10). It is emphasized that the exercises must not cause sudden or severe pain in the tendon, but muscle soreness is to be expected.

Progression is performed individually and with a progression of 2-10%. This is generally accepted as a reasonable progression in resistance training and for exercise therapy for painful tendinopathy and even though specific research on Achilles tendon rupture is lacking is seems a safe precaution to prescribe in the early rehabilitation of Achilles tendon rupture.[31]

New treatment - **Strength exercises**:

- **Isometric contraction** of the leg muscles inside the immobilising orthosis. Short time under tension (TUT) and load in the beginning and then progression as the patient feels comfortable. Progression of load will be allowing to push the forefoot against the bottom of

the walker with more pressure. Position: can be seated, standing or lying down with bent or straight knee.

- **Seated heel-rise** with heel on wedges in the walker boot and with open straps to allow movement. The wedges under the heel prevents excessive dorsiflexion of the foot. Progressing with external weight on the knee. To ensure contraction of the gastrocnemius and not just the flexor muscles to the toes, the contraction will be monitored with ultrasound. Position: seated with bent knee in 90 degrees and possibly a cushion on the chair to compensate for the higher heel in the walker with wedges.
- **Resistance strength exercise with elastic band**. This exercise is part of the usual treatment, but will be started earlier and with progress to a stronger elastic band (from yellow to red/green/blue). The patient is instructed to do plantarflexion from neutral position. They are not allowed to pull the foot in dorsiflexion beyond neutral foot position. Position: seated with bend or straight knee.

General information (as given with current treatment):

All patients receive general information about Achilles tendon rupture, tendon healing, choice of treatment and risks. The long term prognosis of the Achilles tendon rupture is associated with lack of muscle strength and physical function and therefore forms the rationale for progressing the exercise therapy.

- **Circulatory exercises**. The patients are instructed to do circulatory exercises to prevent edema and loss of muscle in the whole leg. The exercises are toe curls, flexion and extension for knee and hip. From week three **Active range of motion (ROM)** is allowed outside the walker boot, 3x10 rep 5 times per day. ROM for dorsiflexion is restricted beyond neutral position of the foot. Position: seated with bent or straight knee. It is important that the position is secure with no risk of sudden movement of the foot caused by externally forces (nearby persons, animals or other moving objects).

Exercise descriptors

Table of Toigo and Boutellier Exercise descriptors available in appendix A

Schedule of the exercise program:

Exercises		Iso	Heelrise Iso ROM	Heelrise Iso ROM	Elastic 1 Heelrise Iso ROM	Heelrise Iso stand Elastic 1 ROM	Elastic 2 Heelrise Iso stand Elastic 1 ROM	Elastic 2 Heelrise Iso stand Elastic 1 ROM	Elastic 2 Heelrise Iso stand Elastic 1 ROM
Weeks	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Immobilizing	Walker, 3 wedges			Walker, 2 wedges		Walker, 1 wedge		Walker, no wedge	
Weight bearing	Non WB		P- WB, 2 crutches		P-WB, 1-2 crutches		Full WB, crutches for long walk		
Rationale		A. Facilitation		B. Initiation of load			C. Progression to more load		
Total exercise dose (time under tension)		Facilitation of muscle activity by isometric contraction without ROM		Slow controlled movement to avoid peak forces on tendon while prioritizing long TUT to maintain/increase strength			Improve strength (go to failure IF THEY ARE comfortable with it)		
Progression		Progress from A to B: If patient feel comfortable doing facilitating exercises If clinical screening is OK at "2 week follow-up" (no tendon gap, equal ATRS, no pain during exercises).		Progress from B to C: If patient feel comfortable doing "initiation of load" exercises. If exercises are managed well a. with regards to Toigo descriptors, b. without persistent pain or discomfort during and after exercises, c. no compensating movements while performing exercises.			Progress from C to exercise and mobilize without walker: The decision to discontinue the walker is done at the Outpatient clinic. The exercises should provide the foundation for the patient to be confident in future decisions of choosing sufficient amount of load to improve the muscle performance while still avoiding too much strain on the healing tendon (i.e. avoid strenuous load, avoid stretching in dorsiflexion with load)		

Blue is usual treatment. Orange is the new additional treatment. Iso is isometric contractions. Elastic 1 is light load(yellow) and Elastic 2 is progression of load to stronger elastic band (red, blue, green). Heelrise is seated. ROM is unloaded range of movement.

11b Criteria for discontinuing or modifying allocated interventions

Each exercise session begins with assessing the progression of the tendon healing. In the first weeks with immobilisation, where physical examination is not possible, the patient is asked if there has been any constant or sudden pain or swelling and if there has been any excessive load to the tendon. In the following six weeks with the removable walker boot, there will also be a physical examination (as procedure in the outpatient clinic) of the tendon and muscle structure, and a measure of the Achilles Tendon Resting Angle (ATRA).[32]

In case of deviation from the protocol or adverse events, the primary investigator MC and the chief orthopaedic foot surgeon ILK will decide to either continue with modifications or to withdraw the patient from the study. (Further description in section 21a and appendix B)

11c Strategies to improve adherence

During the first visits the patients are informed about the importance of adherence to the exercise intervention. At the sessions the primary investigator will motivate the patients to perform the exercises. To ensure adherence to the home exercise program there will be a pamphlet with detailed description of the exercises. At each session the primary investigator will ask about the home exercises and the patients can ask questions.

11d Relevant concomitant care and intervention that are permitted or prohibited during the trial

During the first nine weeks of treatment the patients are advised to avoid activities with high load on the foot, concentrate on oedema prophylaxis and training for a better overall result. Most activities of daily living will be possible, but is advisable to take sick leave from work in the first two to nine weeks or longer depending on the workload.

12. Outcomes

For this feasibility study there are several outcome of interest, but no predefined single primary outcome. The main focus will be to test the feasibility of the exercise intervention by setting values for fulfilment of a range of outcomes and process variables deemed of importance to patients and safety. The outcomes will concern the patient's acceptability of the intervention, adherence to the intervention and safety of the healing tendon.

The exercise program is considered feasible if:

1. The acceptability of the exercise program is 80%
    a. Defined as: ≥13/16 patients will rate the acceptability of the intervention as "acceptable"
2. The adherence to the exercise program is 50%
    a. Defined as: ≥13/16 patients will perform ≥ 50% of the exercise sessions possible from start to end of week 9

Outcomes:

Patient acceptability: The patients will rate their acceptability (willingness) to perform the exercises on a 7-point Likert scale ranging from "very unacceptable" to "very acceptable". This is not a measure of whether the patient's symptoms have improved to normal physical function or any other satisfactory level at the specific time, but if it matches, their expectations of the content of an

exercise program in this early phase and how they tolerate performing the exercises. The intervention program is categorised as "Unacceptable" if rated as the three lower scores ("very unacceptable" to "slightly unacceptable") and categorised as "Acceptable" if rated as the four higher scores ("neither acceptable or unacceptable" to "very acceptable")

- Clinical relevance: When developing a new exercise program it is essential to investigate if the patients are willing to perform the exercise program. If the intervention is unacceptable to the patient it is not feasible to embark on a large scale RCT. To categorise the intervention program as "Acceptable", it is considered important that the patients does not rate it as "unacceptable".

Compliance with the intervention: The patients will register the number of training sessions and exercises they perform each day in a training journal. The compliance is measured as the mean number of exercise sessions they perform. The timeframe will be from the day they start the exercises to the end of week 9.

- Clinical relevance: the exercise program is based on home exercises which should be easy to understand and perform without the need for supervising of a physiotherapist, as this will be both time consuming and with much higher costs. Total compliance to the exercise program is not expected, but even then reporting concerning exercise compliance are very poor with compliance as low as 45% or less for chronic diseases.[33-35] The magnitude of this exercise program should leave room for patients with higher physical level or motivation, but the success rate should reflect the reality of compliance for most patients.

Secondary outcomes

The fear of re-rupture. When asked, the patients mention the fear of re-rupture and feeling the "pop" of the tendon as the worst thing that could happen again. This could influence the willingness to participate in the early exercises. The Tampa scale of Kinesiophobia (TSK) is used and validated for backpain, but has previously been used for Achilles tendon rupture evaluation[36] as the questions about kinesiophobia could have associations to how patients with Achilles tendon rupture manage rehabilitation and return to sports. The questionnaire consists of 17 items concerning pain and kinesiophobia and has 4 answers from "Strongly disagree" to "Strongly agree". During the exercise intervention period and at 3 months follow-up the patients will fill out the score and subsequently they are asked to rate the appropriateness of the score on a 7 point Likert scale ranging from "strongly disagree" to "strongly agree". Measured at 2 weeks, 10 weeks and 3 months.

The most frequently used patient reported outcome for Achilles tendon rupture is the **Achilles Tendon total Rupture Score (ATRS)**.[37] It contains 10 questions about physical performance in an 11-point Likert scale from zero to ten with a total sum score of maximally 100. The scale only has labels for 0 and 10 ("major limitations/symptoms" and "no limitations/symptoms"). The questionnaire will be filled out by the patients at baseline for a pre-rupture level and at the 3 months follow-up.

International Physical Activity Questionnaire (IPAQ) short form Danish version. It consists of 7 items concerning physical activity as time spent performing vigorous and moderate activities, the time spent walking and sitting during the past week. The IPAQ gives an estimate of the total weekly

physical activity measured in MET-minutes per week and total minutes spent sitting.[38] The questionnaire will be filled out by the patients at baseline for a pre-rupture level and at the 3 months follow-up.

Achilles tendon resting angle (ATRA) is validated as an indirect measure of the Achilles tendon length.[32,39,40] It is measured in degrees between the axis of the fibula (from malleol to proximal head) and the line from the tip of the fibula to the head of the Fifth metatarsal bone. The ATRA will be measured at 10 weeks and at 3 months followup.

Achilles tendon properties - length measured by ultrasound using Barfods Ultrasound length measure for tendon length[41] will be performed at 10 weeks and 3 months.

Achilles tendon properties – cross-sectional area measured by ultrasound at the rupture site[42] will be performed at 10 weeks and 3 months.

Delay in start of exercises. At the two week visit to the outpatient clinic all patients will be clinical assessed when the immobilising orthosis is removed. The progression of the treatment is based on a combination of clinical assessments of the tendon structure, no palpable gap at the rupture and a foot position in equinus. Delay in starting the exercise program is measured in days from start to end of week 9.

Safety and Adverse events. The number of serious and minor adverse events is registered in a pre-defined list based on Common Terminology Criteria for Adverse Events[43] and the patients will be asked open questions at each session. Serious Achilles tendon injury adverse events are re-rupture, non-union of the tendon or deep vein thrombosis (DVT). Muscle soreness or mild pain is considered inevitable and normal when initiating exercises after a period of immobilisation. Measured at 10 weeks and 3 months follow-up.

Muscle endurance is measured in the seated position with the MuscleLab measurement system (Ergotest Technology, Oslo, Norway).[44] External weight load on the knee is calculated to 50% of the bodyweight. A linear encoder is attached to the heel of the patient's shoe. When heel-rise is performed, the string is pulled and the sensor measures the muscle endurance. Measured at 3 months follow-up.

13. Participant timeline

Time schedule of enrolment

FEASIBILITY STUDY	**STUDY PERIOD**						
	Enrolment	**Post-allocation**					**Close-out**
TIMEPOINT	***Day 1-7***	***Week 2***	***Week 3-4***	***Week 5-6***	***Week 7-8***	***2 months***	***3 months***
ENROLMENT:							
Eligibility screen	X						
Informed consent	X						

INTERVENTIONS:							
Facilitation of muscle		←	—	—	→		
Resistance exercise			←	—	—	→	
ASSESSMENTS:							
Prescore ATRS, IPAQ	X						
Demographics	X						
FEASIBILITY OUTCOMES:							
Patient acceptability		X	X	X	X	X	X
Compliance with the intervention		X	X	X	X	X	X
SECONDARY OUTCOMES:							
Adverse events		X	X	X	X	X	X
PROM: ATRS, IPAQ							X
Tampa scale of Kinesiophobia TSK		X				X	X
Agreement of TSK		X				X	X
Physical measures (ATRA, UL of tendon length and cross-sectional area)						X	X
Seated heel-rise endurance test							X
Delay in intervention start						X	

14. Sample size considerations

Since this is a feasibility study and we are primarily interested in estimates of feasibility and acceptability, no formal sample size calculation will be performed. Estimated number of participants is 16, which seems appropriate compared to the estimations for the following RCT. The overall incidence of Achilles tendon ruptures presenting at our hospital is approximately 80 per year.

15. Recruitment Strategies for achieving adequate participant enrolment to reach target sample size

The participants are recruited in the Emergency department at Aalborg University Hospital or at the Orthopaedic Outpatient Clinic. All relevant subjects in this region will pass through these departments.

All medical and administrative staff involved in treating the patients will be informed of the project and notified of the inclusion/exclusion criteria. There will be written information for staff and patients.

On a daily basis, the referral lists will be searched to retrieve all incoming journals for new acute Achilles tendon ruptures. Patients potentially eligible for the project will be contacted by the Primary Investigator to explain the study. If the patient is potential eligible, an early appointment in the outpatient clinic is arranged, where the patient receive the oral information about the project. Final inclusion will take place at this meeting if the eligibility is confirmed.

Patients will be given the possibility of contacting the project manager by phone or Email, if they have questions. The intervention will take place at the hospital and be coordinated with the usual appointments in the outpatient clinic.

Methods: Assignment of interventions (for controlled trials)

16-17

N/A

Methods: Data collection, management, and analysis

18. Data collection methods

18a Plans for assessment and collection of outcome.

Baseline data will be collected at the first appointment in the outpatient clinic. During the intervention the patients will be followed closely and monitored on compliance to the exercise program, progression of tendon healing and adverse events. At every session there will be an assessment of the clinical measures and the patient's evaluation of the intervention. Assessment of outcome takes place after three months and will include patient reported questionnaires and physical measurements of leg strength and tendon length.

18b Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols.

Each appointment will be registered in the hospitals booking system and this features a possibility of having text messages prior to the appointments. If the patients fail to attend an appointment, the study manager will call the patient and offer another appointment. If the patient decides to leave the study, the reason for leaving will be registered.

19 Data management

Data will be entered in REDCap hosted at Aalborg University Hospital. It is a secure web application for building and managing online surveys and databases. Some baseline data will be imported from the Danish Achilles tendon Database DADB. Both databases has secure logged entry. Any paper forms will be kept in a locked cabinet in the Physiotherapy at the study site. All

data will be kept for 10 years after completion of the study in accordance with The European Code of Conduct for Research Integrity.

20. Statistical methods

20a

STATA ver. 15 will be used for the statistical analysis.

The following criteria will have to be completed to conclude feasibility of the intervention:

1. ≥13/16 patients will rate the acceptability of the intervention as "acceptable"
2. ≥13/16 patients will perform ≥ 50% of the exercise sessions possible from start to end of week 9

Feasibility will be presented as:

Patients acceptability as median and quartiles. Criteria fulfilment of 80% as number and percentage of patients scoring "acceptable". Adherence to the intervention(compliance) as number of fulfilled sessions and percentage. Criteria fulfilment of 50% as number and percentage of patients performing ≥50% of the exercises. The feasibility of the main outcomes will be measured at 10 weeks and the secondary outcomes at 3 months follow-up. Descriptive information will be registered at baseline: Age, sex, height, weight, IPAQ, ATRS. Baseline and follow-up data will be presented as means with standard deviations.

Reasons for exclusion and for withdrawal will be summarised. Safety will be presented as number and percentage of patients reporting adverse events divided in major and minor events. Time from treatment start to beginning exercises as mean days and range.

20b Methods for any additional analyses (eg, subgroup and adjusted analyses)

N/A

20c Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)

The intention-to-treat principle is used for analyses and all participants are included in the analyses regardless of the acceptability or compliance to the intervention.

Methods: Monitoring

21. Data monitoring.

21a Composition of data monitoring committee (DMC);

Safety of the tendon healing has great importance in this feasibility study. There will be a data monitoring committee(DMC) with the principal purpose of monitoring adverse events. The study setup will aim at preventing adverse events by monitoring the tendon healing and setting threshold values for initiation and progressing the exercises in the intervention. The DMC will be composed of the principal investigator (MC), the chief orthopaedic foot surgeon (ILK) and an orthopaedic surgeon not otherwise involved in the study. All symptoms and adverse events will be registered by the principal investigator (Appendix B). The DMC will assess and grade symptoms that are not within normal trauma reactions or normal exercise reactions and especially events considered a serious or possible serious adverse event. DMC will decide, whether to delay the proceeding of the intervention or the patient should be withdrawn from the study due to the adverse event (See section 11b). The adverse events will be graded 1 to 5 according to the Common Terminology Criteria for Adverse Events v4.03.[43]

21b

If the rate of re-rupture or other serious adverse events is noted to be exceptionally high or increases rapidly after the intervention has been implemented, the data monitoring committee can recommend and decide to terminate the trial. No formal stopping rules has been set, as this is a feasibility study.

22. Harms. Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct

All patients receive information about possible adverse events relative to the Achilles tendon rupture in general and to the specific intervention. In case of serious adverse events they are encouraged to seek immediate medical attention and for minor adverse events to contact the principal investigator by phone. At each session the patients will answer questions of possible adverse events during and between the sessions. The primary investigator will be monitoring a predetermined set of key points at each session.

23. Auditing

N/A

Ethics and dissemination

24. Research ethics approval

Before initiation of the project the study protocol, informed consent and patient information will be approved by:

- The Physiotherapy and Occupational therapy department and the Orthopaedic Surgery at Aalborg University Hospital

- The Ethics committee of North Denmark Region

25. Protocol amendments

26.ab Consent or assent

The primary investigator will obtain informed consent by the participants.

27. Confidentiality

All personal data collected on potential and enrolled participants is collected by telephone screening or at the baseline appointment. Data will be kept secure and for 10 years.

The GDPR – General Data Protection Regulation is followed. The study is registered at The Danish Data Protection Agency at Aalborg University Hospital.

28. Declaration of interests

All authors have no competing interests.

29. Access to data

All authors will have access to the full dataset before publication. The dataset will be stored at the sponsor site, Aalborg University hospital.

30. Ancillary and post-trial care

During and after completion of the study the included patients will be followed in the outpatient clinic and in The Danish Achilles tendon Database (DADB). Any serious adverse event occurrence will be reported and consulted with the Chief foot surgeon (ILK) the same day for re-ruptures or DVT and within 3 days for minor adverse events.

31. Dissemination policy

31a Plan for publication

The results of the study will be published in an international peer-reviewed journal for example the Journal of Pilot and Feasibility Studies or the Journal of Orthopaedic & Sports Physical Therapy (JOSPT). The preliminary title is: Development and feasibility of an early progressive strength exercise programme for acute Achilles tendon rupture.

The results will also be presented at relevant physiotherapy and orthopaedic conferences. Guidelines and the exercise protocol will be made available for online download, to ensure translation of the research results into useful information for clinical practice.

31b Authorship eligibility guidelines and any intended use of professional writers

All co-authors are expected to make substantial scientific contributions that will qualify them as co-authors according to the International Committee of Medical Journal Editors (ICMJE) recommendations for authorship[45]:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

MC will draft the manuscript with input from all the authors. MSR, ILK, JAZ and KGS will all participate with valuable scientific contributions to the manuscript.

Expected author list: Christensen M, Silbernagel KG, Zellers JA, Rathleff MS, Kjær IL

31c Plans for granting public access

Data will be available upon reasonable request.

Appendices

32. Informed consent materials:

33. Biological specimens:

None

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Appendix A. Table of the three exercises in the Feasibility study.

Toigo & Boutellier exercise descriptors	**Isometric contraction**	**Seated heel-rise**	**Elastic band**
X1 Load magnitude	15-20 RM	15-20 RM Progress to 15RM week 6/7 First step is to increase repetitions and second step is to add more load	15-20 RM Progress to 15RM week 6/7 First step is to increase repetitions and second step is to add more load
X2 number of repetitions	5	10-15	10-15
X3 number of sets	5	3	3
X4 rest btw sets	5 sec	10 sec	10 sec
X5 number of exercise interventions	Every hour (approx 15 hours per day) for week 2-3, then change to 5 times per day in week 4-9 as warm-up exercise.	5 per day	5 per day
X6 duration of the experimental period	Week 2 to 9	Week 3 to 9	From week 5 to 9
X7 Fractional and temporal distribution of the contraction modes per repetition and duration (s) of one repetition	5 sec	3s shortening 2s isometric 3s lengthening	3s-2s-3s (Focus is on the concentric phase. Important not to push beyond the neutral position in the eccentric phase)
X8 Rest in-between repetitions	2	2	2
X9 Time under tension	125 s per session 1875 s per day (hourly) 625 s per day (5 times)	240s per session 1200s per day	240s per session 1200 s per day
X10 Volitional muscular failure	No	No	No
X11 Range of motion	No range of motion. The foot is immobilized in equinus according to the number of wedges.	From plantarflexed foot position on the wedges to more plantarflexed, when performing the heel-rise	Dorsiflexion above neutral is not allowed. Full plantarflexion allowed.
X12 Recovery time in-between exercise sessions	1 hour	3 hours	3

X13 Anatomical definition of the exercise (exercise form)	Isometric contraction is performed inside the walkerboot with the foot in equinus according to the weekplan. Push the forefoot against the bottom of the walker and feel the contraction of the leg muscles as if you are going to make a heel-rise, but the walker boot restricts your motions. Extend the big toe to minimize the activity of the muscles for the big toe and increase activity of the leg muscles.	Seated heel-rise with leg in walker with "the wedges of the week". Open straps and liner of walker. Knee in 90 degrees position. Hold one hand at the back of the walker to stabilize. Extend the big toe. Lift the heel up from the walker/wedges. Make sure that you are using the leg muscles and not pulling up the leg with your thigh muscles. Rest the foot on the forefoot pad rather than on the toes alone. Progression: add weight on knee (either sandbag/rice, water bottle, upper body.	Performed seated with straight knee. Wrap the elastic band around the forefoot and hold both ends in the hand. Tighten the band, but make sure that the foot is not pulled beyond 90 degrees. Extend the big toe. Press the foot down against the tightened elastic band as far as you can move the foot. Hold the position and then slowly pull up the foot again, but still with a tightened band. Progression: Change elastic band to other color (more strength)

Borgs scale – Perceived exertion during exercise (/10) is used to guide the patients to progress or regress the load in each exercise. The recommended level being "easy" to "hard" (2-5/10). It is emphasized that the exercises must not cause sudden or severe pain in the tendon, but muscle soreness is to be expected.

Progression:

Progression of the exercises will be a continuous process. There are three main phases: facilitating, initiation of load, progression to more load. When progressing to the next phase or new type of exercise the following criteria has to be observed:

The load magnitude of the present exercise should be accomplished with the patient feeling comfortable doing the exercises and without persistent pain or discomfort during and after exercises.

Appendix B. Adverse events / safety protocol

Feasibility of an early progressive strength exercise program for acute Achilles tendon rupture.

Collecting information about safety and adverse events.

Questions of adverse events will be asked at each exercise session, before the intervention starts.

Part 1.

Open questions to the patient:

Have you experienced any symptoms since the last time you were here?

- Symptoms from your Achilles tendon, lower leg or foot?
- Symptoms from other parts of the body?

Have you experienced any new trauma or large load since last time you were here?

- On your Achilles tendon?
- To other parts of the body?

The response is registered as formulated by the patient.

Part 2.

Specific questions. Have you experienced any of the listed symptoms?

Symptoms	Yes /No	Comments. Description, location, cause, time, other scores (eg VAS)	Grade assessment. The specific symptoms are rated on C1-C7 or other relevant – if not possible then on the general scale (“C general”) (C=CTCAE)
Pain		Describe	C1
- Pain on VAS scale		If you have (or had) pain then place the marker at the scale corresponding to your pain. (Use A4 paper with precise measures or numeric scale in Redcap)	
Cramps		Describe	C7 Myalgia
Swelling/edema		Describe	C3 Localysed edema or C4 Edema limbs

Discomfort, unease, itch, sleeping sensation		Describe	C general
Breathing difficulties		Describe	C5 Thromboembolic event
Exercise induced pain in leg muscles during or after the exercises.		Describe	C7 Myalgia
Other? Describe nature of symptoms.		Describe	C general is used if no specific topic is applicable

Part 3:

Objective assessment by principal investigator.

Symptoms	Yes /No	Comments. Description, location, cause, time, other scores (eg VAS)	Grade assessment. The specific symptoms are rated on C1-C7 or other relevant – if not possible then on the general scale ("C general") (C=CTCAE)
Achilles tendon palpation – is there a gap?			C2 Muskuloskeletal deformity
Achilles tendon pain at palpation			C1 Pain
Achilles tendon length v ATRA			C2 Muskuloskeletal deformity
Muscle pain			C7 Myalgia
Local edema at Achilles tendon			C3 Localised edema
Edema in foot-ankle or lower leg			C4 Edema limbs
Redness or pressure marks			C8 Skin Ulcerations
Signs of DVT – pain, edema, tension in musculature			C5 Thromboembolic event
Other Specify			Cgeneral is used if no specific topic is applicable

How to grade the severity of adverse events

Grades (CTCAE) of the typical events. Consult CTCAE document if others are needed.

Cgenerel

Grade refers to the severity of the AE. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*.
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL**.
Grade 4	Life-threatening consequences; urgent intervention indicated.
Grade 5	Death related to AE.

C1: Pain (page 59)

Definition: A disorder characterized by the sensation of marked discomfort, distress or agony.

Grade 1	Mild pain
Grade 2	Moderate pain; limiting instrumental ADL
Grade 3	Severe pain; limiting self care ADL
Grade 4+5	- -

C2: Musculoskeletal deformity (Herunder re-ruptur og manglende heling) (page 124)

Definition: A disorder characterized by of a malformation of the musculoskeletal system.

Grade 1	Cosmetically and functionally insignificant hypoplasia
Grade 2	Deformity, hypoplasia, or asymmetry able to be remediated by prosthesis e.g., shoe insert) or covered by clothing
Grade 3	Significant deformity, hypoplasia, or asymmetry, unable to be remediated by prosthesis or covered by clothing; disabling
Grade 4+5	- -

C3:Localized edema (page 58)

Definition: A disorder characterized by swelling due to excessive fluid accumulation at a specific anatomic site

Grade 1	Localized to dependent areas, no disability or functional impairment
Grade 2	Moderate localized edema and intervention indicated; limiting instrumental ADL
Grade 3	Severe localized edema and intervention indicated; limiting self care ADL
Grade 4+5	- -

C4: Edema limbs (page 55)

Definition: A disorder characterized by swelling due to excessive fluid accumulation in the upper or lower extremities.

Grade 1	5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection
Grade 2	>10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour; limiting instrumental ADL
Grade 3	>30% inter-limb discrepancy in volume; gross deviation from normal anatomic contour; limiting self care ADL
Grade 4+5	- -

C5: Thromboembolic event (page 193)

Definition: A disorder characterized by occlusion of a vessel by a thrombus that has migrated from a distal site via the blood stream.

Grade 1	Venous thrombosis (e.g., superficial thrombosis)
Grade 2	Venous thrombosis (e.g., uncomplicated deep vein thrombosis), medical intervention indicated
Grade 3	Thrombosis (e.g., uncomplicated pulmonary embolism [venous], nonembolic cardiac mural [arterial] thrombus), medical intervention indicated
Grade 4	Life-threatening (e.g., pulmonary embolism, cerebrovascular event, arterial insufficiency); hemodynamic or neurologic instability; urgent intervention indicated
Grade 5	Death

C6: Gait disturbance (page 57)

Definition: A disorder characterized by walking difficulties.

Grade 1	Mild change in gait (e.g., wide-based, limping or hobbling)
Grade 2	Moderate change in gait (e.g., wide-based, limping or hobbling); assistive device indicated; limiting instrumental ADL
Grade 3	Disabling; limiting self care ADL
Grade 4+5	- -

C7: Myalgia (page 124)

Definition: A disorder characterized by marked discomfort sensation originating from a muscle or group of muscles.

Grade 1	Mild pain
Grade 2	Moderate pain; limiting instrumental ADL
Grade 3	Severe pain; limiting self care ADL
Grade 4+5	- -

C8: Skin Ulcerations (page 186)

Definition: A disorder characterized by circumscribed, inflammatory and necrotic erosive lesion on the skin.

Grade 1	Combined area of ulcers <1 cm; nonblanchable erythema of intact skin with associated warmth or edema
Grade 2	Combined area of ulcers 1 – 2 cm; partial thickness skin loss involving skin or subcutaneous fat
Grade 3	Combined area of ulcers >2 cm; full-thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to fascia
Grade 4	Any size ulcer with extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures with or without full thickness skin loss
Grade 5	Death

Other:
Bruising: (page 88)
Fall (page 89)
Generalized muscle weakness (page 121)