Study protocol and statistical analysis plan

Evaluation of the Effectiveness of Extracorporeal Shockwave Therapy in Patients With Patellar Tendinopathy on Its Micromorphology

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Study design and description

This work is designed as a prospective cohort study, in which the effects of low-energy focused extracorporeal shock wave therapy (ESWT) in patients with patellar tendinopathy (PT) on its micromorphology will be monitored. It is estimated that at least 21 patients will participate. In addition, there will be a small control group of healthy tendons which will be monitored to observe magnitude of natural changes.

Patients in both groups will have same program. The research within one patient will last a total of 16 weeks from the initial to the final examination. Potential participants will be selected based on the recommendation of a specialist doctor and their suitability will be assessed according to the inclusion criteria. They will then be invited to an initial examination. This will include an objective examination by a physiotherapist, a subjective assessment by the patient and an ultrasonographic (USG) examination followed by a micromorphological analysis using special software.

Patient selection

Patient will be included in the study if they meet these inclusion criteria:

- is a recreational athlete performing intensive sport activity loading patellar tendon (running, jumping, strength training etc.) at least 3 days in a week for minimum of 1 hour per session,
- is in age between 18-40 years,
- has a patellar tendon pain, which limits (at least in part) the quality of normal daily or sports activities,
- has clinical manifestation of PT (pain and impaired function) confirmed by clinician,
- has symptoms only in one leg, the other one is asymptomatic.

Patient will not be included if:

- any contraindication for ESWT is present (according to International Society for Medical Shockwave Treatment (ISMST) consensus at https://shockwavetherapy.org),
- is aware of any symptomatic mechanical tendon damage in the past (e.g., partial or complete rupture in relation to the injury),
- neurological, oncological, or systemic disease (e.g., neuropathy, lupus or rheumatic arthritis) coexists,
- is/was already treated for PT elsewhere (e.g., platelet-rich plasma therapy, physiotherapy)
- is using blood thinning medications or statins.

Initial and final examination

During the initial and final examinations, the several tasks to the patient will be performed. Firstly the anamnestic data will be collected, then the area of greatest pain will be localized by palpation.

Secondly, the patient will be asked to complete a validated Victorian Institute of Sports Assessment - Patella questionnaire, which assesses the subjectively perceived severity of the disease and partly its impact on the quality of normal daily or sports activities.

The patient's maximal pain will be assessed using a standardized numerical rating scale (NRS) of pain. The patient will be asked about the morning and maximum pain that could be caused by various factors.

Lastly, the ultrasonographic (US) examination of patient's AT in both legs will be performed. This examination is described in the following chapter.

Both, inital and final examinations in each patient will be performed by only one person (the investigator of the study). Follow-ups will be in the day of the last ESWT application (for NRS and VISA-P) and at 15 week (for all outcomes)

Ultrasonographic examination

US examination will be performed with a Mindray DC-70 machine with a linear probe type L12-3E with a frequency of 12 Hz in the preset “MSK” mode. The whole area of patellar tendon will be monitored from the apex patellae to the insertion site on the tibia by longitudinal and transverse imaging.

The values of anteroposterior tendon width at the anteroposterior widest point will be collected using the measuring instruments included in USG machine.

After that, the preset will be changed to the specific setting, and three pictures of each leg (symptomatic and asymptomatic) will be saved in long axis for subsequent micromorphological analysis using Spatial Frequency Analysis software (SFA). SFA is a non-invasive, specialized method which analyzes the US image. In particular, it analyzes the anisotropic B-mode speckle pattern arising from within a tissue type in the spatial frequency domain and is capable of detecting and comparing collagen fascicles organization, spacing, and density across various parameters. Mean of those three values will be used for statistical analysis.

ESWT application

The low-energy focused ESWT will be applied using the BTL-6000 FSWT machine with piezoelectric generator and a coupling pad which modulates penetration depth to 0-35 mm. The setting is chosen based on ISMST guidelines (https://shockwavetherapy.org): Energy Flux Density (EFD) between 0.14-0.18 mJ/mm2 due to patient tolerance, frequency at 5 Hz. A total of 2000 shocks will be applied semi-statically to the most US defined pathological area in patellar tendon followed by 2000 shocks dynamically to the quadriceps muscle always using a contact gel. The set parameters will not change during the study and will remain the same for each patient.

Data analysis

The normality of the data distribution will be determined by calculating the Shapiro-Wilk p value. Independent t-tests (or Mann Whitney U tests for non-parametric) will be performed for each parameter to compare baseline values between symptomatic and asymptomatic limb for US and SFA parameters. In addition, paired t-tests (or Wilcoxon tests) will be performed for each parameter, evaluated in each group separately (symptomatic, asymptomatic) between baseline and final values. To reach effect size, Cohen’s d will be calculated for paired t-tests and biserial rank correlation for non-parametric Wilcoxon test.

Intergroup statistical significance between baseline and follow-up values of morphological parameters will be evaluated using two-way ANOVA or non-parametric Kruskal-Wallis test. Statistical significance between time periods in VISA-P and NRS parameters will be evaluated using repeated measures ANOVA or non-parametric Friedman test with repeated measures.