Official Title of the study:

Effectiveness of night splinting after percutaneous needle fasciotomy in Dupuytren's contracture - a randomised controlled multicenter trial

Date:

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Statistical Analysis Plan

Study design

This randomized controlled trial aims to evaluate the treatment effect of a night splint in patients with Dupuytren's contracture. It contains two treatment arms: (1) percutaneous needle fasciotomy (PNF) combined with a night splint and finger training guided by a physiotherapist and (2) PNF without a night splint and finger training guided by a physiotherapist. Following a baseline assessment, participants that meet the eligibility criteria and consent to participation are randomly assigned to either one of the treatment groups at a 1:1 allocation ratio. In total, 154 patients are randomized according to Soares and Wu's big stick design and stratified by center (Berger VW, Antsygina O. A review of randomization methods in clinical trials. Clin Invest 2015. 5(12). The randomization sequence was generated by Riccardo Lo Martire, statistician at the Center for Clinical Research (CKF) in Dalarna (Rv4.1.2; randomizeR v2.0.0). The sequence was prepared in sequentially numbered opaque sealed envelopes by a research nurse at each center that was not involved in the recruitment process and distributed on a one-to-one basis following patient enrolment.

Active extension was defined as primary outcome. Secondary outcomes are active flexion and grip strength, subjective measurements as experienced health related quality of life (EQ-5D), pain on a visual analog scale, functional and cosmetical results in the 'Unité Rhumatologique des Affections de la Main' (URAM) as well as the study questionnaire. All outcomes will be measured both before and after treatment at all follow-ups by a physiotherapist, except extensions deficit which even will be measured directly after treatment with PNF. Complications will be monitored continuously at every visit defined as aberrance from expected recovery, more exact defined as recurrence, sensational disfunction, infection, flexor tendon injury, nerve injuries and impaired healing.

Number of patients and power calculation

Based on the primary outcome extension deficit, the sample size was calculated with a non-inferiority hypothesis under asymptotic normality. A difference of 10° was chosen as the non-inferiority margin, because 10° is not clinically relevant, the true difference between groups was assumed to be 0°, and the standard deviation of treatment effect was assumed to be 20° based on data from previous published studies (Jerosch-Herold 2011, Kemler 2012). With 80% power and a 97.5% confidence interval (alpha = 0.025), 64 participants are needed in each treatment group. With an expected loss to follow-up of 20%, the number of participants was increased to 154 (=64*2*1.2).

Data analyses

Analyses will be conducted primarily according to the intention-to-treat principle. The primary outcome will be analyzed in a repeated measures linear mixed-effects model. Fixed effects are time (factor: 2 weeks, 3 months, and 12 months from baseline), treatment group (PNF with night splint vs. PNF without night splint), their interaction, and the baseline measurement of total active extension (TAE). The planned random effects are the patients within centers, with an unstructured covariance matrix for the temporal dependency within patient.

Once the data from the 36-month follow-up is collected, the same model will be repeated including also the 36 month-measurement. Non-inferiority will be declared if the lower boundary of the two-sided 95% confidence interval of the marginal mean difference in extension at 12 months is larger than -10° (PNF with night splint - PNF without night splint).

For the secondary outcomes, the primary analysis model will be used to generate confidence intervals for the outcomes of active flexion and grip strength at 12 months, while bootstrap confidence intervals will be generated for the median difference of pain intensity on a visual analog scale, EQ-5D index, and URAM questions at 12 months; however, without a formal test of a non-inferiority hypothesis.