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Protocol Article

Adjuvant steroid to percutaneous needle fasciotomy for Dupuytren's contracture. An RCT study protocol

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ABSTRACT

INTRODUCTION. Percutaneous needle fasciotomy (PNF) is a non-invasive treatment option for finger flexion contractures caused by Dupuytren's disease. Variations in PNF techniques include the use of corticosteroid injection. In the presented randomised controlled trial, we compare the efficacy of PNF +/- corticosteroid injection in terms of reducing the recurrence rate.

METHODS. This study is performed as a two-armed, randomised controlled trial with a two-year follow-up. Patients will be allocated 1:1 to either PNF with corticosteroid injection (n = 200) or PNF with saline injection (n = 200). Follow-up is conducted at 90 days, one year, and two years after treatment. A finger goniometer will be used to assess finger extension deficit. Treatment complications and adverse events will be recorded, and patient-reported outcomes will be registered utilizing hand-specific and quality-of-life questionnaires.

CONCLUSIONS. This study is expected to be the first randomised controlled trial to compare PNF +/- single corticosteroid injection in a large cohort of patients with Dupuytren's contracture. The results will contribute to evidence-based recommendations for the treatment of Dupuytren's contracture.

FUNDING. The trial is funded by grants from the Graduate School of Health at Aarhus University, the Danish Rheumatism Association, the Danish Medical Association Foundation and the AP. Møller Foundation.

TRIAL REGISTRATION. The trial is registered with the CTIS (EU CT: 2022-501549-57-00) and Clinicaltrials.gov (NCT05440240).

Dupuytren's disease is a benign and chronic hand disease that affects up to one in three people over the course of a lifetime [1, 2]. The disease causes fibroproliferative changes in the aponeurotic fibers in the palm, which may range from palpable nodules in the palm to permanent finger flexion contracture [3], resulting in a hooked appearance and inability to fully extend the finger, also known as Dupuytren's contracture (DC). This may ultimately lead to impaired function of the hand and disability in daily activities [4].

DC can neither be prevented nor cured but can be treated surgically by releasing the flexion contracture. Open surgery, mainly by limited fasciectomy, in which the pathological DC tissue is removed, has until recently been the most applied method for DC in Europe [5]. Drawbacks of open surgery, including the need for general anaesthesia and prolonged recovery due to wound healing, have increased the popularity of minimally invasive techniques such as percutaneous needle fasciotomy (PNF) and injectable *Clostridium histolyticum* collagenase

(Xiapex) [6]. However, Xiapex was withdrawn from the European market in 2020. PNF is performed under local anaesthesia in which a fine syringe needle is used to perforate the Dupuytren cord repeatedly until it is weakened, after which the finger can be extended mechanically [7, 8]. The PNF technique has shown reliable clinical results regarding correction of the flexion deformity, along with fast recovery and safety [9-12]. Although several definitions exist, recurrence after PNF is common and has been reported to be 21.8% in the MCP joint five years after PNF, higher than that of more invasive treatments such as open fasciectomy (5.3%).

The described PNF technique varies and may include the use of corticosteroid injection [13-15]. Corticosteroids are hypothesised to modify disease progression in DC by softening the nodules [16]. The rationale behind combining corticosteroids with PNF lies in the potential synergistic effect of these modalities.

To date, only one randomised controlled trial has assessed the use of corticosteroids in PNF [15, 17]. The results seem promising in decreasing the recurrence rate when multiple injections of corticosteroids were applied within the first three months post-operatively [17]. No randomised trials exist comparing PNF with a single corticosteroid injection versus PNF alone.

In the current randomised controlled trial, we plan to compare the efficacy of PNF +/- single corticosteroid injection in terms of the ability to reduce DC recurrence within a two-year follow-up period.

Methods

Study design

This study is an investigator-initiated, randomised, controlled superiority trial following the CONSORT guidelines. Patients will be randomised 1:1 to one of two interventions: either PNF with corticosteroid injection (n = 200) or PNF with isotonic saline injection (n = 200) and followed at 90 days, one year, and two years post-operatively.

Study settings and patients

The study was initiated at Silkeborg Regional Hospital, Denmark. The first patient was enrolled in January 2023. Plans are in place to invite other hospitals to participate.

Patients are recruited in the outpatient clinic. A general practitioner refers patients to our clinic on suspicion of DC. All referred patients will be assessed for eligibility by an orthopaedic surgeon or specially trained PNF nurse dedicated to the project. The inclusion and exclusion criteria are defined in **Table 1**.

TABLE 1 Inclusion and exclusion criteria.

Inclusion criteria
≥ 45 yrs
DC of ≥ 20° PED in MCP joint measured with a finger goniometer
DC of either II-V finger, excluding the thumb due to angular deformity
Well-defined/palpable cord
Received oral and written information about the trial prior to inclusion
Willingness to participate and signed written informed patient consent form
Exclusion criteria
Legally incapacitated
Previous study inclusion with another finger ray
Isolated PIP or DIP joint contracture[a]
Previous hand surgery of the affected finger for any reason
Known allergy to the study medication
Anticoagulant therapy[b]
Pregnancy or lactation
Insulin-dependent diabetes mellitus
Ongoing systemic infection or local infection at the site of the procedure
Rheumatoid arthritis
Amyloidosis or mucopolysaccharidosis
Unable to communicate, cooperate or participate in follow-up
Unable to speak or read Danish language

DC = Dupuytren's contracture; DIP = distal interphalangeal; MCP = metacarpophalangeal; PED = passive extension deficit; PIP = proximal interphalangeal.
a) Defined as MCP joint contracture < 20° PED, regardless of the deficit in the PIP or DIP joint
b) Acetylsalicylic acid is not an exclusion criterion.

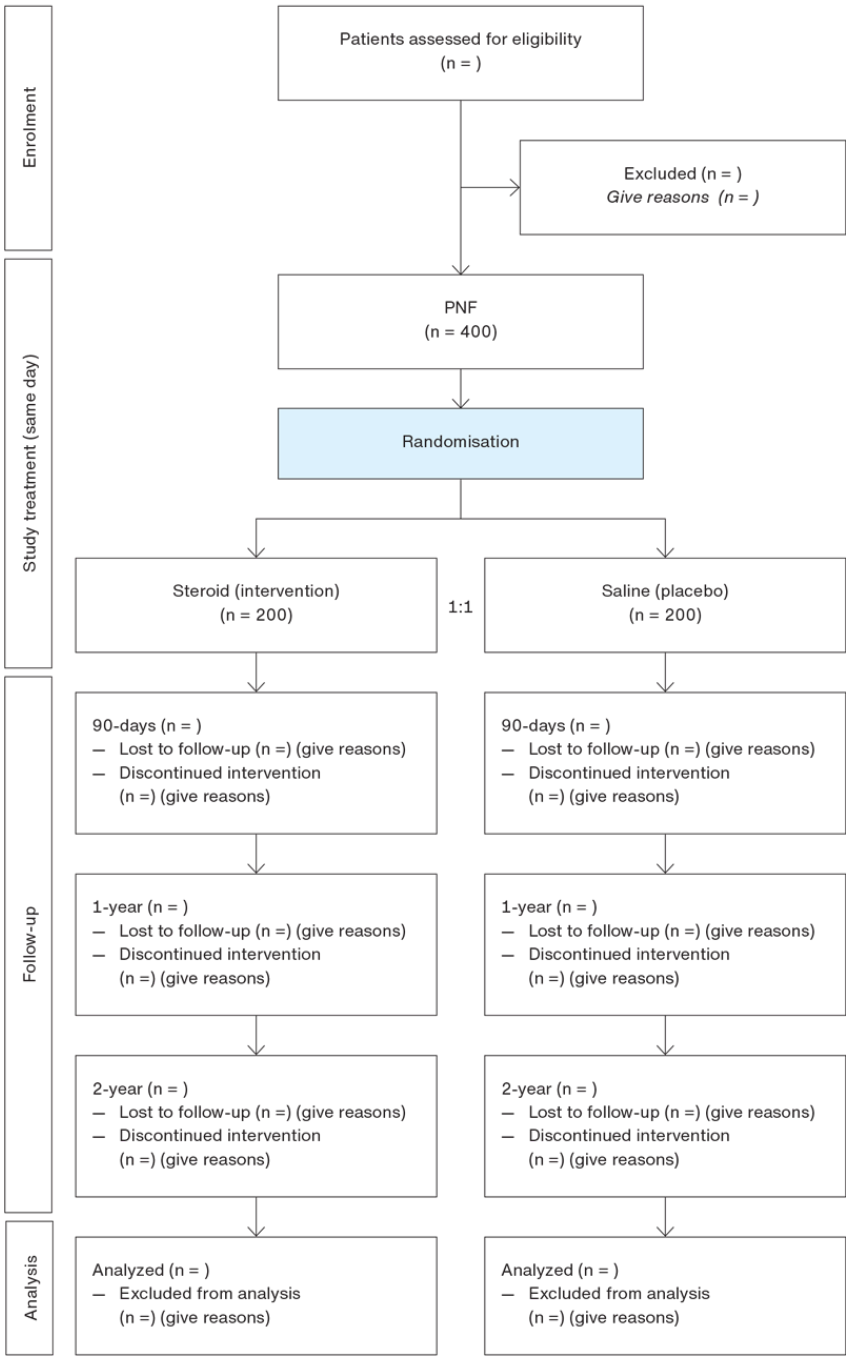
Patients will be included at the person level. If a patient presents with more than one DC-affected metacarpophalangeal (MCP) joint, the most affected finger ray is chosen for study inclusion.

The study population, including excluded patients, will be recorded and presented in a CONSORT flowchart.

Study procedures

The study flowchart is shown in **Figure 1**.

FIGURE 1 CONSORT study flow chart.



All participants will be treated with PNF and hereafter randomised into one of two treatment groups.

Percutaneous needle fasciotomy procedure

Percutaneous needle fasciotomy is performed in an outpatient setting. Following the standard disinfection procedure and sterile draping, 0.1-0.2 ml of 1% lidocaine with epinephrine is injected into chosen sites of the Dupuytren cord using a small, 25-gauge syringe needle. The anaesthetic is injected only intradermally to maintain full sensibility of the PNF-treated finger during the entire procedure.

The technique, by which the cord is then weakened, is a combination of repeated needle-tip perforations into the

cord and cautious pendulum cutting of the cord, with a 25-gauge needle at a slow pace and simultaneously passively stretching of the finger to rupture the Dupuytren cord. When the Dupuytren cord is sufficiently weakened, the finger can be stretched manually, and any potential residual cord strings can be ruptured slowly but forcefully. An additional local anaesthetic may be required to achieve a final manipulation at the end of the treatment, but only after the perforation/cutting has concluded [8, 10].

PNF is performed by an orthopaedic surgeon or specially trained PNF nurse.

Sufficient correction of the MCP joint contracture, defined as < 20 passive extension deficit (PED), measured at the end of the PNF procedure, is a prerequisite to inclusion in the study. At this point of the surgery, the patient is randomised to receive either corticosteroid injection (intervention) or saline injection (placebo), and the study drug is administered before applying a sterile dressing.

Intervention group: corticosteroid injection

A dose of 1 ml methylprednisolone 40 mg/ml is mixed with 1 ml of lidocaine and injected subcutaneously into the treated area of the DC cord.

Placebo group: saline injection

A total of 2 ml of standard isotonic sterile saline is injected subcutaneously into the treated area of the DC cord.

Randomisation and blinding procedure

Patients will be randomised 1:1 into two groups with 200 patients in each group. The randomisation is a computer-based, real-time process performed in the Research Electronic Data Capture (REDCap) system hosted at Aarhus University. The randomisation is stratified by hospital and gender. For each stratum, the allocation ratio is 1:1.

The patient will be randomised *after* PNF to ensure that the surgeon/PNF nurse is unaware of which allocation arm the patient is randomised to when performing the PNF procedure. The randomisation result will be passed on to the surgeon/PNF nurse on a note without being revealed to the patient, who is blinded to the treatment until the two-year follow-up. The surgical nurse prepares the syringe with the study drug.

The same procedure is used for all patients, regardless of whether corticosteroid or saline is administered. The patients can be slightly sensitive to needle insertion. Still, most will not experience discomfort because the skin is already locally anaesthetised from the PNF, and they cannot differentiate which injection type is given. Methylprednisolone is a cloudy white, odourless liquid. Saline is transparent. Therefore, blinding is not feasible for the surgeon. However, the patient is blinded to the given injection by a curtain/surgical drape obstructing their line of sight.

Follow-up

Independent occupational therapists, blinded to the given intervention, will conduct patient follow-ups at 90 days, one year and two years. The patients will complete a questionnaire.

Data collection and outcome

Data will be entered into and stored in a web-based electronic case report form (eCRF) in REDCap, specifically designed for this purpose.

Baseline characteristics

Age and gender will be collected. Further information about smoking, alcohol consumption, job status, family predisposition, diabetes, epilepsy, co-morbidities, previous hand trauma, multiple fingers being affected by DC

and/or previous DC treatments will be obtained by interview.

Primary outcome

The primary outcome parameter is recurrence, defined as ≥ 20&; PED in the MCP joint after two years. This primary outcome will be measured with a finger goniometer and analysed as a dichotomised value, defined as intervention success or failure. If the patient maintains an MCP joint < 20&; at the two-year follow-up, the endpoint is considered a success. If the patient presents an MCP joint ≥ 20&;or has received a new procedure in the MCP joint before the two-year follow-up, the endpoint is considered a failure.

Secondary outcomes

Secondary outcome parameters are shown in **Table 2.**

TABLE 2 Secondary outcomes.

Clinical outcome
Change in MCP joint PED: %
Straight MCP joint: 0-5 degrees
PED of MCP, PIP, DIP-joints: degrees
Total PED: degrees
Max. pulp-to-palm distance: mm
Tabletop test: positive/negative
Reoperation: yes/no
Safety
Complications and adverse events
Patient-reported outcome measures
Quick DASH
Southampton Dupuytren's Scoring Scheme
General health assessed using the EQ-5D-5L
Global rating of change scale for patient satisfaction

DASH = Disability of the Arm, Shoulder and Hand; DC = Dupuytren's contracture; DIP = distal interphalangeal; EQ-5D-5L = EuroQol 5-dimensions, 5-level version; MCP = metacarpophalangeal; PED = passive extension deficit; PIP = proximal interphalangeal.

Before inclusion and at each follow-up timepoint, the PED of the MCP, proximal interphalangeal (PIP) and distal

interphalangeal (DIP) joints of the project finger will be measured with a finger goniometer. Pulp-to-palm distance will be measured with a ruler, and a tabletop test will be performed.

Adverse events, defined as any harmful or unwanted reactions and treatment complications, will be recorded systematically on the day of surgery and at follow-up time points.

Before inclusion, the patient completes the questionnaires in the outpatient clinic. At defined follow-up time points, follow-up questionnaires will be sent to the patients by mail or post.

Statistics

Sample size calculation

The sample size calculation was performed on simple frequencies of patients reaching the primary outcome parameter given a two-sided alpha (risk for type 1 error) of 0.05, a power of 95% and a group ratio of one. The estimation was based on two previous studies reporting recurrence after PNF. Assuming that 2% in the corticosteroid group [9] and 12% in the saline group [18] would reach the primary outcome after two years, 334 patients will be needed. Incorporating a drop-out rate of 17%, a total of 400 patients are planned for inclusion in the study population.

General statistical approach

Data independence will be ensured at the patient level (one treated finger per patient, and a patient can only participate in the study once).

Normally distributed data will be assessed by visual inspection of qq plots.

The primary data analysis will be performed on the intention-to-treat population. A secondary per-protocol analysis will be performed, excluding patients not attending follow-ups.

If the data are normally distributed, comparisons between groups concerning baseline characteristics and outcome parameters will be analysed by t-test and reported as means with 95% confidence intervals (CI). The Wilcoxon rank-sum test will be applied for categorical or nonparametric data, reported as medians with ranges. Dichotomised outcomes will be analysed using the χ^2 square test or Fisher's exact test, reported as proportions with 95% CI.

Adverse events and complications will be represented in a table.

All analyses will be performed in R Studio.

Ethics and monitoring

The medicine used in this study is commercially available and widely used in medical practice. Corticosteroid injections are already used in the PNF treatment regimen at some orthopaedic departments nationally and internationally. Thus, patients are not expected to be subjected to any unknown risks.

The study is registered with ClinicalTrials.gov (NCT05440240) and approved by the Health Research Ethics Committee and The Danish Medicines Agency (EU CT: 2022-501549-57-00). It will be conducted in accordance with the Helsinki Declaration. Oral and written informed patient consent will be obtained before study inclusion. All personal data will be stored securely to ensure confidentiality before, during and after the trial.

The Good Clinical Practices (GCP) Unit at Aarhus University Hospital will monitor the study process according to the Danish Pharmaceutical Trials Act (Project ID: 2022-985). The authors will also monitor any adverse events.

Dissemination of results will be performed irrespective of the nature of the results.

Discussion

The current trial will provide important new knowledge about the use of corticosteroids in PNF treatment for DC, a common pathology in the general population. To our knowledge, it is the first randomised controlled trial to evaluate whether add-on corticosteroids improve the short-/long-term effect of PNF and whether these drugs entail a higher complication rate. We also believe that the study will benefit surgeons in their decision-making process for treatment and benefit the considerable number of patients affected by DC.

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Conflicts of interest none. Disclosure forms provided by the authors are available with the article at ugeskriftet.dk/dmj

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