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DupuytrEn Treatment EffeCtiveness Trial (DETECT): a protocol for prospective, randomised, controlled, outcome assessor-blinded, three-armed parallel 1:1:1, multicentre trial comparing the effectiveness and cost of collagenase clostridium histolyticum, percutaneous needle fasciotomy and limited fasciectomy as short-term and long-term treatment strategies in Dupuytren's contracture

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ABSTRACT

Introduction Dupuytren's contracture (DC) is a chronic fibroproliferative disorder of the palmar fascia which leads to flexion contracture in one or more fingers. There is no definitive cure for DC, and treatment aims at relieving symptoms by releasing the contracture using percutaneous or operative techniques.

Methods and analysis We planned a prospective, randomised, controlled, outcome assessor-blinded, three-armed parallel 1:1:1, multicentre trial comparing the effectiveness and cost of (1) collagenase clostridium histolyticum injection followed by limited fasciectomy in non-responsive cases, (2) percutaneous needle fasciotomy followed by limited fasciectomy in non-responsive cases and (3) primary limited fasciectomy during short-term and long-term follow-up for Tubiana I–III stages DC. We will recruit participants from seven national centres in Finland. Primary outcome is the rate of success in the treatment arm at 5 years after recruitment. Success is a composite outcome comprising (1) at least 50% contracture release from the date of recruitment and (2) participants in a patient-accepted symptom state (PASS). Secondary outcomes are (1) angle of contracture, (2) quick disabilities of the arm, a shoulder and hand outcome measure (QuickDASH), (3) perceived hand function, (4) EQ-5D-3L, (5) rate of major adverse events, (6) patient's trust of the treatment, (7) global rating, (8) rate of PASS, (9) rate of minimal clinically important improvement, (10) expenses, (11) progression of disease, (12) progression-free survival, (13) favoured treatment modality, (14) patients achieving full contracture release and >50% improvement and (15) patient satisfaction with the treatment effect. Predictive factors for achieving the PASS will also be analysed.

Ethics and dissemination The protocol was approved by the Tampere University Hospital Institutional Review Board and Finnish Medicine Agency. The study will be performed according to the principles of good clinical practice. The results of the trial will be disseminated as published articles in peer-reviewed journals.

Trial registration number NCT03192020; Pre-results.

Strengths and limitations of this study

- Long-term follow-up of effectiveness and cost of treatment strategies rather than single interventions.
- Simulates current clinical practices with wide inclusion of population affected by the disease because of the primary public-funded healthcare system.
- There are other potential strategies that could be used.
- Study is performed in Finland, and cost-effectiveness analysis may not be fully generalisable to other countries.
- Patients with several affected digits or both hands affected may be treated with a primary intervention for each digit on several occasions which may cause variance in the short-term follow-up.

INTRODUCTION

Background

Dupuytren's contracture (DC) is a genetically regulated[1 2] fibroproliferative disorder of the palmar fascia. The estimated global prevalence among whites is 3%–6%.[3 4] Prevalence rises with age and is 12% at age 55 years and 29% at age 75 years.[5] However, not all patients have a contracture, some have only asymptomatic soft tissue changes. The affected palmar fascia gradually forms thick cords which cause flexion contracture in one or more fingers. The contracture most often develops in the metacarpophalangeal (MP) joint or proximal interphalangeal (PIP) joint of the ring and little fingers.[6] Typically, washing one's face or putting gloves on becomes difficult.

There is no definitive cure for the pathological process in DC. The treatment aims at relieving the contracture by cutting or excising the cords, limiting the range of motion (ROM) of the fingers. The options can be divided into two categories: (1) open surgical excision and (2) percutaneous division of the cords using a needle or collagenase solution. Open excision of fascial cords (limited fasciectomy, LF) was the standard treatment until recently, while collagenase clostridium histolyticum (CCH) injection has gained more popularity lately.[7] In an outpatient clinic, collagenase is injected inside the cord, which is ruptured by gentle force after a day or two. In percutaneous needle fasciotomy (PNF), the cord causing the contracture is divided with a hypodermic needle leading to release.

Rationale of the study

Multiple comparisons of efficacy of the three treatment options have been made.[8–20] In summary, in Tubiana I–III stages of the contracture (<135° of extension deficit), the two percutaneous treatments show comparable short-term efficacies, while the LF yields better angular contracture release when compared with PNF in severe stages of the disease.[16] However, although the angular release is more complete after LF compared with PNF, the patients can be more satisfied with the percutaneous treatment.[16] Although CCH has not been compared with LF in a randomised controlled trial, non-randomised comparative studies suggest that the release of contracture is equivalent, but patients return to work and daily activities in a shorter time after CCH.[21] Over longer periods, the recurrence probably occurs earlier after percutaneous treatments compared with LF.[17 22] The cost-effectiveness of the three treatments has not been compared in prospective randomised studies. Cost analyses show that PNF is the cheapest option followed by CCH and LF when single interventions are compared.[11 23–25] Cost comparisons, however, are affected by the price allocated for each treatment. Currently, there are insufficient data to determine if one treatment is more cost-effective than others.

DC is a chronic condition, and the recurrence is almost inevitable during long-term follow-up. This results in repeated interventions which can be performed either in a percutaneous or open manner with good results. Hence, in the clinical realm, the disease can be approached using three long-term strategies: (1) the cords are initially divided by PNF and patients who eventually fail to respond undergo surgery; (2) the cords are initially dissolved with CCH and patients who eventually fail to respond undergo surgery; and (3) the cords are treated with surgery both primarily and in the case of recurrence.

Studies concerning efficacy or costs of a single intervention are not sufficient to determine effectiveness (ie, how the treatment works in everyday practice) of treatment strategies. Instead, effectiveness should be assessed by comparing treatment strategies, which are used in normal practice and can include several interventions. Outcomes should be patient-centred and also include the payer's perspective (eg, patient seeking further treatment). Surgeon-centred outcomes (eg, angular measurements) are of less value when the patient continues functioning well and is not in need of further treatment. LF, CHH and PNF have all shown efficacy in contracture release, but there is an obvious need to assess the effectiveness of different treatment strategies in long-term follow-up.

Study aim and hypothesis

Our primary aim is to compare the effectiveness and cost of three treatment strategies over 5 years of follow-up: (1) PNF followed by surgical LF in patients who fail to respond; (2) CCH followed by surgical LF in patients who fail to respond; and (3) LF as the primary (and secondary) treatment modality (figure 1) in patients suffering from Tubiana I–III stages (20°–135° total passive extension deficit, TPED) of DC. The secondary aim is to compare the clinical outcomes of the three aforementioned treatment strategies at 3 months, 2 years, 5 years and 10 years.

METHODS AND ANALYSIS

Trial design

The trial design of DETECT is a multicentre, randomised, controlled, assessor blinded, three-armed 1:1:1, superiority trial with three parallel groups.

Study setting

The participants will be recruited from seven national tertiary and secondary referral centres in Finland that have at least one practising specialist in hand surgery (lead investigator, LI). Because of the nationwide public healthcare system, each of the participating hospitals is expected to see most of the DC cases in the population. To be eligible, the investigators must have a specialist degree in hand surgery, and they must have performed each of the three treatments more than ten times prior to the study commencement. All the LIs will participate in training to standardise measurements and execution of treatments before participating in the trial.

Information on the trial and approval of the patient

The LI will inform the patients about the trial. A written information form about the study is given to the patient.

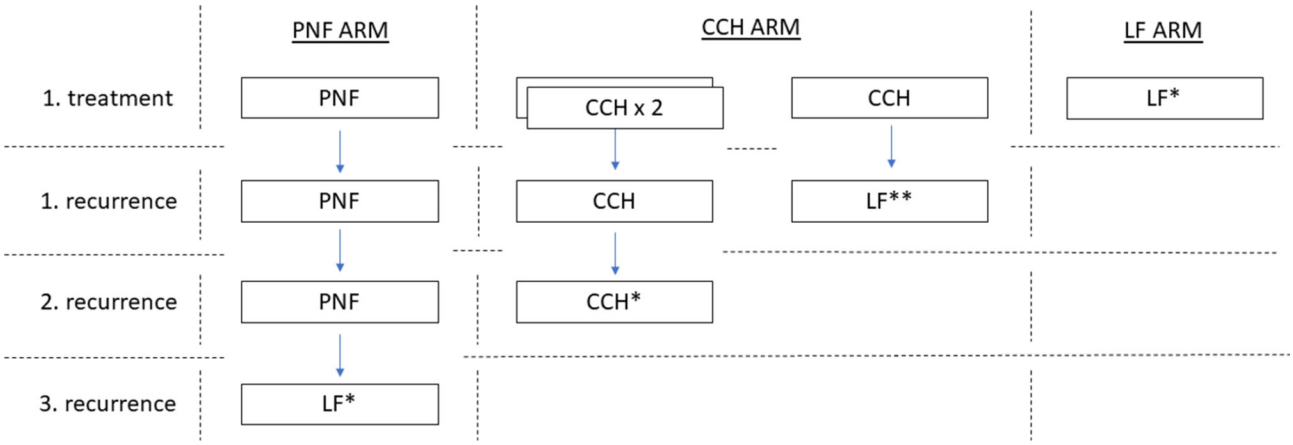

Figure 1 Four examples of possible scenarios in the different treatment strategy arms. *Success; **Success not achieved but patient does not want new treatment. CCH, collagenase clostridium histolyticum; LF, limited fasciectomy; PNF, percutaneous needle fasciotomy.

The LI will obtain the consent from the participants and collect the baseline data prior to the randomisation.

Participants

The LI will screen all the patients, who are referred to the study centres under the diagnosis of DC. The inclusion criteria are (1) patients with ≥20° passive extension deficit (PED) in MP or PIP joint, or TPED of ≥30° in MP and PIP joints of finger/fingers II–V; (2) age>18 years; (3) a palpable cord; (4) provision of informed consent; and (5) the ability to fill out the Finnish versions of the questionnaires. The exclusion criteria are (1) recurrent contracture in the finger to be treated, (2) neurological condition causing the loss of function of the finger to be treated, (3) contraindication for CCH (Xiapex/Xiaflex), (4) pregnant or breast feeding, (5) total TPED>135° (Tubiana stage IV[26]) in the finger to be treated, (6) rheumatoid arthritis, (7) previous fracture in the finger to be treated that affects the ROM of the MP or PIP joint and (8) age>80 years.

Baseline assessment

Baseline assessment includes sex, age, handedness, involved fingers (rays), involved joints, history of treatment in other fingers than treated in the trial, duration of symptoms, DC in family, history of smoking, occupation, education, knuckle pads, Peyron or Ledderhose disease, comorbidities, quick disabilities of the arm, a shoulder and hand outcome measure (QuickDASH), EQ-5D-3L, VAS function, state of contracture (static or dynamic), patient's trust of the treatment and angle of contracture including TPED, PED of each joint and ROM. Patients, who are allocated to the LF arm, will be assessed for their functional and angular scores during recruitment and on the day of the intervention. Both measurements will be reported. Intervention day values are used in the primary analysis.

Randomisation and blinding

A centralised allocation system will be used. After the recruitment and baseline assessment, the LI receives a randomisation code from the coordinating research assistant (CRA) via phone. The concealment of allocation is ensured, as the LI is not aware of the sequence and the randomisation code is released only after the patient data are given to the CRA. The patients are allocated 1:1:1 with a random block size. The dominantly affected joint (greater PED, MP or PIP joint) will be used as a stratification criterion. In participants with several affected rays which fulfil the criteria for treatment, if any of the PIP joints has more extension deficit than the MP joint, the patient will be stratified and later analysed as having predominantly PIP joint contracture. The patient is scheduled for treatment within 3 months from the inclusion. If the patient has inclusion criteria fulfilling contracture in both hands, the follow-up time starts from the latter intervention (if both hands are not treated at the same visit). Patients with multiple affected rays are randomised to one treatment arm, and each patient (not ray) is analysed as one subject.

The patient, LI and CRA are not blinded to the allocation. Allocation is concealed from the blinded outcome assessor (BOA) of each centre. Before measurement, patient will dress sterile glove to the hand and is instructed not to discuss the treatment with the BOA. The BOA does not participate in the care at any other point of the study.

Interventions

In the CCH arm, 0.58 mg collagenase will be injected into the cord. The finger is straightened under local anaesthesia 1–3 days after in the outpatient clinic. If the patient is not satisfied with the outcome, the patient is offered a new CCH injection, if there is a palpable cord. Treatment can be performed up to three times. Interval between the injections is 4 weeks. The patient can also choose no further treatment or LF after the first intervention, if they do not want to have the same treatment again. If no

Table 1 The assessment time points

Outcome	Preoperatively	3 Months*	2 Years†	5 Years†	10 Years†
Rate of success		X	X	X	X
Patient's trust of the treatment	X				
QuickDASH	X	X	X	X	X
Perceived hand function	X	X	X	X	X
EQ-5D-3L	X	X	X	X	X
MAEs		X	X	X	X
Angle of contracture	X	X	X	X	X
Patients achieving full contracture release and >50% improvement		X	X	X	X
Patients achieving PASS		X	X	X	X
Global rating		X	X	X	X
Rate of MCII		X	X	X	X
Expenses			X	X	X
Progression of disease‡			X	X	X
Progression-free survival			X	X	X
Favoured treatment modality			X	X	X
Patient satisfaction with the treatment		X	X	X	X
Predictive factors for achieving PASS		X	X	X	X

*Follow-up visit will be 3 months from the last treatment.
†Follow-up visit will be 2, 5 or 10 years from primary visit.
‡Clinically relevant progression is defined as rate of patients who contact the study centre because they are not in PASS because of recurrence or extension of the disease, and at least 20° flexion contracture is observed in ray which patient wants to be treated. Clinically irrelevant progression is measured as ΔTPED in those who have no reinterventions during the follow-up.
EQ-5D-3L, Euroqol Five Dimensions Three Level Questionnaire; MAEs, major adverse events; MCII, minimal clinically important improvement.; PASS, patient-accepted symptom state; QuickDASH, quick disabilities of the arm, a shoulder and hand outcome measure.

palpable cord exists, the patient can choose between no further treatment and LF.

In the PNF arm, the cord will be divided under local anaesthesia with a hypodermic needle in 1–3 levels to release the contracture as completely as possible. If the patient is not satisfied with the outcome, the patient can choose between another PNF, no further treatment and LF.

In the LF arm, the procedure is performed in an operation theatre. After the skin incision, the cord is exposed and excised. If extension lag exists after the excision of the cord, a gentle passive manipulation is performed to extend the finger. If there is still extension lag, the surgeon will decide if the volar structures and collateral ligaments are released. Similarly, skin grafts and night splint can be used based on surgeon's judgement. Standardised instructions for rehabilitation are given to the patient for self-implemented physiotherapy.

Study outcomes

Study outcomes and follow-up time points are summarised in table 1.

Primary outcome

Primary outcome is the rate of success in the treatment arm after 5 years of follow-up. Success is a composite outcome comprising (1) at least 50% contracture release from the recruitment and (2) patient is in a patient-accepted symptom state (PASS, ie, patient is satisfied with the current state of symptoms and does not feel the need for any further treatment). Success is defined and analysed in patient level. If the patient has multiple affected rays in the time of allocation, each must meet the 50% improvement criteria so that the participant is defined as success. In this study, PASS is defined by the question: 'Would you be satisfied and not in need for any other treatment if the functional impairment caused by the contracture would remain the same as it is today for the rest of your life?'

The PASS is a relevant patient-centred outcome measurement which reflects the overall state in which patients consider themselves well.[27] It is a state of the symptoms between complete remission and subjective dissatisfaction with the symptoms. It is subjective and can vary between the patients, although it can be remarkably stable within subjects.[28] It has been used in musculoskeletal studies and shows stability over time. Although the PASS has not been assessed in DC, a simple question about patient satisfaction has correlated well with questionnaires of hand function (QuickDASH and Southampton Dupuytren Scoring Scheme) and how willing the patient is to undergo treatment again after CCH injection.[9] Furthermore, 50% of contracture release

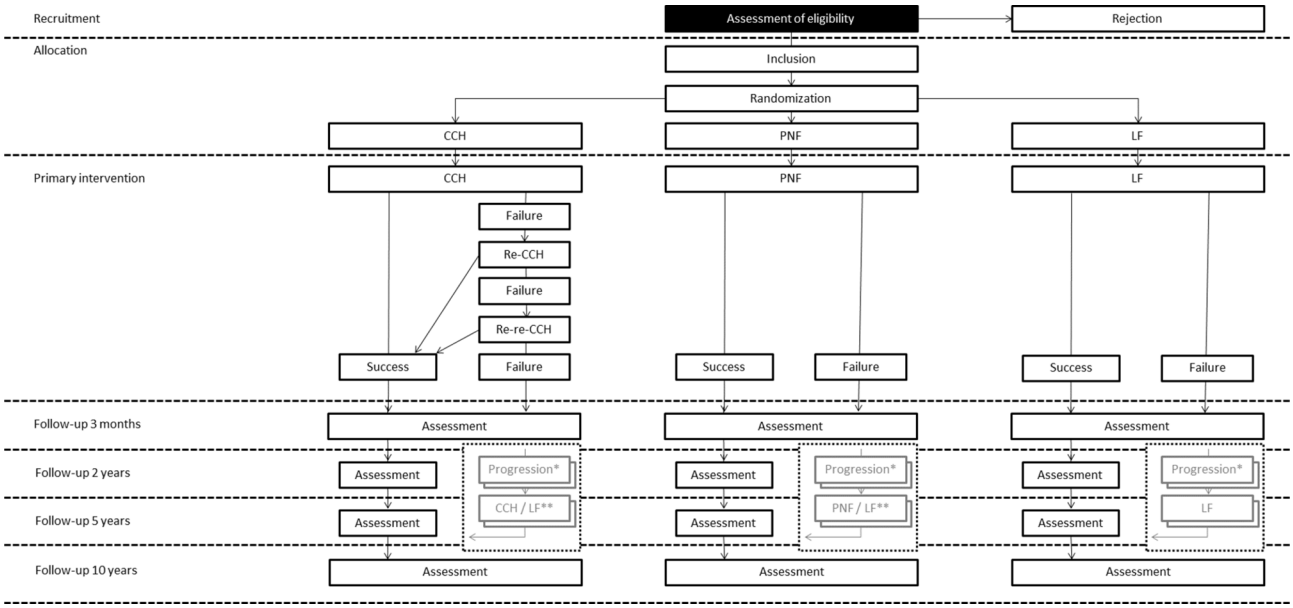

Figure 2 The assessment and treatment plan. *Clinically relevant progression is diagnosed in this trial when the patient contacts an outpatient clinic, because the disease has recurred or manifested in another finger (extension of disease) and the patient requests further treatment; that is, patient is not in a patient-accepted symptom state anymore, and at least 20° flexion contracture is observed. Note that the patient's request for treatment is not limited to follow-up visits. The secondary treatment can be carried out whenever the patient requests it, but no sooner than 3 months after the primary intervention. **The patient will be treated with the same intervention as allocated primarily. However, the patient has right to refuse CCH or PNF and can request LF. If there is no palpable cord, the surgeon can decide to perform LF instead of CCH or PNF. CCH, collagenase clostridium histolyticum; LF, limited fasciectomy; PNF, percutaneous needle fasciotomy.

was considered clinically significant in a previous study, which assessed the efficacy of CCH.[18 29] The rationale for including objective measurement (50% contracture release) is to avoid situation where patients report being in PASS only because they were treated or they do not want to go through further treatments.

Secondary outcomes

Secondary outcomes are listed in table 1 and explained in online supplementary appendix 1.

Progression of the disease

Progression of disease is measured and reported in three levels: (1) rate of reinterventions in the arm due to recurrence or extension of the disease (clinically relevant progression); (2) costs of reinterventions (impact of progression); and (3) change in TPED in those patients who do not require further treatments (clinically irrelevant progression).

Recurrence or extension is treated if the patient contacts the study centre and requires new treatment (ie, patient is not in the PASS anymore) and at least 20° flexion contracture is observed in one of the joints which patient wants to be treated. However, if over 20° flexion contracture is noted at the study follow-up points, but the patient considers themselves to be in a PASS and not in need of further treatment, it will not be defined or treated as clinically relevant progression. The costs of reinterventions are measured and reported for each arm. Clinically irrelevant progression is measured in ΔTPED in treated rays (average Δ/ray when multiple rays are treated) in those patients who do not seek further treatment during the follow-up.

The LI will treat progression according to the allocation. In the CCH and PNF arms, LF can be performed if any of the following conditions is met: (1) patients refuse percutaneous treatment, because they are not satisfied with the results; (2) the cord causing the contracture is not palpable; or (3) the percutaneous treatment fails to achieve PASS (figure 2). Patients in the LF arm will not be offered PNF or CCH at any point of the study.

Sample size

For the sample size calculation, the results from previous studies were used, in which patients had undergone CCH or PNF.[14] Based on these studies, we expect to find success rates of 60%–80% for all treatment arms. To detect a 20% difference in the success rate between the groups with a power of 80% and using a two-sided type I error rate of 5%, our trial requires 84 patients in each group or a total of 252. To allow 10% loss during follow-up, we will recruit 278 patients.

Adherence and discontinuation

High adherence to the treatment is expected because all therapies are in use, all have been proven efficacious and the care is affordable due to national healthcare insurance. We are assuming adherence over 90% for the follow-up. A multicentre study design will help to enlist the required number of patients. At the time of the recruitment, the LI of the centre will tell the patient, that the treatment can be changed from the CCH and PNF

to the LF, if adequate improvement of hand function is not achieved at the 3-month postoperative evaluation and after that at any point. Patients can quit the study at any point and if they do, the data collection is stopped and only the data collected until that point are used in the study.

Statistical plan

All analyses will be performed on the intention-to-treat principle, defined as including all patients who will be randomised in the study. The descriptive statistics will be presented as means with SDs, as medians with IQR or as counts with percentages. The most important values and differences between groups will be expressed with 95% CIs. X^2-based tests or the Mantel-Haenszel combined test will be used to compare the prevalence of the primary endpoint. The statistical significance between groups will also be evaluated by generalised linear models with appropriate distribution and link functions. In the case of violation of the assumptions (eg, non-normality), a bootstrap-type test or non-parametric method will be used. Repeated measures will be analysed using generalised linear mixed models with an unstructured correlation. The fixed effects will be group, time and the group–time interaction. To control for clustering, study centre is included as random effect in primary outcome analysis. Hand and ray are added as random effects in TPED analysis. Time-to-event analysis will be based on the product limit estimate of the cumulative 'survival' function or Poisson regression models. Cost analyses will be performed using a generalised linear regression model with log link and gamma variance functions. The variance function will be selected based on Park test and Akaike's information criterion. A recycled prediction simulation will estimate the incremental cost. The minimal clinically important improvement (MCII) will be determined with receiver operating characteristic (ROC) regression. The ROC analysis will be performed separately for each treatment arm and for different stages of the disease. The cut-off values for the different stages are 0°–45°, 45°–90° and 90°–135°. The normality of variables will be evaluated with the Shapiro-Wilk W test. Hommel's adjustment will be applied to correct levels of significance for multiple testing, if appropriate. In case of missing data, we will use multiple imputation method. All statistical analyses will be performed using Stata (the most recent version available) (StataCorp LCC, College Station, TX, USA).

ETHICS AND DISSEMINATION

All the treatments are widely used in DC, and they are considered equally safe. The protocol is registered with clinicaltrials.gov (trial identifying number NCT03192020, table 2). The study protocol was composed according to the Standard Protocol Items: Recommendations for Interventional Trials statement. Any protocol amendments are communicated to the LIs and the data safety and monitoring committee (DSMC). Approval of the institutional review board and Finnish Medicine Agency will be requested before implementation of the amendments. The amendments are also reported in the clinicaltrials.gov registry. The protocol and results will be reported in peer-reviewed journals, and the data from the trial will be available on request. The members of steering committee, writing committee and LIs of each centre are eligible for authorship of the publications. Principal investigators (OL and TK) will identify writing committee, which is responsible for the reporting of the data.

At each centre, the data are collected and entered directly into the trial electronic database, E-lomake (Eduix Oy, Tampere, Finland). The database is password protected. All electronic data will be entered with the patient's trial number and a separate paper log of patients is kept in each study centre. The junior investigator, the principal investigators and DSMC are the only ones who have access to the final dataset, and there is no disclosure of contractual agreements that limit such access. Data are shared by request anonymously. Data will be stored after the trial for 15 years.

Data management

The DSMC will be established that consists of one statistician, one clinician familiar with clinical trials and one clinician familiar with DC. All major adverse events (MAEs) will be documented in detail, and will be reported to the DSMC. We will consider any MAE that can be attributed to the intervention and requires hospitalisation of the patient. All the MAEs will be reported within 48 hours. Participants who suffer an MAE will be given adequate medical treatment and will be entitled to apply compensation from the Finnish Patient Insurance Centre or Pharmaceutical Injuries Insurance.

We will not conduct interim analyses outside the planned follow-up points. The study will be monitored by an independent assessor before commencement of the study, during and after recruitment of the participants and after completion. This study will be conducted in accordance with the Declaration of Helsinki. The principles of good clinical practice will be followed and respected.

DISCUSSION

This comparative effectiveness research study will assess the short and long-term effectiveness and cost of three commonly used treatment strategies for DC, a chronic fibroproliferative disease that cannot be cured. The treatment aims at reducing the functional deficit caused by the contracture. Recurrence is almost inevitable if the follow-up is long enough. Therefore, we aim to compare the effectiveness of treatment strategies rather than efficacy of single interventions. In this respect, our study is different from other studies assessing the efficacy of a single intervention in short-term follow-up.

We chose a primary outcome that comprises both objective and subjective stand points: successful treatment is defined as significant improvement of the contracture (50%) as well as the patient achieving a state in which

Table 2 The content of the trial registry

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT03192020
Date of registration in primary registry	16 June 2017
Date and version identifier	19 June 2017, V.5.5
Source(s) of monetary or material support	–
Primary sponsor	Tampere University Hospital, Teiskontie 35, 33520 Tampere, Finland
Secondary sponsor	University of Tampere
Contact for public queries	Olli V Leppänen, Email: olli.leppanen@fimnet.fi.fi, Tel: +358–3–311611
Contact for scientific queries	Olli V Leppänen, Email: olli.leppanen@fimnet.fi, Tel: +358–3–311611
Public title	Trial Comparing Treatment Strategies in Dupuytren's Contracture (DETECT)
Scientific title	DupuytrEn Treatment EffeCtiveness Trial (DETECT): prospective, randomised, controlled, outcome assessor-blinded, three armed parallel 1:1:1, multicentre trial comparing effectiveness and cost of collagenase clostridium histolyticum, percutaneous needle fasciotomy and limited fasciectomy as a short and long-term treatment strategies in Dupuytren's contracture
Countries of recruitment	Finland
Health condition(s) or problem(s)	Dupuytren contracture
Intervention(s)	Collagenase clostridium histolyticum, percutaneous needle fasciotomy and limited fasciectomy
Key inclusion and exclusion criteria	Inclusion: patients with ≥20° passive extension deficit in MP or PIP joint, or TPED of ≥30° in MP and PIP joints of finger/fingers II–V, age>18 years, palpable cord, provision of informed consent and ability to fill Finnish versions of questionnaires.
	Exclusion: recurrent contracture, neurological condition or previous fracture affecting finger to be treated, contraindication to collagenase clostridium histolyticum, pregnant or breast feeding, TPED>135°, rheumatoid arthritis and age>80 years
	Allocation: randomised
	Intervention model: parallel assignment
	Masking: single blind (outcome assessor)
Study type	Primary purpose: treatment
Date of first enrolment	September 2017
Target sample size	278
Recruitment status	Recruiting
Primary outcome(s)	Primary outcome is the rate of success in the treatment arm after 5 years of follow-up.
Key secondary outcomes	Rate of success, entrustment of the treatment, QuickDASH, perceived hand function, EQ-5D-3L, MAEs, angle of contracture, global rating, rate of MCII, expenses, progression, progression-free survival, favoured treatment modality, patient satisfaction and PASS

EQ-5D-3L, Euroqol Five Dimensions Three Level Questionnaire; MAEs, major adverse events; MCII, minimal clinically important improvement; MP, metacarpophalangeal; PASS, patient-accepted symptom state; PIP, proximal interphalangeal; QuickDASH, quick disabilities of the arm, shoulder and hand score; TPED, total passive extension deficit.

they consider themselves well and not in need for any other treatment (PASS). When the patient is subjectively not in need of further treatment, the goals of both the patient and healthcare provider are met. The rationale for including angular cut-off is to avoid situation where patient claims being in PASS only to avoid further treatments. We will report degree of contracture release in each treatment arm to further facilitate the comparison between the arms.

All the treatment modalities of this study have been proven efficacious for contracture release. The reported differences in the primary results are small or negligible in Tubiana I–III stages of the diseases. The rates of recurrences of the different treatments are difficult to compare as the definition of recurrence and follow-up times heavily affects the interpretation of results.[30] We expect to find higher rate of progression of disease and, thus, higher rates of secondary interventions after

percutaneous treatments. Instead of reporting progression of the disease as dichotomous phenomenon, we will assess the progression in three levels: (1) rate of reinterventions (clinically relevant progression including both recurrence and extension), (2) total costs (impact to the society) and (3) deterioration of contracture (ΔTPED) compared with the situation after primary intervention in patients who have no further interventions (clinically irrelevant progression). This approach is transparent and circumvents having an arbitrary cut-off point in a gradually progressing phenomenon.

It is not feasible to include all the possible strategies in one study. Furthermore, patients with several affected rays or both hands affected may undergo a primary intervention for each digit over several occasions followed by short convalescence periods. In these cases, the follow-up point may be longer than planned for some of the rays. This may have a small effect on the primary efficacy results at the 3-month follow-up, but we expect that at the 2-year and 5-year follow-up points, the time difference will be negligible. We will try to complete the primary intervention in one visit whenever possible and expect that the proportion of patients having multiple primary interventions will be <10%. To safeguard against bias arising from this, we will report the inconsistency and adjust the analysis if there is a difference. Finally, position of adjacent joint may affect the angular measurement values particularly in PIP joint level.[31] We control this by standardising the position of the joints during the measurement (online supplementary appendix 1).

In conclusion, this study compares the short and long-term effectiveness and cost of three different treatment strategies of DC. We will use a pragmatic approach and primarily assess the rate of solved functional problems from both the patient's and healthcare provider's perspective. Long-term follow-up will give a better understanding of the cost-effectiveness of the treatment strategies. This is important because of the soaring incidence of the interventions along with the increase in elderly populations, in which DC is common, in western countries.

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Contributors MPR, literature search and writing the protocol; TK: writing and reviewing the protocol; HG, commenting on and reviewing the protocol; AR, commenting on the protocol and conducting the power analysis of the trial; HK, statistical plan of the trial, power analysis and writing the protocol; AM, commenting on the protocol; OVL, writing and reviewing the protocol. All the authors will read the final versions of the protocol and manuscripts. The authors will take responsibility for the validity of the data.

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Disclaimer None of the funders will have any role in the collection, management, analysis and interpretation of data; writing of the report or the decision to submit the report for publication.

Competing interests MPR, shoulder arthroscopy course paid for by Arthrex and nerve repair course paid for by Axone. TK, cadaver course paid for by Articular Finland and lecture fee from Summed.

Patient consent Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

Ethics approval The Regional Ethics Committee of Tampere University Hospital) and the Finnish Medicines Agency (FIMEA) have approved the study protocol.

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