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Median nerve Decompression at the carpal tunnel alone versus Median nerve Decompression at both the carpal tunnel and the Lacertus fibrosus in adults with carpal tunnel syndrome (MeDe): study protocol for a randomised controlled trial

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Study protocol

Keywords: carpal tunnel syndrome, proximal median nerve compression, Lacertus syndrome, double crush, nerve decompression, carpal tunnel release, Lacertus release

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Additional Declarations: No competing interests reported.

Abstract

Background: Carpal tunnel release is the most commonly performed surgical procedure in patients diagnosed with carpal tunnel syndrome (CTS). Nevertheless, up to 43% of patients experience residual symptoms, necessitating secondary surgical interventions in approximately one out of eight carpal tunnel releases. These residual symptoms may be attributable to proximal median nerve compression (PMNC), which can potentially be alleviated by performing a Lacertus release. However, diagnosing PMNC poses a challenge, as standard diagnostic tools like physical examination, electromyography (EMG) and ultrasound lack the specificity to distinguish between CTS and PMNC. Consequently, PMNC often goes undetected and untreated during initial evaluations. This randomised trial compares patient-reported outcomes following median nerve decompression at the carpal tunnel alone versus median nerve decompression at both the carpal tunnel and the Lacertus fibrosus in individuals with CTS.

Methods: This multicentre superiority trial compares patient-reported outcomes following median nerve decompression at the carpal tunnel alone versus median nerve decompression at both the carpal tunnel and Lacertus fibrosus in adults with CTS. The inclusion criteria are adult patients (≥ 18 years) with CTS, as confirmed by electromyography or ultrasound. The primary outcome is the Boston Carpal Tunnel Questionnaire Symptom Severity Scale (BCTQ SSS) score at twelve months follow-up. Secondary outcomes are the total BCTQ score, BCTQ Functional Status Scale (FSS), residual and persistent symptoms, recurrence, pillar pain, sensibility, tip-pinch strength, Return to work, Quality of life assessed with the EQ-5D-5L questionnaire, cost-effectiveness and cost-utility, additional surgical interventions, and complications. Sample size calculation showed that 110 patients must be randomised. The estimated time for inclusion will be 12 months.

Discussion: The MeDe study will provide evidence of whether **Me**dian nerve **De**compression at the carpal tunnel combined with **Me**dian nerve **De**compression at the Lacertus fibrosis results in better patient-related outcomes and quality of life compared to **Me**dian nerve **De**compression at the carpal tunnel alone in adult patients with Carpal Tunnel Syndrome.

Trial registration: registered in the CCMO Registry on ToetsingOnline.nl on 24-09-2024 with registration number NL87289.100.24 and OMON number NL005174

Trial registration number: NL87289.100.24 and OMON number NL005174 (MEC-U reference number:R24.082)

Registration URL: https://onderzoekmetmensen.nl/en/trial/57619

Structured summary {1b}

Item	Description
Primary Registry and Trial Identifying Number {4}	Overview of Medical Research in the Netherlands (OMON), NL-005174, https://onderzoekmetmensen.nl/nl/trial/57619, registered on 24 September 2024
Secondary Identifying Numbers	CCMO register (ToetsingOnline): NL87289.100.24; MEC-U: R24.082
Source(s) of Monetary or Material Support	None. This investigator-initiated study has not received any external funding or material support.
Primary Sponsor and contact information {3b}	Board of Directors - Maasstad Ziekenhuis, Rotterdam, the Netherlands. Maasstadweg 21, 3079 DZ Rotterdam Phone number: +31 (0)10 291 3042 E-mail: SecretariaatRvB@maasstadziekenhuis.nl
Role of sponsor and funder {3c}	This is an investigator-initiated trial without external funding. The sponsor enables the conduct of the trial at the participating sites. The investigators are responsible for the design, conduct, data analysis, interpretation and reporting of the trial, and for the decision to submit results for publication.
Contact for Public Queries	Maasstad Ziekenhuis – S. Poggio Voormolen Spijkenisse Medisch Centrum – S. Poggio Voormolen Phone number: +31646560865 E-mail: poggiovoormolens@maasstadziekenhuis.nl
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Public Title	**MeDe** study
Scientific title	**Me**dian nerve **De**compression at the carpal tunnel alone versus **Me**dian nerve **De**compression at both the carpal tunnel and the Lacertus fibrosus in adults with carpal tunnel syndrome (MeDe): study protocol for a randomised controlled trial.
Countries of Recruitment	The Netherlands

Health Condition(s) or Problem(s) Studied	Carpal tunnel syndrome
Intervention(s)	Intervention: carpal tunnel release combined with Lacertus fibrosis release. Comparator: carpal tunnel release alone.
Key Inclusion and Exclusion Criteria	Inclusion: adults (≥18 years) with CTS confirmed by EMG and/or nerve ultrasound who choose surgical treatment. Exclusion: previous median nerve decompression at the ipsilateral wrist or forearm; severe thenar atrophy; simultaneous nerve decompression in the ipsilateral arm; neurological disorders affecting peripheral nerves; malunion of the distal radius; impaired hand function; pregnancy; insufficient comprehension of the Dutch language.
Study Type	Multicentre, open-label, parallel group randomised controlled superiority trial; allocation ratio 1:1.
Date of First Enrolment	6 May 2026
Sample Size	110
Primary outcome(s)	Boston Carpal Tunnel Questionnaire Symptom Severity Scale (BCTQ SSS) score at 12 months.
Key Secondary outcome(s)	BCTQ Functional Status Scale and total score; residual and persistent symptoms; recurrence; pillar pain; secondary surgery; complications; sensibility; tip-pinch strength; return to work; quality of life (EQ-5D-5L); cost-effectiveness and cost-utility.
Ethics Review	Approved by the Medical Research Ethics Committees United (MEC-U), reference R24.082, on 18 August 2025.
Individual Trial Participant Data sharing statement	Data sharing is not applicable to this article as no datasets were generated yet for the current protocol manuscript. Final trial dataset will only be accessible to sponsor and coordinating investigators, but can be shared on request.

Protocol version {2}

Version 3.4, 3 September 2026

Introduction

Background and rationale {9a}

In the Netherlands, 22500 carpal tunnel releases are performed yearly [1]. Success rates range between 75-90%, however, up to 43% of patients have residual symptoms following carpal tunnel release [2–4]. Requiring secondary surgical interventions in approximately one out of eight carpal tunnel release (CTR) cases [5].

Recent studies show that residual symptoms following carpal tunnel release may be caused by a proximal median nerve compression, isolated or combined with compression at the carpal tunnel [6, 7]. A proximal median nerve compression may be treated effectively with a Lacertus release [7]. Lacertus release is performed under regional or local anaesthetics in the outpatient clinic, similar to a carpal tunnel release. However, diagnosing a PMNC can be challenging since physical examination, electromyography (EMG) and nerve ultrasound lack the specificity to distinguish between carpal tunnel release (CTS) and proximal median nerve compression (PMNC) [8].

There is no consensus on the optimal treatment for residual symptoms following carpal tunnel release. Theoretically, residual symptoms may be minimised by combining median nerve decompression at the carpal tunnel with proximal median nerve decompression through a Lacertus release.

We conducted a retrospective analysis of 50 patients who underwent a carpal tunnel release combined with Lacertus release in our outpatient clinic since January 1 2023. All patients had a minimum follow-up period of three months, and no complications, such as bleeding, infection, seroma or nerve damage, were observed or reported. Two patients experienced minor bruising around the Lacertus release incision, and three reported a temporary bruised sensation in their arms. These minor issues were resolved without additional treatment within two to three weeks.

This randomised trial compares patient-reported outcomes following median nerve decompression at the carpal tunnel alone versus median nerve decompression at both the carpal tunnel and the Lacertus fibrosus in individuals with CTS.

Explanation for the choice of comparator {9b}

The comparator is carpal tunnel release alone, median nerve decompression at the wrist and the standard surgical treatment for CTS. It is performed approximately 22500 times annually in the Netherlands [1]. Comparing the combined procedure with the current standard of care will determine whether adding Lacertus release improves patient-reported outcomes compared to those of carpal tunnel release alone.

Objectives {10}

The primary objective is to determine which treatment is superior: carpal tunnel release alone or carpal tunnel release combined with Lacertus release in adult patients. Secondary objectives are functional status, residual and persistent symptoms, recurrence, pillar pain, sensibility, tip-pinch strength, return to work, quality of life, cost-effectiveness and cost-utility. To assess harms, we will compare the incidence of complications and secondary or revision surgeries between groups.

Methods: Patient and public involvement, and trial design

Patient and public involvement {11}

Patients were involved in the initial design of this trial, as they were involved in the structure of the follow-up visits and proofread the patient information form (PIF). The public was not involved in the design of this trial. Participants can receive a summary of the results in plain language after completion of the trial.

Trial design {12}

The MeDe study is a multicentre, open-label, parallel-group randomised controlled superiority trial comparing median nerve decompression at the carpal tunnel alone with median nerve decompression at both the carpal tunnel and the Lacertus fibrosus in adults with CTS. Participants are randomised in a 1:1 ratio.

Methods: Participants, interventions and outcomes

Trial setting {13}

The trial is conducted at two hospitals in the Netherlands: the Maasstad Ziekenhuis in Rotterdam, a non-academic teaching hospital, and the Spijkenisse Medisch Centrum in Spijkenisse, a non-teaching hospital. Patients are recruited at the outpatient clinics of both hospitals. Both procedures are performed there under local or regional anaesthesia.

Characteristics of the people who are needed for the trial

The expected demographic characteristics of the trial population, based on the PRO EDI core characteristics are summarised in Table 1 [9, 10].

Table 1. PRO EDI participant characteristics

Characteristic	The people the MeDe study expects to see included
Age	Following the inclusion criteria, adults (≥18 years) with a diagnosed CTS, confirmed by EMG or ultrasound will be included. In Dutch general practice, incidence peaks in the 45-64 age group [11]. We therefore expect mainly middle-aged adults, with a substantial proportion aged 65 or over. Age will be recorded in years.
Sex	Both males and females will be included. In Dutch general practice, CTS is about three times more common in females than in males [11]. Therefore, we expect roughly three quarters of study participants to be female. Sex and gender are recorded with a single self-reported question, with the response options man, woman and other. If missing, sex will be recorded as registered in the medical record.
Gender	Gender is not recorded separately from sex; participants self-report their sex and gender in a single question with the options man, woman and other. We expect mainly men and women to be included.
Race, ethnicity and ancestry	Following the ethics-approved data collection plan, ethnicity is not recorded. We expect participants to reflect the ethnically diverse area of Rotterdam and Spijkenisse [12]. However, following the exclusion criteria, patients assessed to be unable to complete Dutch questionnaires are excluded, which may under-represent people with limited understanding of the Dutch language.
Socioeconomic status	Occupation (blue- vs white-collar) and employment status are recorded. Blue-collar work has been associated with an increased risk of CTS in both men and women [13, 14]. We therefore expect a considerable proportion of participants to have blue-collar occupations, although patients of all socioeconomic backgrounds are eligible.
Geographic location	Participants are recruited in the Netherlands at Maasstad Ziekenhuis (Rotterdam, urban) and Spijkenisse Medisch Centrum (Spijkenisse, smaller town). The trial is coordinated from the Maasstad Ziekenhuis.
Other relevant characteristics	Patients who are pregnant at the time of the surgery are not eligible for inclusion, as pregnancy-related CTS frequently resolves after delivery and would confound the assessment of treatment effects.

Eligibility criteria for participants {14a}

All adult patients (≥18 years) at the outpatient clinic with CTS confirmed by EMG or nerve ultrasound who choose surgical treatment are eligible for inclusion.

CTS diagnosis will be confirmed by EMG or nerve ultrasound conducted by a clinical neurophysiologist or neurologist. EMG measures the sensory latency difference in the fourth finger by comparing the median and ulnar nerve conduction velocities. A sensory latency difference smaller than 0.6 milliseconds is considered negative for CTS. Nerve conduction may be immeasurable in cases of severe compression neuropathy or due to subsequent nerve damage. In cases of diagnostic uncertainty, nerve ultrasound will be utilised. Nerve ultrasound measures the cross-sectional area of the nerve in the wrist at the height of the carpal tunnel and in the forearm at the height of the distal 1/3. An area larger than 11 square millimetres at the carpal tunnel and 9 square millimetres or smaller at the forearm is considered positive for CTS.

The exclusion criteria are:

- Previous surgical decompression of the median nerve at the ipsilateral wrist or forearm
- Severe thenar atrophy: Examination of the thenar is based on clinical observation. The presence of thenar muscle atrophy is scored as none, mild, or severe.
- Simultaneous nerve decompression in the ipsilateral arm (e.g. cubital tunnel, Guyon and radial nerve release).
- Neurological disorders affecting peripheral nerves (e.g. spinal cord compression or injury, muscular dystrophy, dystonia, amyotrophic lateral sclerosis (ALS))
- Malunion of the distal radius
- Impaired hand function
- Pregnancy
- Inability to complete study forms due to insufficient comprehension of the Dutch language

Eligibility criteria for sites and those delivering interventions {14b}

Participating sites are hospitals in which both carpal tunnel release and Lacertus release are routinely performed. All procedures are performed by surgeons experienced in both carpal tunnel release and Lacertus release.

Who will take informed consent? {32a}

Patients are informed about the study by the treating physician after the decision has been made to proceed with surgical treatment for carpal tunnel syndrome. The study and the informed consent process are discussed face-to-face by the investigator, after the patient showed interest in the study and agreed to be informed. The patient is provided with PIF and the consent form, along with a return envelope. Should the patient have any questions regarding the study, they are encouraged to contact the investigator (by telephone). If, after the consideration period, the patient has no further questions, decides to participate and returns the signed consent form, randomisation will take place.

There is a minimum interval of one week between the initial provision of study information and the signing of the informed consent form. Deviations from this interval are permitted if preferred by the participant. Particpants can consult an independent expert with question surrounding the trial.

Additional consent provisions for collection and use of participant data and biological specimens {32b}

Not applicable. No biological specimens are collected in this trial.

Intervention and comparator

Intervention and comparator description {15a}
The intervention group will receive a carpal tunnel release supplemented with a Lacertus release. This

combination of carpal tunnel and Lacertus release is the standard treatment for median nerve double crush syndrome.The control group receives the standard treatment consisting of a carpal tunnel release, which is performed as the standard open procedure according to routine clinical practice at the participating sites. In the intervention group, both procedures are performed sequentially in a single session, adding approximately 5-10 minutes to the operative time. All procedures are performed by surgeons experienced in both carpal tunnel release and Lacertus release.

Lacertus Release Surgical Procedure

Local or regional anaesthesia is administered. The patient is positioned supine with the arm extended on an arm board. The surgical site is sterilised, and a tourniquet is applied to the upper arm to control bleeding.

A transverse incision is made on the forearm's volar (anterior) aspect, approximately 3cm distal of the elbow crease. This incision is placed over the palpable brachioradialis and biceps tendon.

The subcutaneous tissue is dissected to expose the fascia overlying the flexor pronator muscles. The brachial fascia is identified and incised to reveal the underlying Lacertus fibrosus (also known as the bicipital aponeurosis). The Lacertus fibrosus is a tendinous band extending from the biceps tendon medially across the forearm. Care is taken to avoid injury to the underlying structures, particularly the median nerve, which lies deep and slightly medial to the Lacertus fibrosus. The Lacertus fibrosus is incised transversely. The surgeon ensures that the median nerve is fully decompressed and that there are no remaining constrictive bands.

Haemostasis is achieved using electrocautery as needed. The incision is closed in layers: the subcutaneous tissue is approximated with absorbable sutures, and the skin is closed with non-absorbable or absorbable sutures.

In both groups, a sterile dressing is applied for 3-5 days. The patient is instructed to use the arm normally and to monitor for signs of complications.

Criteria for discontinuing or modifying allocated intervention/comparator {15b}

Participants can leave the study at any time for any reason without any consequences if they wish to do so. The investigator can decide to withdraw a participant from the study for urgent medical reasons. All patients who withdraw after informed consent has been given, but before the surgical procedure, will be replaced. Their data will be analysed according to the intention-to-treat principle, allowing us to obtain a comprehensive database of consecutive patients and avoid attrition bias. An end-of-study form will be completed, and the drop-out reason will be recorded.

Strategies to improve adherence to intervention/comparator {15c}

Both the intervention and the comparator consist of a single surgical procedure performed by the surgeon, so no specific strategies to improve adherence are required. The allocated procedure is recorded in the operative report and will be checked against the randomisation outcome before surgery.

Concomitant care permitted or prohibited during the trial {15d}

Simultaneous nerve decompression in the ipsilateral arm (e.g. cubital tunnel release) is prohibited in this trial. All other care is permitted according to standard clinical practice.

Ancillary and post-trial care {34}

The sponsor/investigator has liability insurance in accordance with article 7 of the Medical Research Involving Human Subjects Act (WMO). The sponsor (also) has insurance, which is in accordance with the legal requirements in the Netherlands (Article 7 WMO). This insurance provides cover for damage to research participants through injury or death caused by the study. The insurance applies to the damage that becomes apparent during the study or within 4 years after the end of the study.

After completion of the 12-month follow-up, participants will continue to be treated according to standard clinical practice.

Outcomes {16}

The primary outcome is the Boston Carpal Tunnel Questionnaire Symptom Severity Scale (BCTQ SSS) at twelve months follow-up. The BCTQ is a carpal tunnel syndrome-specific, patient-reported outcomes instrument that comprises two subscales: the Symptom Severity Scale (SSS), which includes eleven questions about CTS symptoms, and the Functional Status Scale (FSS), which includes eight questions about overall functional status, each scored from 1 to 5. The sum of the scores for each subscale is divided by the number of questions in that subscale. The maximum score is 5.0, indicating the worst possible condition. The lowest score is 1.0, with no CTS symptoms [15]. The BCTQ SSS and FSS will be collected at baseline, six weeks, three months, six and 12 months. See the SPIRIT figure for an overview of the measurement timeline (Figure 1) [16].

Secondary outcomes:

- BCTQ FSS
- BCTQ Total score: a weighted mean of the BCTQ SSS and FSS score.
- Anchor questions regarding patient satisfaction will be used to analyse the minimal clinically important difference (MCID) at 12 months.
- Residual symptoms: the presence of preoperative symptoms after carpal tunnel release (yes/no) will be assessed at six weeks, three, six and 12 months.
- Persistent CTS: preoperative symptoms have never completely disappeared after carpal tunnel release (yes/no), will be assessed at six weeks, three, six and 12 months [17].

- Recurrence: recurrence of median nerve compression symptoms (including CTS) is defined as an asymptomatic period after carpal tunnel release of three months minimum, followed by a recurrence of preoperative symptoms [18]. Recurrence will be assessed at six and 12 months.
- Pillar pain: the presence of tenderness or pain in the thenar or hypothenar area around the hook of the hamate and the unciform process of the trapezium [17]. Pillar pain will be assessed at six weeks, three, six and 12 months.
- Secondary surgery: This includes, but is not limited to, nerve decompression, internal or external neurolysis, and flap reconstruction in the ipsilateral arm. It will be assessed at six weeks, three, six and 12 months.
- Complications/adverse events, such as infection, seroma, and tendon and neurovascular damage, will be monitored and registered at all time points: six weeks, three, six and 12 months.
- (Return to) work: will be assessed using the QuickDASH work module and an additional question to investigate the time it takes to Return to Work. It will be assessed at baseline, six weeks, three and six months.
- Sensibility: monofilament test on the tuft of the 3rd digit and the proximal thenar. The tuft of the 5th digit and the distal thenar will be measured and used as a reference. Sensibility will be tested at baseline, three and 12 months.
- Tip-pinch strength: tip-to-tip pinch strength of the first and second digit will be measured with a Baseline Pinch Gauge. The mean of three measurements will be taken at baseline, three and 12 months.
- Cost-effectiveness of intervention: measured with health care resource utilisation and costs (iMCQ, iPCQ); at six weeks, three months, six and 12 months. Cost-effectiveness will be measured as costs per unit change in the BCTQ [19].
- Quality of life: will be assessed using the 5-level EuroQol (EQ-5D-5L) questionnaire at baseline and 12 months [20].
- Cost-utility analysis will be described as cost per quality adjusted life years (QALYs). QALYs will be measured by the EQ-5D-5L; at baseline and 12 months.
- Patient Demographics: age, sex, labour (blue versus white collar), hand dominance and medical history regarding comorbidities and hand-specific conditions will be assessed at baseline.
- Physical examination may include but is not limited to, sensibility of the thenar, proximal thenar, hypothenar, tuft of digits 3 and 5, tip-pinch strength measured by the OK sign and the flexor pollicis longus (FPL) and flexor digitorum profundus of the index finger (FDP2) separately, scratch collapse test over the carpal tunnel and Lacertus fibrosis, and Phalen and Tinel test. Physical examination will be assessed at baseline, three and 12 months.

Continuous outcomes will be summarised as mean with standard deviation (SD) for normally distributed data, or median with interquartile range (IQR), for non-normally distributed data. Dichotomous outcomes will be summarised as numbers and percentages at each time point.

Harms {17}

All adverse events reported by the patient or observed by the treating physician or researcher will be recorded. Adverse events are assessed systematically at each follow-up point by asking participants in the questionnaire whether they experienced any problems during recovery, and by physical examination at the three month and twelve month visit. Serious adverse events (SAEs) will be reported through the web portal 'het Onderzoeksportaal' of the Central Committee on Research Involving Human Subjects (Dutch CCMO) and to the Medical Research Ethics Committees United (MEC-U), which approved the protocol. SAE reporting will take place within 7 days after the sponsor has first knowledge of an SAE resulting in death or is life-threatening. All other SAEs will be reported within 15 days.

Adverse events (AEs) are defined as:

- Wound infection treated with incision and drainage or antibiotics
- Postoperative bleeding
- Tendon damage
- Neurovascular damage
- Seroma
- Complex regional pain syndrome (CRPS) defined according to the Budapest criteria
- Secondary surgery

All AEs will be followed until they have abated, or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures as indicated, and/or referral to the general practitioner or a medical specialist. SAEs need to be reported till end of study within the Netherlands, as defined in the protocol.

Participant timeline {18}

Adapted from the SPIRIT 2025 participant timeline template [16].

Sample size {19}

Sample size calculation is based on our primary endpoint, the change in BCTQ SSS score at twelve months. The score for an individual without any CTS symptoms is 1.0. The higher the score, the worse the symptoms. We hypothesised a superior (lower) BCTQ SSS score in the intervention group and used the results from two published studies for our sample size calculation. We assume that a difference of at least 0.5 scores is clinically important. This MCID for the BCTQ SSS is based on the pooled MCID threshold of 1.0 and the reported MCID range between 0.88 and 1.55 for the BCTQ SSS [21].

With a two-sided significance level of 0.05 and a standard deviation of 0.7, a two-group Student's T-test has 90% power to detect a difference of 0.5 between scores in the control and intervention groups, based on an MCID of 1.0 in the control group, if at least 50 patients per group or 100 patients in total are

included [22]. Accounting for approximately 7.5% drop-out due to lost-to-follow-up and assuming that, eventually, the Mann -Whitney U test as the non-parametric counterpart of the T-test with a relative efficiency of 0.955 has to be applied for distributional reasons, 110 patients will initially be included. A power of 90% seems advisable to generate convincing evidence to change clinical practice amongst surgeons who might have a preferential attitude to the treatment choice

Recruitment {20}

All consecutive adult patients with CTS who choose surgical treatment at the outpatient clinics of the inclusion sites are screened for eligibility and, if eligible, approached for inclusion. Recruitment progress is monitored by the coordinating investigators.

Assignment of interventions: randomisation

Sequence generation: who will generate the sequence {21a}

The randomisation sequence is computer-generated by Castor EDC [23]. The investigators have no access to the sequence.

Sequence generation: type of randomisation {21b}

Participants are randomised in a 1:1 ratio using variable block randomisation, without stratification.

Allocation concealment mechanism {22}

To ensure allocation concealment, randomisation will be automated (using Castor software) and password-protected [23]. The allocation will be revealed only after the participant has signed the informed consent form and been enrolled in Castor.

Implementation {23}

After signing informed consent, patients will be randomly assigned to the intervention or control group. Participants are enrolled by the investigators, who register them in Castor EDC. Castor EDC then allocates participants to one of the study arms, independently of the investigators. Afterwards, the allocation is communicated to the treating surgeon and participant prior to surgery.

Assignment of interventions: blinding

Who will be blinded {24a}

This is an open-label trial. Participants, surgeons and investigators will not be blinded to treatment allocation, as both treatments are visually different for the treating physician, the investigator and the patient.

How will be blinding be achieved {24b}

Not applicable, as this is an open-label trial.

Procedure for unblinding if needed {24c}

Not applicable, as treatment allocation is not blinded.

Data collection and management

Plans for assessment and collection of outcomes {25a}

Measurements and data collection will take place at five time points as shown in Figure 1. The time points are at baseline (T0), six weeks (T1), three months (T2), six months (T3) and 12 months (T4) after surgery. At T0, informed consent will be obtained, baseline characteristics and physical examination tests will be gathered, sensibility and tip-pinch strength will be measured, and patients will need to complete questionnaires. T2 is a standard outpatient visit, where the monofilament and tip-pinch strength will be measured. T4 is an extra visit where the researcher measures sensibility and tip-pinch strength. All data are recorded in an electronic case report form in Castor EDC [23].

Plans to promote participant retention and complete follow-up {25b}

At T1, T2, T3 and T4, the patient will be asked to complete questionnaires by email, and reminders will be sent automatically. When a patient does not respond, we will contact the patient by telephone or obtain a paper questionnaire through a home visit or telephone interview.

Data management {26}

All data will be collected by one of the investigators and stored in an online, password-protected database (Castor EDC) with an audit trail. To promote data quality, range checks and required fields are added to the data entry fields where appropriate, and any change to an entered field requires a reason, which is recorded in the audit trail. All source data will be stored for 15 years after the publication of the results of this trial.

Confidentiality {33}

Patient data is handled confidentially and is accessible only to members of the research team. After randomisation, patients receive a study identification number (pseudonymised). The subject identification list will be accessible only to the principal investigator, study coordinator, and monitor.

Statistical methods

Statistical methods for primary and secondary outcomes {27a}

Baseline patient characteristics and physical examination tests will be described using descriptive statistics. The primary outcome, the difference in BCTQ SSS score between both groups at twelve

months, according to the intention-to-treat principle, will be analysed using the unpaired t-test or Mann-Whitney U test, depending on the data distribution, and reported as the difference between groups with 95% confidence interval. For secondary outcomes, trends in BCTQ SSS and FSS scores along the different follow-up moments will be assessed using a generalised linear mixed model for repeated measurements, calculating the marginal mean differences. Furthermore, the number of complications, re-interventions and cross-overs will be determined using a Fisher Exact or a Chi-square test. A two-sided p-value < 0.05 will be considered statistically significant.

Both cost-effectiveness (CEA) and cost-utility analysis (CUA) will be performed from a social and healthcare perspective. For the calculation of medical costs, we will use charges published in Dutch guidelines as a proxy for actual costs. Intramural costs (i.e. additional diagnostics, number of hospital visits, in case of hospital admission, the length of stay, etc.) are collected from the electronic health record. Productivity costs will be registered in detail by the iPCQ. The iMCQ and the iPCQ are validated by the Institute of Medical Technology Assessment (Erasmus University, Rotterdam, The Netherlands). The primary economic outcome for the CEA is the cost-per-unit change in CTS symptoms, which closely relates to the clinical outcome measure (BCTQ SSS). The primary economic outcome for the CUA is the cost per QALY. QALYs will be measured based on the Dutch tariff for the EQ-5D-5L. Differences between groups will be assessed after correction for bias and using accelerated non-parametric bootstrapping to account for sampling variability, generating 5,000 replications. Results will be presented graphically using cost-effectiveness planes [24, 25]. The time horizon will be one year.

Who will be included in each analysis {27b}

The primary analysis will follow the intention-to-treat principle and include all participants in the groups to which they were randomised. A per-protocol analysis, including only participants who received their allocated procedure following the randomisation, will be performed as a sensitivity analysis.

How missing data will be handled in the analysis {27c}

Missing data will be minimised by sending automated e-mail reminders and by contacting non-responders by telephone, home visit or telephone interview. If no contact is made, a non-responder analysis will be performed using baseline data and, where available, data on possible complications.

Methods for additional analyses (e.g. subgroup analyses) {27d}

Following the study protocol, no subgroup analyses are planned. A per-protocol analysis will be performed as a sensitivity analysis.

Interim analyses {28b}

In accordance with the study protocol, no interim analyses are planned. In accordance to section 10, subsection 4, of the WMO, the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardise participant health or safety. The sponsor will notify the review

committee without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the review committee. The investigator will take care that all participants are kept informed.

Protocol and statistical analysis plan {5}

The trial protocol is available in this publication of the study protocol. The statistical analysis plan is included in the protocol and described under 'Statistical methods' {27a} – {27d}. No separate statistical analysis plan has been developed. Any changes to the planned analyses will be reported and justified in the final trial report.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {3d}

The study sponsor is enabling the study. The lead investigator is NS and is mainly involved in the study design, writing the report, deciding to submit the report for publication and delegating activities. The coordinating investigators (SPV and ID) are responsible for day-to-day coordination, data collection and management and writing of the report. The participating surgeons are involved in data collection, and MK is responsible for data analysis. The study team meets at least every two months, and more often when required. There is no trial steering committee or separate patient and public involvement group.

Composition of the data monitoring committee, its role and reporting structure {28a}

This study is labelled a low-risk study, according to the risk classification for investigator-initiated research of the Maasstad Ziekenhuis, therefore a data safety monitoring board is not required. The risk classification is documented in the trial master file of the study.

Frequency and plans for auditing trial conduct {29}

The study will be monitored at least once by an independent monitor in compliance with Good Clinical Practice (GCP). A written report from the monitor will be discussed with all participating members of the study's project group.

The sponsor/investigator will submit a summary of the progress of the trial to the review committee once a year. Information will be provided on the date of inclusion of the first participant, numbers of participants included and numbers of participants that have completed the trial, serious adverse events, other problems, and amendments.

Protocol amendments {31}

Substantial amendments are changes to the research that will only be implemented after receiving a favourable opinion from the MEC-U. Non-substantial amendments will not be notified to the review

committee, but will be recorded and filed by the sponsor. The trial registration in OMON will be updated accordingly.

Dissemination policy {8}

The results of this trial will be submitted for publication in a peer-reviewed journal, and possibly presented at national or international conferences. The results will also be reported in the trial registry. Within one year of the study's end, the investigator or sponsor will submit a final report on the study results, including any publications or abstracts of the study, to the review committee. Participants can receive a summary of the results in plain language after completion of the trial if requested.

Discussion

Participants in the intervention group will receive the standard treatment for carpal tunnel syndrome, supplemented with a lacertus release. This combined procedure is already routinely performed in clinical practice when a double crush syndrome of the median nerve is suspected. As described in the "Retrospective analysis of carpal tunnel release combined with Lacertus release" outcomes from 50 patients treated in our clinic support the safety and feasibility of this approach. Both the carpal tunnel release and Lacertus release will be performed sequentially under local anaesthesia, with a modest increase in operative time of approximately 5–10 minutes.

There are negligible additional risks for participants, as both procedures are considered standard surgical treatments. Our clinical experience also indicates that patients do not perceive the combined procedure as more burdensome. Postoperative complaints are typically focused on the wrist incision, with minimal discomfort reported from the forearm site. In clinical practice, some patients require a second surgical procedure for Lacertus release after an initial carpal tunnel release, resulting in two separate recovery periods. By combining the two procedures, we aim to reduce the overall recovery time and shorten the duration of symptoms, potentially benefiting participants and being more cost-effective due to fewer patients requiring second surgical treatments.

Therefore, the burden of participation is considered low, and the potential for direct benefit justifies the conduct of this study.

Trial status

This manuscript is based on the approved protocol version 3.4, dated 3 September 2026. Recruitment began on 6 May 2026 and recruitment is expected to be completed in May 2027.

Abbreviations

LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

AE	Adverse Event
ALS	Amyotrophic lateral sclerosis
BCTQ	Boston Carpal Tunnel Questionnaire
CCMO	Central Committee on Research Involving Human Subjects; in Dutch: Centrale Commissie Mensgebonden Onderzoek
CEA	Cost-effectiveness analysis
CRPS	Complex regional pain syndrome
CTS	Carpal tunnel syndrome
CTR	Carpal tunnel release
CUA	Cost-utility analysis;
EMG	Electromyography
FDP2	Flexor digitorum profundus of the index finger
FSS	Functional status scale
FPL	Flexor pollicis longus
GCP	Good Clinical Practice
iMCQ	Medical consumption questionnaire
iPCQ	Productivity cost questionnaire
IQR	Interquartile range
MEC-U	Medical Research Ethics Committees United
MCID	Minimal clinically important difference
PIF	Patient information form
PMNC	Proximal median nerve compression
QALY	Quality adjusted life year
(S)AE	(Serious) Adverse Event
SD	Standard deviation
SSS	Symptom severity scale
Sponsor	The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.

UAVG	Dutch Act on Implementation of the General Data Protection Regulation; in Dutch: Uitvoeringswet AVG
WMO	Medical Research Involving Human Subjects Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen

Declarations

Acknowledgements

Not applicable

Authors' contributions {3a}

- NS is the lead investigator and is mainly involved in supervising the trial and formulating the study design, writing the report, deciding to submit the report for publication and delegating activities.
- SPV and ID are the coordinating investigators are and are mainly involved in the day-to-day coordination of trial, including: data collection, management, analysis, interpretation of data and writing of the report.
- JJ, SPV, GN, SP, HC and NS are involved in data collection and writing of the report
- MK is involved in data analysis and interpretation.

An artificial intelligence (AI) language tool (Claude) was used to assist in language-editing of the manuscript and assist in the translating of the ethics approval documents. The authors take full responsibility for the submitted content. Authorship of future publications from this trial will be determined according to the ICMJE criteria. All authors read and approved the final manuscript.

Sources of funding and other support {7a}

This study has not received any external funding or material support. It is conducted with the departmental resources of the Maasstad Ziekenhuis, Rotterdam, the Netherlands.

Availability of data and materials {6}

The final trial dataset will be accessible to the principal investigator, coordinating investigators and the trial statistician. This study does not involve the publication of individual participant data; therefore, consent for publication is not applicable. All datasets generated or analysed during the study will be available from the corresponding author upon reasonable request, in accordance with data sharing principles (General Data Protection Regulation).

Ethics approval and consent to participate {30}

This study will be conducted according to the principles of the Declaration of Helsinki (2024) and in accordance with the WMO and other guidelines, regulations and Acts like the General Data Protection

Regulation (in Dutch: Uitvoeringswet Algemene Verordening Gegevensbescherming). This study is approved by the Medical Research Ethics Committees United (MEC-U) on 18 August 2025 with reference number: R24.082. Written informed consent is obtained from all participants before randomisation takes place. The original letter of approval is provided in the Supplementary Material.

Consent for publication

This study does not involve the publication of individual participant data; therefore, consent for publication is not applicable.

Competing interests {7b}

The authors declare that they have no competing interests.

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Figures

	TRIAL PERIOD						
	Enrolment		Post-randomisation				Close-out
TIMEPOINT	T_0 (baseline)	0 (randomisation)	*Surgery*	t_1 (6w)	t_2 (3m)	t_3 (6m)	t_4 (12m)
ENROLMENT:							
Eligibility screen	X						
Informed consent	X						
Randomisation		X					
INTERVENTION/ COMPARATOR:							
CTR + Lacertus release			X				
CTR alone			X				
ASSESSMENTS:							
Demographics	X						
Physical examination	X				X		X
BCTQ (SSS,FSS)	X			X	X	X	X
Residual and persistent symptoms				X	X	X	X
Recurrence						X	X
Pillar pain				X	X	X	X
Sensibility (monofilament)	X				X		X
Tip-pinch strength	X				X		X
Return to work (QuickDASH)	X			X	X	X	
EQ-5D-5L (Quality of life)	X						X
iMCQ, iPCQ				X	X	X	X
Anchor questions							X
Secondary surgery				X	X	X	X
(Serious) adverse events				X	X	X	X

CTR, carpal tunnel release; BCTQ, Boston Carpal Tunnel Questionnaire; SSS, Symptom Severity Scale; FSS, Functional Status Scale; QuickDASH, Quick Disabilities of the Arm, Shoulder and Hand; EQ-5D-5L, EuroQol 5-dimension 5-level questionnaire; iMCQ, Medical Consumption Questionnaire; iPCQ, Productivity Cost Questionnaire.
Follow-up timepoints are releative to the date of surgery.

Figure 1

Participant timeline: Schedule of enrolment, interventions, and assessments.