COMPARISON OF CONVENTIONAL AND COOLED RADIOFREQUENCY TREATMENT OF THE GENICULAR NERVES VERSUS SHAM PROCEDURE FOR PATIENTS WITH CHRONIC KNEE PAIN: A MULTICENTRE, DOUBLE BLIND, RANDOMISED CONTROLLED TRIAL

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The aim of the COGENIUS trial is to investigate the effect of the two types of RF treatment on individuals experiencing chronic knee pain that is resistant to conservative treatments. For this purpose, the efficacy and cost-effectiveness of cooled...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Joint disorders
Study type	Interventional

Summary

ID

NL-OMON56136

Source
ToetsingOnline

Brief title
COGENIUS

Condition

- Joint disorders
- Bone and joint therapeutic procedures

Synonym

Chronic knee pain, ostheoarthritis

Research involving
Human

Sponsors and support

Primary sponsor: Ziekenhuis Oost-Limburg
Source(s) of monetary or material Support: niet-commerciële sponsor (Ziekenhuis Oost-Limburg;Genk;België) die funding ontvangt voor deze studie van de Belgisch overheid (Federaal Kenniscentrum;KCE)

Intervention

Keyword: cooled, Genicular, pain, radiofrequency

Outcome measures

Primary outcome

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

score (range 0-96) at 6 months post-intervention.

Secondary outcome

• WOMAC score collected at baseline and 1-, 3-, 6-, 12- and 24-months

post-intervention.

• Pain intensity assessed by the mean numerical rating scale (NRS) (0-10) of

the 4 days prior to each visit. Collection of NRS will happen at screening,

baseline and 1-, 3-, 6-, 12- and 24-months post-intervention.

• The proportion of patients with a pain reduction of at least 50% assessed by

the NRS compared to baseline calculated at 1-, 3-, 6-, 12- and 24-months

post-intervention*.

• Health-related quality of life assessed by the EuroQoL-5D-5L (EQ-5D-5L)

collected at baseline and 1-, 3-, 6-, 9-, 12- and 24-months post-intervention.

• Physical functioning assessed by goniometry by using the CJOrtho app, *timed

up and go* test and 6-min walk test collected at baseline and 1-, 3-, 6-, 12- and 24-months post-intervention.

• Mental health status assessed by the Hospital Anxiety and Depression Scale (HADS) and Pain Catastrophizing Scale (PCS) collected at baseline and at 1-, 3-, 6-, 12- and 24-months post-intervention.

• Patient Global Impression of Change (PGIC) collected at 1-, 3-, 6-, 12- and 24-months post-intervention.

• Patient*s satisfaction assessed by 7-point Likert scale at 1-, 3-, 6-, 12- and 24-months post-intervention.

• Medication use measured by:

- the Medication Quantification Scale III (MQS III) collected at baseline and at 1-, 3-, 6-, 9-, 12- and 24-months post-intervention.

- Opioid dependence at 1-, 3-, 6-, 9-, 12- and 24-months post-intervention visit.

• The incidence of related adverse events. Active capture during each study contact to assess specific symptoms and adverse events related to RF intervention.

• Health care resource utilisation, including adverse events, additional or re-interventions to the index knee, pain medication, visits to a range of medical specialists, general practitioner visits, and other health care providers, is assessed at baseline and 3, 6, 9, 12 and 24 months post-intervention.

Adverse events (including hospitalisations), knee interventions and pain medication are actively monitored and captured during each

study contact. Three questions regarding medical specialist,

general practitioner visits, and other health care providers are added to

questionnaires package completed by patients at baseline, 3, 6, 9, 12 and 24

months.

• Productivity loss due to sickness assessed by the Work Productivity and

Activity Impairment (WPAI) questionnaire6 at baseline, 1, 3, 6, 9, 12 and 24

months.

Study description

Background summary

Chronic knee pain remains a disabling disease despite current treatment strategies. There is an increase in the prevalence of osteoarthritis (OA) of the knee in the general population. A total knee replacement is a viable alternative for severe knee OA that does not respond to conservative therapy. Unfortunately, up to 53% of patients who undergo a total knee replacement develop persistent post-surgical pain (PPSP). There is momentarily no effective therapy for PPSP.

A radiofrequency (RF) treatment applies high frequency current on the nerve responsible for pain conduction, resulting in an interruption of the transmission of pain. This can be applied to the nerves innervating the knee joint * the superolateral, superomedial and inferomedial genicular nerves * and could be an alternative, minimally invasive treatment for patients with knee OA who fail conservative treatments and for patients with PPSP. Data from the recent literature indicates that this treatment leads to a reduction of pain intensity and could result in an improvement of knee function, of the psychological state of the individual, and finally in an increase in health-related quality of life. Furthermore, RF of the genicular nerves could help avoid or delay a total knee replacement therefore potentially contributing to cost reduction. Both cooled and conventional RF treatments are reported in the literature to improve pain. The use of water to cool the RF electrodes results in an increased lesion size by removing heat from adjacent tissue, allowing power delivery to be increased. As a consequence, cooled RF could result in a higher chance of success and longer duration of effect. Until now, the studies performed on cooled RF are industry initiated and a direct

comparison between conventional, cooled and a sham procedure is lacking.

Study objective

The aim of the COGENIUS trial is to investigate the effect of the two types of RF treatment on individuals experiencing chronic knee pain that is resistant to conservative treatments. For this purpose, the efficacy and cost-effectiveness of cooled and conventional RF will be compared to a sham procedure in patients suffering from knee OA and PPSP after total knee replacement.

Study design

A prospective, multicentre, double blind, randomised controlled pragmatic trial with three study groups with a 2:2:1 randomisation ratio

Intervention

There are two intervention groups: cooled and conventional radiofrequency (RF) treatment of the superolateral, superomedial and inferomedial genicular nerves. A sham procedure with placement of three needles in the subcutaneous area of the superolateral, superomedial and inferomedial genicular nerves with injection of local anaesthetic which will mimic the intervention(s) mentioned above.

Study burden and risks

Patients in the three intervention groups have the opportunity to benefit from optimization of usual care and of positive treatment effects of the RF intervention (pain relief, functional improvement, improved quality of life). Potential side effects of the RF intervention are hematoma, infection, temporary increase of pain, hyperesthesia, paraesthesia and neuralgia or paralysis, superficial burns, damage to collateral nervous tissue or soft tissue, failure of technique and allergy. Potential side effects of the sham procedure are due to skin penetration (hematoma, infection) and allergy to the local anaesthetic used. The additional risks associated with either intervention options are expected to be very low, and we conclude that this trial can be categorised as a *Low intervention* clinical trial for the following reasons:
* The RF equipment device used for the study intervention has a CE Marketing Authorisation in Europe.
* The RF equipment device is used in accordance with the indication as mentioned in the European Marketing Authorisation.
* The additional (monitoring) study procedures do not deviate from routine clinical practice in the Netherlands, apart from the use of more standardised functional tests and questionnaires. These study procedures do not add

additional safety risks to the study subjects.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Signed written informed consent must be obtained before any study assessment is performed.
* Adult patients (Age >= 18 years old).
* Chronic anterior knee pain (> 12 months) that is moderate to severe (defined as NRS > 4 on most or all days for the index knee either constantly or with motion).
* Unresponsive (meaning insufficient pain reduction or intolerance) to conventional treatments ongoing for at least 12 months prior to inclusion. Conventional treatments must include all of the following: active

physiotherapy, pharmacological treatment of pain and, in case of OA patients, intra-articular infiltration.
* Only for patients with OA: Radiologic confirmation of knee osteoarthritis of grade 2 (mild), 3 (moderate) or 4 (severe) noted within 12 months prior to the screening for the index knee according the Kellgren Lawrence criteria 54 diagnosed by an independent radiologist with experience in musculoskeletal imaging on Rx or MRI.55 If imaging will need to be performed at screening it is recommended to perform an MRI instead of Rx. Imaging with MRI will enable the independent radiologist to perform a better estimation of the grade of OA.
* Only for patients with PPSP after TKA: Patients with PPSP after TKA need to have had a negative orthopaedic work-up.

Exclusion criteria

* Local or systemic infection (bacteraemia) at the time of inclusion.
* Evidence of inflammatory arthritis or an inflammatory systemic disease responsible for knee pain.
* Intra-articular injections (steroids, hyaluronic acid, platelet enriched plasma, *) in the index knee during the 3 months prior to procedure.
* Pregnant, nursing or planning to become pregnant before the study intervention. Participants who become pregnant after the study intervention during the follow-up period will not be excluded.
* Chronic widespread pain e.g. fibromyalgia.
* Patients with unstable psychosocial disorder.
Unstable psychosocial disorder is defined as:
o any untreated psychiatric conditions
o any psychiatric condition where the treating medication is not stable the last 3 months prior to inclusion
o patients currently treated by a psychiatrist and the psychiatrist could not confirm that the psychosocial disorder is stable.
Patients treated by a general practitioner are considered to have a stable condition.
* Allergies to products used during the procedure (lidocaine, propofol, chlorhexidine).
* Uncontrolled coagulopathy defined as supratherapeutic dose of anticoagulation medication.
* Uncontrolled immune suppression.
* Participating in another clinical trial/investigation within 30 days prior to signing informed consent.
* Patient is currently implanted with a neurostimulator.
* Current radicular pain in index leg.
* Previous conventional or cooled radiofrequency of the genicular nerves of the index knee. Previous RF of the index knee other than of the genicular nerves is not an exclusion criterium.
* Patients with therapy-resistant bilateral knee pain defined as patients who

fulfil the inclusion criteria for pain in each knee i.e., patients who experience chronic knee pain (> 12 months) in both knees that is moderate to severe (defined as NRS > 4 on most or all days either constantly or with motion) and that is unresponsive (meaning insufficient pain reduction or intolerance) to conventional treatments ongoing for at least 12 months prior to inclusion. Conventional treatments must include all of the following: active physiotherapy, pharmacological treatment of pain and, in case of OA patients, intra-articular infiltration.
* Patients who have a planned TKA in the near future defined as patients who already have agreed on a date for the TKA procedure.
* Patients who are unwilling or mentally incapable to complete the study questionnaires.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-01-2023
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	31-10-2022
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	05407610
CCMO	NL80503.068.22