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Early Venous Reflux Ablation (EVRA) ulcer trial

Submission date
02/10/2013

Recruitment status
No longer recruiting

Registration date
03/10/2013

Overall study status
Completed

Last Edited
24/09/2020

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
A large number of patients (around 1% of the adult population) suffer from an ulcer (break in the skin surface) near the ankle. In most people, such an injury should heal up within a week or two. However, when there is an underlying problem with the skin, ulcers do not heal and may result in longstanding (chronic), painful, smelly and embarrassing wounds. The ulcers are often due to varicose veins in the legs, which can cause skin breakdown and ulcer formation. To get the ulcer to heal, the current best treatment is to wear a tight compression bandage with multiple layers, with which about 60% of these ulcers will heal within 24 weeks. There is evidence that treatment of the varicose veins by surgery will prevent the ulcer from returning after it has healed. Recent studies have suggested that newer techniques of treating varicose veins, such as injecting a medicine into the varicose vein (sclerotherapy) or treating the vein with heat ablation to seal it (using laser or radiofrequency), in an outpatient setting may help the ulcers to heal more quickly and (like surgery) reduce the chance of the ulcer coming back. These techniques can be carried out in the outpatient setting and are much better tolerated by patients in comparison to surgery. The aim of this study is to see whether early treatment of varicose veins using sclerotherapy or heat ablation helps with healing.

Who can participate?
Men and women, aged 18 or over, with a leg ulcer and varicose veins.

What does the study involve?
Patients will be randomly allocated to one of two treatments: either compression bandaging with treatment of varicose veins after the ulcer has healed (the current best treatment), or compression bandaging and early treatment of the veins. Participants will be followed-up for 1 year via monthly telephone calls with the research nurse and will undergo routine leg ulcer care in community or hospital (or both) settings, in accordance with the local standard. Participants will attend a 6-week clinic visit and complete questionnaires at baseline, 6 weeks, 6 months and 12 months. We will look at the number of ulcers healed in both patient groups and the speed at which the ulcers healed. We will also ask the patients to comment on any changes in their quality of life following treatment. Furthermore, we will look at the costs of the two treatments.

What are the possible benefits and risks of participating?
Both of these treatments are routinely offered to most patients with venous leg ulcers, and therefore the risks of taking part in this study are the same as the risks of having treatment

outside of the study. The information gained from the study may help doctors and patients make future decisions as to the best approach (early endovenous treatment compared to standard therapy of compression bandages) to treating venous ulcers in the future. If early treatment of varicose veins improves healing rates in patients with leg ulcers, there will be significant cost savings for the NHS as well as great benefits for the patients.

Where is the study run from?
Imperial College Trials Unit (ICTU) at Imperial College London (UK).

When is the study starting and how long is it expected to run for?
The study started in September 2013 and will run for 70 months, including an extension to collect longer term follow-up data.

Who is funding the study?
This project is funded by the National Institute for Health Research HTA (project number 11/129 /197).

Who is the main contact?
Francine Heatley (trial manager)
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Study website
www.evrastudy.org

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT03286140

Secondary identifying numbers
HTA 11/129/197

Study information

Scientific Title
A randomized clinical trial to compare early versus delayed endovenous treatment of superficial venous reflux in patients with chronic venous ulceration

Acronym
EVRA

Study objectives
What is the clinical and cost effectiveness of early endovenous treatment of superficial venous reflux in addition to standard care compared to standard care alone in patients with chronic venous ulceration?

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/11129197

Ethics approval required
Old ethics approval format

Ethics approval(s)
South West - Central Bristol research ethics board, 15/08/2013, ref: 13/SW/0199

Study design
Pragmatic multicentre randomized clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Venous disease/leg ulcers

Interventions
Standard therapy consisting of multilayer elastic compression bandaging with deferred treatment of superficial reflux (usually once the ulcer has healed) vs early endovenous treatment of superficial venous reflux (within 2 weeks) in addition to standard therapy.

Participants will be randomized 1:1 to standard compression therapy or early endovenous treatment within 2 weeks in addition to standard therapy.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Time to ulcer healing (from date of randomization to date of healing)

Secondary outcome measures
Current secondary outcome measures as of 15/10/2018:
1. Ulcer Healing Rate: Healing rate will be evaluated in addition to time to ulcer healing to allow comparison with other published studies.
2. Ulcer recurrence/Ulcer Free Time: Will be calculated up to 1 year for each study arm and with the extension, up to 5 years (median approximately 3.7 years). This will allow a very practical and easily understood assessment of the clinical difference between the 2 arms of the study. This will also allow comparison with other studies that have reported this outcome. In order to facilitate accurate calculation of reoccurrence/ulcer free time, clinical follow up will be continued after ulcer healing up to 1 year after randomisation.
3. Quality Of Life (QoL): Disease specific (AVVQ) and generic (EQ5D & SF36) quality of life assessments will be compared at 6 weeks post randomisation, 6 months, 12 months and at one time point between October 2018 and March 2019. The 6-week questionnaire will be given to the patient at the follow-up appointment, whereas other QoL questionnaires will be sent to the patient or completed by the patient via telephone. AVVQ is the most widely utilised disease

specific QoL tool in venous disease and has been extensively validated. A score out of 100 points is calculated, with a higher score indicating more severe QoL impairment. Changes in QoL scores will offer a comparison with other studies and, in the standard treatment arm, will allow an assessment of the natural history of venous ulceration treated with compression.
4. Health Economic Assessment: Cost items in hospital and community care will be recorded for each patient. Standard HRG published tariffs will be used to calculate overall costs. A standard tariff will be applied for each bandage change, although additional treatments administered for the treatment of symptoms or complications directly related to venous ulceration will be included. Utilities (QALYs) will be calculated from generic QoL questionnaire and cost-effectiveness will be analysed.
5. Other Markers Of Clinical Success: The Venous Clinical Severity Score (VCSS) will be assessed at 6 weeks. In addition, the incidence of complications related to the endovenous intervention as well as the presence of residual/recurrent varicose veins will also be assessed at 6 weeks.

Previous secondary outcome measures:
1. Ulcer Healing Rate: Healing rate will be evaluated in addition to time to ulcer healing to allow comparison with other published studies.
2. Ulcer Free Time: Will be calculated up to 1 year for each study arm. This will allow a very practical and easily understood assessment of the clinical difference between the two arms of the study. This will also allow comparison with other studies that have reported this outcome. In order to facilitate accurate calculation of ulcer free time, clinical follow-up will be continued after ulcer healing up to 1 year after randomization.
3. Quality Of Life (QoL): Disease specific (AVVQ) and generic (EQ5D & SF36) quality of life assessments will be compared at 6 weeks post randomization, 6 months and 12 months. The 6-week questionnaire will be given to the patient at the follow-up appointment, whereas other QoL questionnaires will be sent to the patient. AVVQ is the most widely utilised disease-specific QoL tool in venous disease and has been extensively validated. A score out of 100 points is calculated, with a higher score indicating more severe QoL impairment. Changes in QoL scores will offer a comparison with other studies and, in the standard treatment arm, will allow an assessment of the natural history of venous ulceration treated with compression.
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5. Other Markers Of Clinical Success: The Venous Clinical Severity Score (VCSS) will be assessed at 6 weeks. In addition, the incidence of complications related to the endovenous intervention as well as the presence of residual/recurrent varicose veins will also be assessed at 6 weeks.

Overall study start date
01/09/2013

Completion date
30/06/2019

Eligibility

Key inclusion criteria
1. Current leg ulceration of greater than 6 weeks, but less than 6 months duration
2. Able to give informed consent to participate in the study after reading the patient

information documentation
3. Patient age > 18 years
4. Ankle Brachial Pressure Index (ABPI) greater than or equal to 0.8
5. Superficial venous disease on colour duplex assessment deemed to be significant enough to warrant ablation by
the treating clinician (either primary or recurrent venous reflux)

Patients who cannot speak/understand English will be eligible for inclusion and informed consent will be obtained with assistance from translation services as per standard clinical practice. In view of the lack of cross cultural validation for quality of life tools, only healing outcome data will be collected.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
450

Total final enrolment
450

Key exclusion criteria
1. Presence of deep venous occlusive disease or other conditions precluding superficial venous intervention
2. Patients who are unable to tolerate any multilayer compression bandaging will be excluded. However, concordance with compression therapy can be variable for patients at different times. Patients who are generally compliant with compression but unable to tolerate the bandages for short periods will still be eligible for inclusion. A period of noncompliance with compression bandages will not be considered a protocol violation, but a normal variation within the spectrum of standard therapy.
3. Inability of the patient to receive prompt endovenous intervention by the recruiting centre
4. Pregnancy (female participants of reproductive age will be eligible for inclusion in the study, subject to a negative pregnancy test prior to randomisation)
5. Leg ulcer of nonvenous aetiology (as assessed by the responsible clinician)
6. If patient is deemed to require skin grafting they cannot be included

Date of first enrolment
24/10/2013

Date of final enrolment
30/09/2016

Locations

Countries of recruitment
United Kingdom

Study participating centre
Imperial College Healthcare NHS Trust
United Kingdom
-

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
United Kingdom
-

Study participating centre
Worcestershire Acute Hospitals NHS Trust
United Kingdom
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Study participating centre
North West London Hospitals NHS Trust
United Kingdom
-

Study participating centre
Gloucestershire Hospitals NHS Foundation Trust
United Kingdom
-

Study participating centre
Heart of England NHS Trust
United Kingdom
-

Study participating centre

University Hospital Birmingham NHS Trust
United Kingdom
-

Study participating centre
North Cumbria University Hospitals NHS Trust
United Kingdom
-

Study participating centre
The Dudley Group NHS Trust
United Kingdom
-

Study participating centre
The Royal Wolverhampton Hospitals NHS Trust
United Kingdom
-

Study participating centre
York Hospitals NHS Foundation Trust
United Kingdom
-

Study participating centre
Hull & East Yorkshire Hospitals NHS Trust
United Kingdom
-

Study participating centre
The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust
United Kingdom
-

Study participating centre

Central Manchester University Hospitals NHS Foundation Trust
United Kingdom
-

Study participating centre
Frimley Park Hospital NHS Foundation Trust
United Kingdom
-

Study participating centre
Plymouth Hospitals NHS Trust
United Kingdom
-

Study participating centre
Bradford Teaching Hospitals NHS Foundation Trust
United Kingdom
-

Study participating centre
Salisbury NHS Foundation Trust
United Kingdom
-

Study participating centre
Leeds Teaching Hospitals NHS Trust
United Kingdom
-

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
United Kingdom
-

Study participating centre

Taunton and Somerset NHS Foundation Trust
United Kingdom
-

Sponsor information

Organisation
Imperial College London (UK)

Sponsor details
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Research Governance Manager
Joint Research Compliance Office
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Sponsor type
University/education

Website
http://www3.imperial.ac.uk

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
30/04/2018

Individual participant data (IPD) sharing plan
At completion of the study, data will be shared in accordance with the NIHR HTA guidance on study outputs as per the research contract between the secretary of state for health research and Imperial College London. Only anonymised data will be shared under the terms of the consent forms.
Data and associated documentation will be available to users only under a data-sharing agreement that provides for the following:
1. A commitment to using the data only for research purposes and not to identify any individual participant;
2. A commitment to securing the data using appropriate computer technology;
3. A commitment to destroying or returning the data after analyses are completed.
All requests are dealt with on a case-by-case basis. Any request should be submitted to the corresponding author who will then review with the Trial Management Group and sponsor. A record of all access to data will be maintained by the Imperial College Archive team.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	31/05/2018	26/04/2018	Yes	No
Results article	results	01/04/2019	12/02/2019	Yes	No
Results article	results	01/05/2019	30/05/2019	Yes	No
Results article	results	23/09/2020	24/09/2020	Yes	No
HRA research summary			28/06/2023	No	No