Imperial College London

Randomised Controlled Trial of Mechanochemical Ablation versus Cyanoacrylate Adhesive for the Treatment of Varicose Veins

FULL TITLE

A randomised controlled trial of mechanochemical ablation versus cyanoacrylate adhesive for the treatment of varicose veins

SUMMARY

This study will be comparing the treatment of varicose veins using either mechanochemical ablation (MOCA) or cyanoacrylate adhesive (CAE). Patients will be randomised to receiving either MOCA or CAE.

The pain scores, clinical scores, quality of life scores, occlusion and re-intervention rate at 2 weeks, 3, 6 and 12 months as well as the cost effectiveness of each intervention will be assessed.

LAY SUMMARY

Varicose vein disease is a common condition affecting the population. Surgery has been the main treatment method for a long time, but, for the past decade, minimally invasive methods using thermal (heat) technologies were introduced and these were found to be more beneficial, especially, as it enables procedures to be carried out under local anaesthetic. However, these are often associated with pain especially as they use heat and require fluid to be injected around the vein.

More recently, non-thermal methods (no heat method) have been introduced, which do not require injection of fluid around the vein. These are potentially better tolerated, which could be more advantageous when carrying procedures under local anaesthesia. Two of the most common of these non-thermal methods are mechanochemical ablation (rotating tip of a catheter wire with simultaneous injection of chemical) and cyanoacrylate glue (a chemical which makes the walls of the vein stick together). They have been found to have a similar efficacy to the heat methods.

However, there have not been direct comparisons between these non-thermal treatment methods and, hence, why this study is being carried out.

The main aim will be to find out which method causes less discomfort. Secondary objectives will be to assess the pain level over the ensuing few days, change in quality of life, clinical severity score, degree of bruising and inflammation, time to return to normal activities/work, re-intervention rates as well as the cost-effectiveness of each method.

OBJECTIVES

- Primary Objective

  Pain score during saphenous vein ablation

- Secondary Objective

  The secondary objectives would be to compare the two treatment groups with respect to:
  - The pain score at the end of the procedure
  - The quality of life scores at baseline, 2 weeks, 3 months, 6 months and 12 months using the EQ-5D, AVVQ and CIVIQ scores
  - The clinical change using the VCSS at baseline, 2 weeks, 3 months, 6 months and 12 months
  - The pain score over the first 10 days
  - The degree of bruising at 2 weeks (based on a clinical examination)
  - The time taken to return to work and normal activities
  - Occlusion rates at 3 months, 6 months and 12 months
  - Re-intervention rate at 12 months
  - Comparison of the cost effectiveness of each intervention

Background

Varicose veins are common and are known to affect approximately one third of the population[1]. Chronic venous disease (CVD) has been shown to have a negative impact on the quality of life of patients and treatment of varicose veins has been demonstrated to lead to improvement in the quality of life of patients[2-4]. Over the past decade, new endovenous techniques have been introduced and these are felt to be cost-effective, especially, when performed in an outpatient or 'office-based' setting[5]. These endovenous ablation methods (almost exclusively radiofrequency ablation (RFA) or endovenous laser ablation (EVLA) employ mainly thermal energy, to treat varicose veins. The American Venous Forum (AVF) and the National Institute of Clinical Excellence (NICE) guidelines published in July 2013 recommended the use of endovenous thermal ablation techniques, namely radiofrequency ablation (RFA) or endovenous later ablation (EVLA), as first line treatment for truncal reflux[6-8]. Occlusion rates of greater than 90% have been demonstrated in studies looking at these two methods at up to 2 years of follow-up [9-12].

However, because they make use of thermal energy to denature the venous wall, they have the potential of causing pain, skin burns, skin pigmentation, nerve damage and, even, arteriovenous fistula formation[13, 14]. To minimise these possible complications, tumescent anaesthesia has to be infiltrated around the vein to be treated. This, in turn, can be a source of discomfort to patients.

More recently, newer non-thermal, non-tumescent (NTNT) ablation techniques have been introduced in order to reduce these complications. Mechanochemical ablation

(MOCA) and cyanoacrylate adhesive injection (CAE) are two examples of these NTNTs[15, 16]. So far, they have been shown to be less painful than the thermal methods, but also equivalent to them in terms of quality of life improvement, time to return to normal activities and occlusion rates[17, 18]. This, therefore, indicates that they may one day be considered more favourably than endothermal ablation.

NICE has also recently produced interventional procedures guidance for the use of both MOCA and CAE.

However, there has not been any direct head-to-head comparison of these two non-thermal methods. We, therefore, propose to undertake a randomised controlled study comparing mechanochemical ablation and cyanoacrylate adhesive in the treatment of varicose veins.

Description

This will be a randomised clinical trial comparing MOCA to CAE. Patients will be randomised into group A (MOCA) or group B (CAE). Only the endovenous ablation part of the procedure will be randomised while the decision as to whether patients should receive treatment of their varicose tributaries will be at the discretion of the clinical team.

The device used for MOCA (group A) will be the ClariVein® mechanochemical ablation (MOCA) device (Vascular Insights, Madison, CT, USA).

The device used for CAE (group B) will be the VenaSeal™ Closure System (Medtronic, Minneapolis, Minnesota, USA).

Re-intervention of the treated saphenous veins will not be decided until at least 3 months after their initial procedure.

Target Population

Patients referred for treatment of symptomatic varicose veins will be recruited if they are found to have primary great saphenous (GSV) or short saphenous vein (SSV) incompetence on colour duplex scan. Patients will be identified at their clinic appointment and provided with further information regarding the study.

Inclusion Criteria

- Adults over 18 years of age
- Symptomatic GSV or SSV vein reflux > 0.5 seconds on colour Duplex

Exclusion Criteria

- Current DVT

- Recurrent varicose veins
- Arterial disease (ABPI<0.8)
- Vein diameter < 3mm
- Patient who are unwilling to participate
- Inability or unwillingness to complete questionnaires
- Adverse reaction to sclerosant or cyanoacrylate
- Not been involved in another venous trial for at least 6 months

Intervention

On the day of their procedures, patients will be asked to sign a study consent form for inclusion into the study. They will then be allocated a study number.

Patients will be randomised to have MOCA (group A) or CAE (group B) to treat their saphenous veins.

Randomisation will be carried out using an internet-based randomisation service (Sealed Envelope).

At baseline, basic demographic data will be collected from each patient (age, sex, height, weight, number of children, occupation, etc.; see Appendix 1). Patients will also be asked to provide their contact details (address, postcode, emails or telephone numbers) to enable correspondence for follow-up appointments.

Patients will be asked to fill quality of life questionnaires (EQ-5D, AVVQ and CIVIQ) and will have their clinical scores assessed (CEAP and VCSS).

The primary outcome measure will be to record the pain score immediately following completion of the endovenous ablation using a 100mm visual analogue scale (VAS) and a 0-10 number scale.

Once the pain score has been recorded, concurrent phlebectomy or foam sclerotherapy will then be carried out, if deemed necessary by the clinical team. At the end of this part of the procedure, the pain score will again be assessed, using the VAS and number scale.

Patients would be allowed to leave once they have spent a complication free period in the department. On discharge, all patients will be provided with compression stockings to wear for 4 days. They will also be provided with a diary to record their post-procedural pain every day for the first 10 post-operative days using a validated 100mm visual analogue scale (VAS) as well as to record when they return to their normal activities and are back to work.

Patients will also be asked to attend a follow-up for research purposes at 2 weeks, 3 months, 6 and 12 months.

Patients' GP will also be sent a letter to inform them of their patient's participation in the study.

Risks of Procedures

Complications are possible following the varicose vein interventions and they are listed below. "Low risk" indicates that the risk of the complication happening is less than 1% and "moderate risk" indicates that the risk of the complication occurring is between 1-5%.

The possible complications usually associated with the MOCA technique include:

- Bleeding (low risk)
- Infection (low risk)
- Thrombophlebitis (moderate risk)
- Venous thromboembolism (low risk)
- Skin discolouration (low risk)
- Rotating wire getting caught (low risk)

The possible complications usually associated with the CAE method include:

- Bleeding (low risk)
- Infection (low risk)
- Thrombophlebitis (moderate risk)
- Venous thromboembolism (low risk)
- Skin discolouration (low risk)

Follow-up

For research purposes, patients will be asked to attend a follow-up appointment in the outpatient clinic at 2 weeks, 3 months, 6 and 12 months.

Follow-up at 2 Weeks

At the 2 weeks' follow-up, the diary containing details of the pain scores and how soon patients were able to return to normal activities/work will be collected. In addition, patients will be asked and examined for any bruising or phlebitis they have had after their procedure. They will undergo a clinical examination and the Venous Clinical Severity Score (VCSS) will be recorded and will be asked to fill in the EQ-5D, AVVQ and CIVIQ scores. No decision regarding re-treatment will be taken at this point. No risks are expected at this follow-up.

Follow-up at 3 Months, 6 Months and 12 Months

At the 3 months, 6 months and 12 months follow-up, patients will undergo another clinical examination and their VCSS will be recorded. They will also be asked to fill the EQ-5D, AVVQ and the CIVIQ scores. They will have a venous Duplex scan to determine occlusion of the treated vein. This will involve measurement of the vein with anonymised images for analysis.

As from the third month, patients found to have recurrence of their truncal veins will be assessed to see if they are symptomatic and require re-intervention. The method used for re-intervention will be dependent on the choice of the consultant in charge of the patient. No risks are expected to happen at follow-up, although patients with recurrence face possible complications based on the re-intervention procedures they will undergo.

Sample Size and Study Duration

We estimated the sample size needed to observe a mean difference of at least 10mm (standard deviation: 20mm) between the two interventions. With power set at 80% and 5% significance equivalence, we would need to recruit 128 patients (64 patients per group).

If a drop-out rate from follow-up of 30% is estimated, the total number to recruit is 183. If we recruit at least 3 patients per week, this will be approximately a total of 156 patients that could potentially be randomised over the year and 180 patients over 60 weeks (approximately 14 months). Thus, with 12 months follow-up the study will be running for 26 months with a target recruitment of 180 patients.

Settings

This study will be conducted at the Charing Cross Hospital (Imperial College London, UK) as well as the Singapore General Hospital and the Sengkang General Hospital (Singapore).

Funding

This study is currently not receiving any funding, but it is anticipated that application will be made for external funding during the course of the clinical trial.

ETHICAL ARRANGEMENTS

Ethical approval will be sought from a Regional Research Ethics Committee as per the National Research Ethics Service (NRES) and Health Research Authority (HRA). Patients will be screened by Roshan Bootun (or another research fellow), who is also a member of the direct care team, and patients thought eligible will be provided with information material about the trial and varicose veins and its treatments.

They will be invited to attend for their varicose vein procedures another day and will have until then to consider their participation into the trial (more than 24 hours to consider).

On the day of their procedure, they will be asked by Roshan Bootun (or another research fellow/nurse) to confirm their consent by providing a written consent prior to participating in the trial.

DATA HANDLING & DISSEMINATION OF RESULTS

All patient data will be anonymised and stored on a password protected database under the guidelines of the Data Protection Act 1998. Patient records will be kept on paper in the form of the diary card questionnaires and clinical scoring sheets. These will be kept in a locked filling cabinet at the and stored at the Charing Cross Hospital for 10 years in accordance with the Imperial College Trust Policy.

Data and study findings will be presented locally within the hospital, as well as national and international peer reviewed presentations and peer-reviewed journals.

Criteria for Electively Stopping the Trial or Other Research Prematurely

The trial may be stopped prematurely due to loss of equipoise or any major adverse effect as a result of treatment in any of the treatment arms.

Adverse events

No significant adverse events are expected.

Adverse Event (AE): any untoward medical occurrence in a patient or clinical study subject.

Serious Adverse Event (SAE): any untoward and unexpected medical occurrence or effect that:

- **Results in death**
- **Is life-threatening** – *refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe*
- **Requires hospitalisation, or prolongation of existing inpatients' hospitalisation**
- **Results in persistent or significant disability or incapacity**
- **Is a congenital anomaly or birth defect**

REPORTING PROCEDURES

All adverse events should be reported.

Depending on the nature of the event the reporting procedures below should be followed.

Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

Adverse Events (AE)

All such events, whether expected or not, should be recorded.

Serious Adverse Events (SAE)

An SAE form should be completed and faxed to the Chief Investigator within 24 hours.

All SAEs should be reported to the Research Ethical Committee where in the opinion of the Chief Investigator, the event was:

· ‘related’, ie resulted from the administration of any of the research procedures; and
· ‘unexpected’, ie an event that is not listed in the protocol as an expected occurrence

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES SAE form for non-IMP studies.

Local investigators should report any SAEs as required by their Local Research Ethics Committee, Sponsor and/or Research & Development Office.

In the event of any harm to participants in the trial, Imperial College holds Public Liability (“negligent harm”) and Clinical Trial (“non-negligent harm”) insurance policies which apply to this trial.

ETHICS APPROVAL

The Chief Investigator has obtained approval from the xxx Research Ethics Committee and the HRA. The study must be submitted for Site Specific Assessment (SSA) at each participating NHS Trust. The Chief Investigator will require a copy of the Trust R&D approval letter before accepting participants into the study. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

CONSENT

Consent to enter the study will be sought from each participant only after a full explanation has been given, an information leaflet offered and time allowed for consideration. Signed participant consent will be obtained. The right of the participant to refuse to participate without giving reasons will be respected. After the participant has entered the study the clinician remains free to give alternative treatment to that specified in the protocol at any stage if he/she feels it is in the participant’s best interest, but the reasons for doing so will be recorded. In these cases the participants remain within the study for the purposes of follow-up and data analysis. All participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment.

CONFIDENTIALITY

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.

Patient details will be anonymised as each participant will be allocated a study number. The allocated study number key code will be kept on a password protected NHS computer at all sites.

Patient details, including contact information (address, email, telephone numbers etc.), will be recorded on paper form. This paper form will be kept in a locked filing cabinet in a locked Vascular Research Office, located in the Section of Vascular Surgery on Floor 4 North at Charing Cross Hospital (university office). The contact details will be discarded once patients have been advised of the findings of the study (approximately, within 6-12 months following completion of the study).

All anonymised patient details with the allocated study number used as identifier will be stored electronically on a password protected access database on an Imperial College London university computer.

INDEMNITY

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

SPONSOR

Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

FUNDING

There are currently no funders for this study. However, external funding may be sought in the future.

AUDITS

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

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APPENDIX 1: Quality of Life Questionnaire

Hospital Number----------

Date of birth----------

Age **----------**

Occupation----------

Date----------

	MALE	FEMALE
Number of Pregnancies		
Weight/ Kg		
BMI>30	Yes	No
OCP or HRT	Yes	No
Smoker	Yes	No

Past Medical History

	Yes	No		Yes	No
Bleeding disorder	☐	☐	IHD	☐	☐
DVT/PE	☐	☐	Leg ulcers	☐	☐
Diabetes	☐	☐	Hypertension	☐	☐

Medications

Previous treatment to Varicose Veins

Side	Site	Date	Treatment type

Appendix 2: Pre Operative Clinical Assessment

Score	Definition
0	**Asymptomatic**
1	**Symptomatic, but able to carry out usual activities with out compressive therapy**
2	**Able to carry out usual activities only with compressive therapy and/or limb elevation**
3	**Unable to carry out usual activities even with compression and/or elevation**
	Usual activities = patients activities before the onset of disability due to venous disease

Appendix 3: Venous Clinical Severity Score (VCSS)

Please indicate right or left leg or bilateral (R, L or B)

	Absent	Mild	Moderate	Severe
Pain	None	Occasional, non/ no analgesia restricting	With moderate activity, occasional analgesia	Daily, severe limitations, regular analgesia
Varicose veins>4mm	None	Few	Multiple GSV	Extensive GSV and LSV
Venous oedema	None	Evening/ankle	Afternoon/ above knee	Morning/requiring elevation
Skin pigmentation	None	Limited and old/brown	Diffuse lower third/ purple	Wide/ purple
Inflammation	None	Mild cellulitis in marginal area	Moderate involving most of gaiter area	Severe cellulitis or significant eczema
Induration	None	Focal <5cm	Medial or lateral less than lower 1/3	1/3 of lower leg or more
Number of active ulcers	0	1	2	3
Active ulcer duration	None	<3 months	>3 months <12 months	>12 months
Active ulcer diameter(cm)	None	<2	2-6	>6
Compression	Not used or non compliant	Intermittent use	Stockings worn most days	Stockings worn daily
Total				

Appendix 4: Clinical-Etiology-Anatomy-Pathophysiology (CEAP Classification)

Clinical	0	1A	1S	2A	2S	3A	3S	4aA	4aS	4bA	4bS	5A	5S	6
Etiology	Congenital			Primary			Secondary			No venous cause identified				
Anatomy	Superficial			Deep			Perforating			No venous location identified				
Pathology	Reflux			Obstruction			Both			No venous pathology identified				

Class 0 No visible or palpable veins

Class 1 Telangiectasia, reticular veins

Class 2 Varicose Veins

Class 3 Oedema without skin changes

Class 4 Skin changes ascribed to venous disease

4a) Pigmentation or eczema

4b) Lipodermatoscerosis or atrophie blanche

Class 5 Skin changes and healed ulceration

Class 6 Active venous ulcers

A= Asymptomatic

S= Symptomatic

Appendix 5. Quality of Life Questionnaires

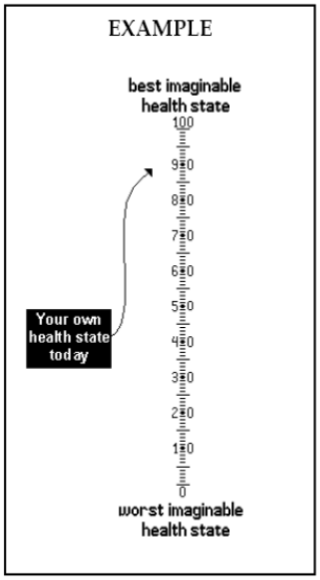
Pre-op questionnaire version 1- 6th August 2009

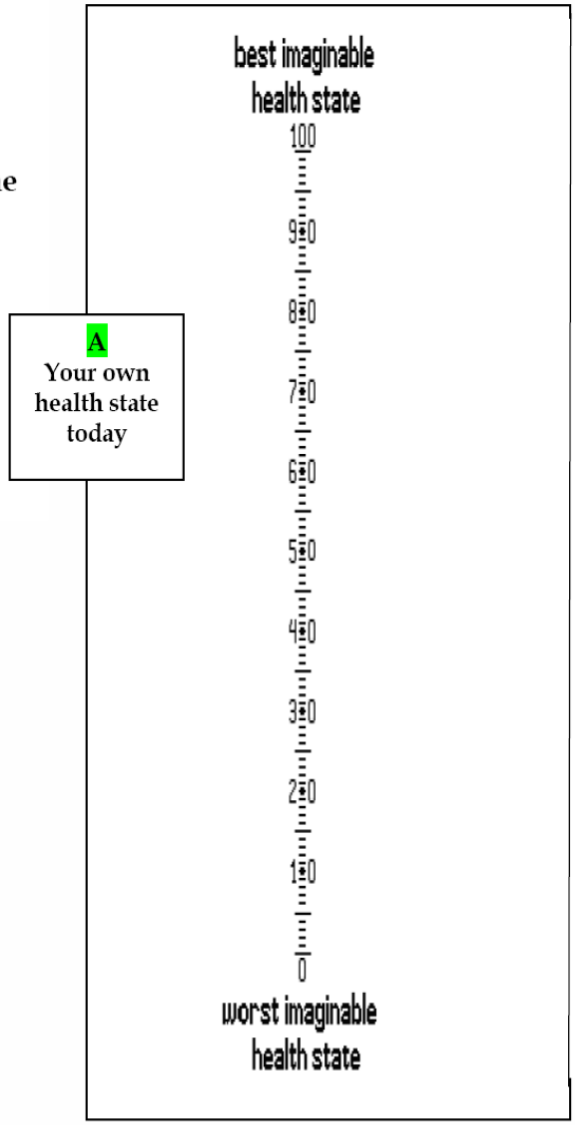
DESCRIBING YOUR OWN HEALTH TODAY

Please indicate on this scale how good or bad your own health state is today.

The best health state you can imagine is marked 100 and the worst health state you can imagine is marked 0.

Please draw a line from box A to the point on the scale that best indicates how good or bad your health state is today.





Your overall general health

Please indicate which statement best describes your own health state. (*Tick only one box in each group*)

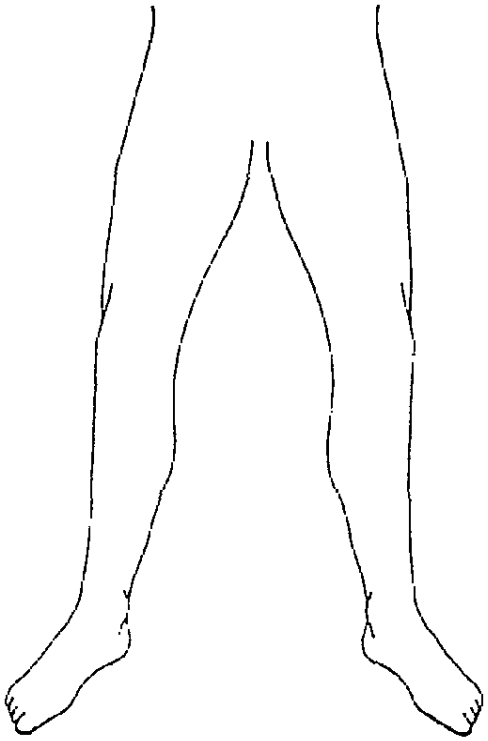
Mobility	I have no problems in walking about	☐
	I have some problems in walking about	☐
	I am confined to bed	☐
Self-care	I have no problems with self-care	☐
	I have some problems washing and dressing myself	☐
	I am unable to wash myself	☐
Usual activities	*For example, housework, family or leisure activities*	
	I have no problems with performing my usual activities	☐
	I have some problems with performing my usual activities	☐
	I am unable to perform my usual activities	☐
Pain/discomfort	I have no pain or discomfort	☐
	I have moderate pain or discomfort	☐
	I have extreme pain or discomfort	☐
Anxiety/depression	I am not anxious or depressed	☐
	I am moderately anxious or depressed	☐
	I am extremely anxious or depressed	☐

Appendix 6: Aberdeen Varicose Vein Questionnaire

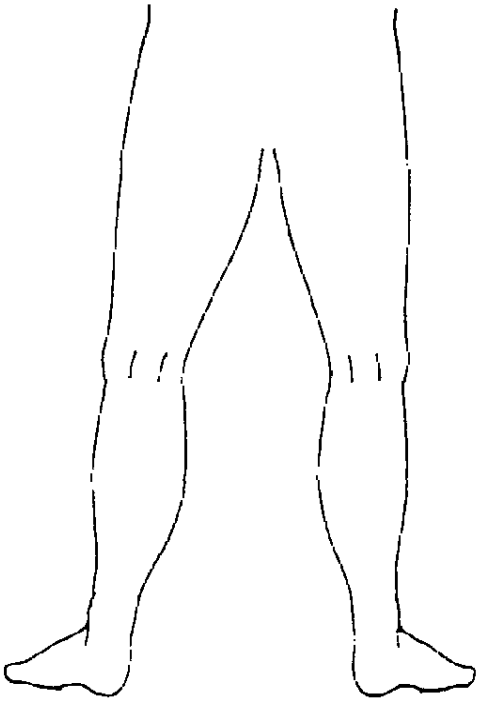
YOUR VARICOSE VEINS

1. Please draw in your varicose veins in the diagram(s) below:-

Legs viewed from front



Legs viewed from back



2. In the last two weeks, for how many days did your varicose veins cause you pain or ache?

(Please tick one box for each leg)

	R Leg	L Leg
None at all	☐	☐
Between 1 and 5 days	☐	☐
Between 6 and 10 days	☐	☐
For more than 10 days	☐	☐

3. During the last two weeks, on how many days did you take painkilling tablets for your varicose veins?

(Please tick one box for each leg)

	R Leg	L Leg
None at all	☐	☐
Between 1 and 5 days	☐	☐
Between 6 and 10 days	☐	☐
For more than 10 days	☐	☐

4. In the last two weeks, how much ankle swelling have you had?

(Please tick one box)

- None at all ☐
- Slight ankle swelling ☐
- Moderate ankle swelling (eg. causing you to sit with your feet up whenever possible) ☐
- Severe ankle swelling (eg. causing you difficulty putting on your shoes) ☐

5. In the last two weeks, have you worn support stockings or tights?

(Please tick one box for each leg)

	R Leg	L Leg
No	☐	☐
Yes, those I bought myself without a doctor's prescription	☐	☐
Yes, those my doctor prescribed for me which I wear occasionally	☐	☐
Yes, those my doctor prescribed for me which I wear every day	☐	☐

6. In the last two weeks, have you had any itching in association with your varicose veins?

(Please tick one box for each leg)

	R Leg	L Leg
No	☐	☐
Yes, but only above the knee	☐	☐
Yes, but only below the knee	☐	☐
Both above and below the knee	☐	☐

7. Do you have purple discolouration caused by tiny blood vessels in the skin, in association with your varicose veins?

(Please tick one box for each leg)

	R Leg	L Leg
No	☐	☐
Yes	☐	☐

8. Do you have a rash or eczema in the area of your ankle?

(Please tick one box for each leg)

	R Leg	L Leg
No	☐	☐
Yes, but it does not require any treatment from a doctor or district nurse	☐	☐
Yes, and it requires treatment from my doctor or district nurse	☐	☐

9. Do you have a skin ulcer associated with your varicose veins?

(Please tick one box for each leg)

	R Leg	L Leg
No	☐	☐
Yes	☐	☐

10. Does the appearance of your varicose veins cause you concern?

(Please tick one box)

- ☐ No
- ☐ Yes, their appearance causes me slight concern
- ☐ Yes, their appearance causes me moderate concern
- ☐ Yes, their appearance causes me a great deal of concern

11. Does the appearance of your varicose veins influence your choice of clothing including tights?

(Please tick one box)

- ☐ No
- ☐ Occasionally
- ☐ Often
- ☐ Always

12. During the last two weeks, have your varicose veins interfered with your work/ housework or other daily activities?

(Please tick one box)

- ☐ No
- ☐ I have been able to work but my work has suffered to a slight extent
- ☐ I have been able to work but my work has suffered to a moderate extent
- ☐ My veins have prevented me from working one day or more

13. During the last two weeks, have your varicose veins interfered with your leisure activities (including sport, hobbies and social life)?

(Please tick one box)

- ☐ No
- ☐ Yes, my enjoyment has suffered to a slight extent
- ☐ Yes, my enjoyment has suffered to a moderate extent
- ☐ Yes, my veins have prevented me taking part in any leisure activities

Appendix 7

C I V I Q-14

SELF-QUESTIONNAIRE PATIENTS

In English language for UK

Many people complain of leg pain. We would like to find out how often these leg problems occur and to what extent they affect the everyday lives of those who suffer from them.

Below you will find a list of symptoms, sensations or types of discomfort that you may be experiencing and which may make everyday life hard to bear to a greater or lesser extent. **For each symptom, sensation, or type of discomfort listed, we would like you to answer in the following way:**

Please indicate if you have experienced what is described in each sentence, and if the answer is 'yes', how **intense** it was. There are five possible answers, and we would like you to circle the one which best describes your situation.

Circle 1	if you feel the symtom, sensation of discomfort described does not apply to you
Circle 2, 3, 4 or 5	if you have felt it to a greater or lesser extent

QUALITY OF LIFE WITH VENOUS INSUFFICIENCY

1) During the past four weeks, have you had any **pain** in your **ankles** or **legs**, and how severe has this pain been?
Circle the number that applies to you.

No pain	Slight pain	Moderate pain	Considerable pain	Severe pain
1	2	3	4	5

2) During the past four weeks, how much trouble have you experienced at **work** or during your **usual daily activities because of your leg problems**?
Circle the number that applies to you.

No trouble	Slight trouble	Moderate trouble	Considerable trouble	Severe trouble
1	2	3	4	5

3) During the past four weeks, have you **slept badly** because of your leg problems, and how often?
Circle the number that applies to you.

Never	Rarely	Fairly often	Very often	Every night
1	2	3	4	5

	During the past four weeks, how much **trouble** have you experienced **carrying out the actions and activities** listed below b**ecause of your leg problems**? *For each statement in the table below, indicate how much trouble you have experienced by circling the number chosen.*				
	No trouble	Slight trouble	Moderate trouble	Considerable trouble	Could not do it
4) Climbing several flights of stairs	1	2	3	4	5
5) Crouching, Kneeling down	1	2	3	4	5
6) Walking at a brisk pace	1	2	3	4	5
7) Going out for the evening, going to a wedding, a party, a cocktail party…	1	2	3	4	5
8) Playing a sport, exerting yourself physically	1	2	3	4	5

	Leg problems can also affect your mood. How closely do the following statements correspond to what you have felt during the past four weeks? *For each statement in the table below, circle the number that applies to you.*				
	Not at all	A little	Moderately	A lot	Completely
9) I have felt nervous/tense	1	2	3	4	5
10) I have felt I am a burden	1	2	3	4	5
11) I have felt embarrassed about showing my legs	1	2	3	4	5
12) I have become irritated easily	1	2	3	4	5
13) I have felt as if I am handicapped	1	2	3	4	5
14) I have not felt like going out	1	2	3	4	5

Appendix 8. Procedural Pain Score

Date:……. **Hosp. No.:-……..**

This is to assess the amount and duration of pain you experience during this treatment.

Please put a mark on the line to indicate the maximum pain score you experience as well as a number between 0-10 to indicate the pain score over 10 (10 = worst pain imaginable).
Also, please indicate the duration of the discomfort.

Example*: If your pain score is roughly about 3 over 10 (10 being the worst pain imaginable), you might want to indicate it as below:*

Discomfort	No pain 0	3 /	Worst pain imaginable 10

Post-Endovenous Ablation

Maximum Discomfort

Maximum Discomfort	No pain 0		Worst pain imaginable 10

	Please Tick
Maximum discomfort lasted ***a few seconds***	
Maximum discomfort lasted ***a few minutes***	
Maximum discomfort lasted ***longer than a few minutes***	

Average Discomfort

Average Discomfort	No pain 0		Worst pain imaginable 10

	Please Tick
Maximum discomfort lasted ***a few seconds***	
Maximum discomfort lasted ***a few minutes***	
Maximum discomfort lasted ***longer than a few minutes***	

Post-tributary Treatment

Maximum Discomfort

Maximum Discomfort	No pain 0	Worst pain imaginable 10

	Please Tick
Maximum discomfort lasted ***a few seconds***	
Maximum discomfort lasted ***a few minutes***	
Maximum discomfort lasted ***longer than a few minutes***	

Average Discomfort

Average Discomfort	No pain 0	Worst pain imaginable 10

	Please Tick
Maximum discomfort lasted ***a few seconds***	
Maximum discomfort lasted ***a few minutes***	
Maximum discomfort lasted ***longer than a few minutes***	

Appendix 9. Patient Diary

Please indicate at what stage you were able to return to work and your normal daily activities (the activities you were able to do prior to treatment).

Please also indicate the day when you stopped wearing the compression stockings (if provided).

(Please tick one box)

	Day I was able to resume my normal activities	Day I returned to work	Day I stopped wearing compression stockings
Day of surgery			
Day after surgery			
2 days after surgery			
3 days after surgery			
4 days after surgery			
5 days after surgery			
6 days after surgery			
7 days after surgery			
8 days after surgery			
9 days after surgery			
10 days after surgery			
>10 days after surgery			

Please return to:

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Appendix 10. Patient Pain Diary (VAS)

Please put a mark on the line to indicate your maximum pain score on each day.
Please also write a score from 0 to 10 for your maximum pain on each day.
***Example**: If your pain score on day 4 is roughly about 5 over 10 (10 being the worst pain imaginable), you might want to indicate it as below:*

Day 4	No pain 0	5 /	Worst pain imaginable 10

Study Diary:

(0 = no pain and 10 = worst pain imaginable)

Day 0	No pain 0		Worst pain imaginable 10
Day 1	No pain 0		Worst pain imaginable 10
Day 2	No pain 0		Worst pain imaginable 10
Day 3	No pain 0		Worst pain imaginable 10
Day 4	No pain 0		Worst pain imaginable 10
Day 5	No pain 0		Worst pain imaginable 10
Day 6	No pain 0		Worst pain imaginable 10
Day 7	No pain 0		Worst pain imaginable 10
Day 8	No pain 0		Worst pain imaginable 10
Day 9	No pain 0		Worst pain imaginable 10
Day 10	No pain 0		Worst pain imaginable 10

Appendix 11. Ecchymosis Score

Patient No.:……..

Date:……

Ecchymosis at 2 weeks		
Grade	***Treated Area with Ecchymosis (%)***	
0	None	
1	<25	
2	25-50	
3	50-75	
4	75-100	
5	Extension above or below treated segment	

Appendix 12. Trial Flowchart