Randomized Controlled Trial Protocol

V0.2

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Title: Does longitudanal or transverse orientation of ultrasound probe improve cannulation success in minimally invasive venous surgery. A randomized controlled trial.

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Trial Locations:

Saolta Hospital Group

Declarations:

The investigators report no conflicts of interest

1. Introduction:

1.1 Background:

Varicose veins are an extremely common disorder[1] and negatively impact on patient quality of life.[2] In recent years minimally invasive venous treatments for varicose veins (MIVT) have emerged as an effective alternative to open surgery. It is associated with a reduction in peri-operative morbidity, recovery time and increased quality of life scores when compared with open surgical stripping[4]. Furthermore, MIVT is now widely carried out under local anaesthesia.

Typically, MIVT requires cannulation, under ultrasound guidance, of either the great or small saphenous vein in the lower extremity to allow subsequent passage of a venous catheter. This cannulation technique is widely used for venous and arterial cannulation throughout the body. It entails utilising an ultrasound probe in either a longitudanal or transverse orientation (to the target vein) to guide an entry needle into a target vessel. The longitudanal orientation, while unstable, offers better visualisation of the vein when performed accurately. Conversely, the transverse approach is very stable with poorer visualisation of the target vessel. As such, no definitve guidance is available to guide treating physicians as to the optimal orientation with a wide variation among practitioners.

The cannulation process for MIVT is often further challenged by both the small calibre and tendency toward vasospasm of target veins. Failure of cannulation may result in greater rates of conversion to open surgery exposing the patient to the the higher rate of morbidity associated with open surgery. More importantly, repeated cannulation results in significant discomfort and hence a reduction in patient satisfaction.

Longitudanal ultrasound orientation during venous cannulation has been suggested by a number of radomised studies to offer superior cannulation rates of cannulation.[5,6] This technique may offer a simple, safe and cost-neutral step to improve cannulation rates in the widely performed MIVT.

1.2 Rationale for study:

The authors question whether orientation of the ultrasound probe (in either a cross-sectional or longitudanal manner) has the potential to improve venous cannulation rates while reducing the perioperative pain associated with challenging access. Thus, we propose a blinded randomized controlled feasibility study to investigate the effects of ultrasound orietation on cannulation rates in MIVT.

2. Aims and Objectives:

2.1 Aim

The aim of this study is to undertake a methodologically robust radomized controlled trial assessing the merits of of ultrasound orietation on cannulation rates in MIVT. The single main research question is " in patients undergoing intervention MIVT for superficial venous reflux, is the orientation of the ultrasound probe in the longitudanal position associated with superior cannulation rates and times and hence a reduction in peri-operative pain when compared to the transverse position."

2.2 Primary Objective

To determine whether the examined ultrasound orientations during cannulation improves cannulation rates.

2.3 Secondary Objectives

a) To assess the effect of orientation on cannulation time

b) To assess the effect of orientation on number of cannulation attempts

c) To assess the effect of orientation on conversion of MIVT to open venous surgery

d) To assess the effect of orientation on vein diameter

e) To assess the complication associated with both orientations

f) To assess patient peri-operative pain

2.4 PICO

Population: Patients with superficial venous incompetance undergoing minimally invasive venous therapy under local anaesthesia

Intervention: Longitudanal orientation of the ultrasound probe during venous cannulation

Comparison: A control group comprising of patients undergoing venous cannulation with the ultrasound probe in the transverse position (90 degree rotation from the experimental group)

Outcomes: Time to cannulation

Cannulation rate

Conversion to open surgery

Vein diameter

Number of cannulation attempts

Complications associated with venous cannulation

Perioperative pain

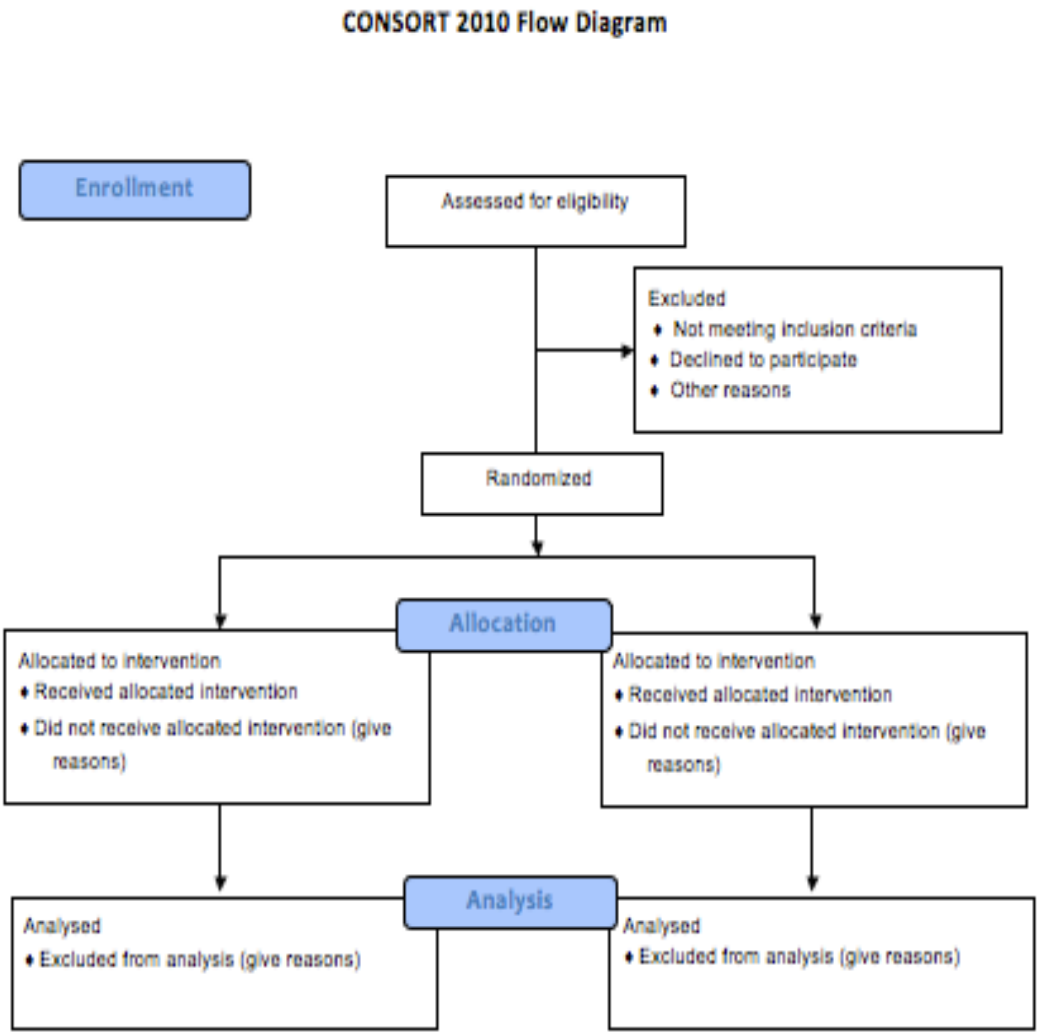
3. Study Methods

3.1 Statement of design

This randomized controlled trial shall be carried out in accordance with the guidance set out by the Consolidated Standards of Reporting Trials (CONSORT) group. http://www.consort-statement.org/

Participants shall be randomized in a 1:1 ratio to one of two parallel groups.

3.2 Study Flow



3.3 Participants:

All consenting patients attending the Vascular Surgical department in the named study loaction with Great Saphenous incompetence suitable for MIVT will be asked re inclusion in the study. Where both legs are being treated only one leg shall be randomised to the study. An initial pilot study will be used to guide potentially larger, powered studies in this area..

3.3.1 Inclusion criteria:

For minimally invasive venous surgery of the lower limb (Clinical-Etiology-Anatomy-Pathophysiology (CEAP) classification score 2 of greater)
Intervention requiring venous cannulation of the axial lower limb vein
Full consent
>18 years
No concomitant deep venous incompetence

3.3.2 Exclusion criteria:

General anaesthesia

3.4 Expected Study Duration:

Ethical approval shall be sought for this trial in February 2019. Pending the outcome recruitment/randomization will commence in April/May 2019 and continue over a twelve month period until April 2020. Subsequent amalgamation and analysis will be performed in May 2020 with the final results expected to be available in June 2020.

3.5 Study Settings:

In this study participants will be recruited from both the Vascular outpatients and day ward at the named trial location. An initial consent and information process (Appendix 1) shall be carried out in the outpatients setting in patients once a patient has been listed for MIVT. Consenting patients and those unsure of particpation will be provided with trial literature for education purposes. Upon re-presentation for their procedure at the original or named site patients will be verbally reconsented for inclusion prior to randomisation. All procedures regardless of site will be carried out by the same surgical team.

3.6 Interventions:

a) *Study group*: Participants randomized to the intervention limb will undergo venous cannulation with the ultraound orientated longitudanally along the target vein. Venous cannulation involves the use of the "Seldinger technique" to puncture a peripheral vein (under ultrasound guidance) and the placement of firstly a wire and subsequently a venous catheter within the vein. The series of steps for the cannulation procedure is standard and will not be changed for the purposes of the trial.

b) *Control group:* Participants in the control limb will undergo MIVT with cannulation performed with the ultrasound in the transverse position.

Following cannulation all procedures will be completed in a standard fashion. All operating surgeons have significant experience (100+) with both ultrasound orientations for cannulation.

3.6.1 Contrindications, cautions and interactions to be considered

There are no contraindications or cautions to be considered when utilising ultrasound for venous cannulation. Currently, the orientation of the ultrasound is at the discretion of the operating surgeon with no guidance provided as to the optimal orientation. No variation in risk has been identified based on ultrasound orientation.

3.7 Outcomes Measures:

Baseline patient demographic data will be collated anonymously from patient medical notes and hospital computer systems. Intra-operative data will be collected prospectively at the time of intervention. Outcome data and definitions are provided below:

- Time to cannulation

  Time in seconds to achieve successful cannulation of superficial vein
- Cannulation rate

  Overall rate of successful cannulations regardless of attempts and time
- Conversion to open surgery

  Number of cases converted to open venous ligation +/- stripping as a results of failure to cannulate the vein successfully
- Vein diameter

Vein diameter in millimeters at the time of cannulation as measured on standardised vascular ultrasound

- Number of cannulation attempts
  Number of skin punctures required prior to successful cannulation of the vein
- Immediate complications
  Any complications identified in either group on the day of intervention
- Perioperative pain
  As defined by the externally validated numeric pain scale (0-10) provided by National Initiative on Pain Control

3.8 Sample size:

As this study is in effect a pilot numbers will be limited to 100 particpants. Similar studies have 200 plus participants[5,6]. Obviously this study will be underpowered however we would hope that our analysis would help guide future powered studies in this area.

3.9 Interim Analysis and stopping guidelines:

As this is a pilot study run over a short time frame we do not envisage a scenario where the trial will be ceased early.

3.10 Randomisation:

a) Sequence Generation: Generation of random sequence will be performed using a computer based random number generator.

b) Randomisation type: Simple randomisation will be used.

c) Allocation concealment: Assignments shall be enclosed in sequentially numbered, opaque, sealed envelopes.

d) Implementation: the allocation sequence and randomization will be undertaken by a clinical third party who has no direct contact with any participant. The recruitment of participants will be carried out by the surgical team. Upon confirmation of consent on the day of intervention a numbered envelope containing randomization data will be randomly selected and the subsequent procedural outcomes will be documented

and sealed within. Those radomised to the study group will undergo cannulation with the probe in the longitudinal orientation. The control group will undergo cannulation in the transverse orientation.

Sealed envelopes will be given to the third party (with overall randomization key) for electronic input of the anonymous data.

3.11 Blinding:

By the nature of the intervention the operating surgeon will not be blinded, however, as screens are used in theatre patients will be blinded to the orientation of ultrasound for cannulation.

3.12 Ethical Approval and Data Protection

Ethical apporval from local ethics bodies will be sought prior to the commencement of the trial. All data will be anonymous and stored within the Department of Vascular Surgery, on an encrypted file. The file and computer will be password protected.

4 Trial Progression:

4.1 Subject withdrawal:

Any participant may voluntarily withdraw consent for participation at any point.

The investigator may withdraw a patient from the study treatment patient:

• Experiences a serious or intolerable adverse event

• Develops, during the course of the study a condition which renders the patient unfit for intervention

• Requires early discontinuation for any reason

4.2 Management of withdrawals:

In this per-protocol analysis patients who voluntarily/ involuntarily withdraw from the study after randomization will be removed from their assigned treatment group. Their data will be stored (with consent) and their withdrawal will be documented in the final report. Replacement participants will be included to maintain target sample size.

4.3 Adverse events:

Adverse events defined as any untoward medical occurrence in a patient enrolled into this study regardless of its causal relationship to study treatment will be recorded and documented in the final report. Any serious morbidities or mortalities will also be reported within 24 hours to the ethics board. An appropriate specialist or the investigatory team shall manage any such events.

4.4 Follow up:

Patients will be followed up in a standardized fashion at 6-weeks in the vascular outpatients department or sooner should the need arise.

4.5 Trial Closure:

The trial shall be completed when a total of 100 participants have been randomized.

5 Confidentiality statement:

All healthcare staff involved in the handling of patient data must preserve and protect confidential patient, employee and business information. All documented study data will be anonymous and held in strict confidence. No information will be released to any third party unless written consent is received. Confidential information includes any individually identifiable information in possession or derived from a provider of health care regarding a patient's medical history, mental, or physical condition or treatment, as well as the patients and/or their family members records, test results, conversations, research records and financial information.

6. References

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