Pain outcomes in a multicentre randomised clinical trial comparing *MechanOChemical ablation versus CyanoAcrylate Adhesive for the treatment of primary truncal saphenous veins incompetence*

A Randomised Clinical Trial

Amjad Belramman MBBS MSc**, Roshan Bootun** BSc MBBS MRCS PhD**, Tjun Yip Tang** MD FRCS (Gen) FAMS**, Tristan R A Lane** MBBS BSc FRCS PhD**, Alun H Davies** MA DM FRCS

Authors

Amjad Belramman MBBS MSc is a Clinical Research Fellow in Vascular Surgery at Imperial College London, United Kingdom. Email: a.belramman17@imperial.ac.uk

Roshan Bootun BSc MBBS MRCS PhD is an Honorary Clinical Research Fellow in Vascular Surgery at Imperial College London, United Kingdom and Vascular Surgery Specialty Training Registrar in the East of England Deanery, United Kingdom. Email: r.bootun@imperial.ac.uk

Tjun Yip Tang MD FRCS (Gen) FAMS is a Consultant Vascular and Endovascular Surgeon at Singapore General Hospital and Sengkang General Hospital, Singapore. Email: tang.tjun.yip@singhealth.com.sg

Tristan R A Lane MBBS BSc FRCS PhD is Consultant Vascular Surgeon at Cambridge University Hospitals NHS Foundation Trust, Honorary Clinical Senior Lecturer, United Kingdom. Email: tristan.lane@imperial.ac.uk

Alun H Davies MA DM FRCS is Professor of Vascular Surgery at Imperial College London and Honorary Consultant Vascular Surgeon at Imperial College Healthcare NHS Trust, London, United Kingdom. Email: a.h.davies@imperial.ac.uk

Corresponding Author:

Prof Alun H. Davies, Section of Vascular Surgery, Department of Surgery and Cancer, Imperial College London, 4N12A, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, United Kingdom. Email: a.h.davies@imperial.ac.uk

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Key Points

Question

Is there a difference in the amount of pain experienced when patients with primary saphenous vein incompetence are treated with mechanochemical ablation or cyanoacrylate adhesive?

Findings

In the MOCCA multicentre randomised clinical trial, the median maximum and “average” pain score were low and similar between the MOCA group and the CAE group.

Meaning

Findings of this study are that both NTNTs have comparable outcomes. Previous studies have demonstrated that the NTNTs also have similar outcomes to ETAs. This would indicate that the main determinant of which interventions to use would be down to cost-effectiveness and clinician and patient opinion.

Abstract

Importance

Endovenous thermal ablations (ETAs) are recommended as first-line treatment of truncal vein reflux and have a short recovery time and are cost-effective. However, ETAs are associated with discomfort during tumescent anesthesia infiltration. To minimise discomfort, non-thermal, non-tumescent ablation techniques, in the form of mechanochemical ablation (MOCA) and cyanoacrylate adhesive injection (CAE), have emerged.

Objective

To assess pain score immediately after truncal ablation using 100-mm Visual Analogue Scale and 10-point number scale.

Design, Setting, and Participants

The MOCCA study was a prospective, multicentre, randomised clinical trial, conducted at three sites between November 2017 and January 2020. There were 392 participants screened, 225 were excluded, and 167 participants underwent randomisation. Four participants did not receive allocated intervention and were included in the intention to treat analysis. Patients were reviewed at 2 weeks, and at 3, 6, and 12 months.

Interventions

Patients with primary truncal vein incompetence were randomised to receive either MOCA or CAE

Main Outcomes and Measures

Primary outcome measure was pain score immediately after completing truncal ablation using 100-mm Visual Analogue Scale (VAS) and 10-point number scale. Secondary outcome measures included degree of ecchymosis; occlusion rates, clinical severity, generic and disease specific quality of life (QoL) scores.

Results

60% were women with mean age 56 years. 92.8% of truncal veins treated were GSV. Demographic data and baseline status was comparable. 47% underwent adjunctive treatment of varicosities. Overall median maximum pain score after truncal treatment was 23mm on VAS and 3

on number scale. There was no difference in pain measured by VAS (MOCA 24mm vs CAE 20mm, p = .230) or number scale (MOCA 4, vs CAE 3, p = .179). Both groups demonstrated significant and comparable improvement in clinical severity, generic and disease specific QoL scores, and complete occlusion rates were similar. Four patients treated with CAE developed minor complications (superficial thrombophlebitis and thrombus extensions).

Conclusions and Relevance

This was the first randomised clinical trial comparing NTNTs techniques directly and demonstrated that both techniques have similar peri-procedural pain score between the MOCA and the CAE techniques.

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Introduction

Varicose veins affect up to one-third of the adult population.[1] They are known to cause a significant detrimental impact on the patient's health-related quality of life (QoL).[1]Varicose veins also carry a growing economic cost due to an aging population and increasing rates of advanced disease. [2] Treatment of symptomatic varicose veins has been shown to improve QoL.[3–5] Endovenous ablation with catheter-based technologies has led to a paradigm shift from open surgery, allowing specialists to perform them in an outpatient or office-based setting.[6] Currently, both the National Institute of Clinical Excellence (NICE) and the American Venous Forum recommend endovenous thermal ablations (ETAs), namely, radio-frequency ablation and endovenous laser ablation, as the first-line treatment of saphenous veins reflux.[7] ETAs demonstrate a short recovery time and are cost-effectiveness when compared to open surgery. Occlusion rates of greater than 90% have been reported for ETA at up to 5 years of follow-up.[8–11] ETAs denature the venous wall using thermal energy, thus they can cause possible complications such as pain, skin burns, skin pigmentation, nerve damage, and even arteriovenous fistula formation.[12,13] To minimise these possible complications, tumescent anaesthesia is infiltrated around the vein, however these injections can increase procedural discomfort.

Foam sclerotherapy is an alternative to ETAs. However, long-term results have shown inferior efficacy compared to other treatment technologies.[14]

To minimise negative aspects of these ETAs, non-thermal, non-tumescent ablation techniques (NTNTs) were recently developed. Since no heat is used, no tumescent anaesthesia is needed. Mechanochemical ablation (MOCA)[15] and cyanoacrylate adhesive injection (CAE)[16] are examples of these NTNTs. NICE has published interventional procedure guidance for both MOCA[17] and CAE.[18] So far, pain was found to be less than[19–24], or comparable to ETAs, [25,26] as well as equivalent to ETAs in terms of QoL improvement, time to return to normal activities or work, and occlusion rates.[27,28] Thus, the NTNTs could, one day, be considered favourable to ETAs.

There has been no head-to-head comparison of the two NTNTs techniques. Therefore, we performed the MOCCA study comparing MOCA with CAE in the treatment of varicose veins, aiming to assess the pain scores after truncal ablation.

Methods

Full details relating to the study design, eligibility criteria, and outcomes are provided in the previously published protocol.[29]

Study Design and Population

The MOCCA study was a prospective, multicentre, randomised clinical trial comparing MOCA to CAE. It was conducted at three sites: Charing Cross Hospital (Imperial College Healthcare NHS Trust) in London, UK; Singapore General Hospital; Sengkang General Hospital. From November 6, 2018, to January 13, 2020, potential participants (eTable 1 in the Supplement) were screened for eligibility.

Randomisation

Enrolment of participants was performed by a study member outside of the treating team. On the day of treatment and after informed consent were obtained; randomisation was carried out by using a web-based computerised randomisation system[30] - blinding after randomisation was not possible for either surgeons or participants due to the nature of the interventions. However, treatment allocation was masked from assessors who carried out follow-up assessments and duplex ultrasound scan (DUS).

Procedures

All interventions were performed under ultrasound guidance using local anaesthesia and carried out according to Instructions for Use (IFU) by vascular surgeons who have experienced in both MOCA and CAE techniques (eTable 2 in the Supplement).

Immediately after completion of the truncal ablation, patients were requested to indicate the amount of pain they had just experienced on a 100-mm Visual Analogue Scale (VAS) and a 10-

point number scale. Patients were provided with a sheet of paper with the scales on to mark their individual scores. Once the pain score was recorded, according to the treating clinical team's discretion, adjunctive procedures was performed if deemed necessary (i.e., concomitant phlebectomy or foam sclerotherapy). Pain scores post adjunctive procedures was also recorded. No routine preoperative or intraoperative pain medication was prescribed. Following interventions, a DUS was carried out to assess the treated truncal vein and the deep venous system. To treat patients similarly, all patients were discharged with instructions to wear class II compression stockings (Credalast, Credenhill Limited, Derbyshire, UK) for four days. Patients were also provided with a diary and instructed to record their post-operative pain for ten days and record when they could return to normal activities, including work and when stopped wearing compression.

Patients attended follow-up visits, had a clinical assessment, and were requested to complete QoL questionnaires at 2 weeks and then at 3-, 6- and 12-months. The diary was collected at 2 weeks. A DUS was performed at 3-, 6- and 12-months. There were four possible findings on post-intervention duplex ultrasound scanning[31]: complete occlusion, proximal occlusion, distal occlusion and open of the saphenous vein.

Outcome measures

The primary outcome measure was assessing the pain score immediately after completing the truncal ablation using a 100-mm VAS and a 10-point number scale. The secondary outcome measures were pain scores post adjunctive procedures; 10 days postoperative pain score; degree of ecchymosis[32]; time to return to normal activities or work; time to stop wearing compression; occlusion rates, clinical severity scores (Venous Clinical Severity Score – VCSS; Venous Disability Score – VDS and Clinical Etiology Anatomy Pathology score)[33,34]; generic (EuroQol 5 Domain 3-Level – EQ-5D-3L and EuroQol VAS)[35,36] and disease specific (Aberdeen Varicose Vein Questionnaire (AVVQ) and chronic venous insufficiency quality of life questionnaire (CIVIQ-14))[37–39] QoL scores.

Power calculations

In previous studies, a difference of 10mm was considered a minimum clinically significant difference.[21,40,41] Therefore, a mean difference of at least 10 mm with a standard deviation of 20 mm between treatment groups in the primary outcome of pain score during truncal ablation as measured by VAS was employed to calculate the sample size. The target sample size was calculated for 80% power of testing and a 5% level of significance, and 64 patients per group were required (128 in total). Allowing for a 30% loss to follow up, the target recruitment was estimated to be 183 patients.

Statistical Analysis

Data were analysed using IBM SPSS Statistics version 27.0.1 (IBM, Armonk, NY), Stata version 17.0 (StataCorp., College Station, TX) and Wizard version 2 (Evan Miller, Chicago, IL) on an intention-to-treat basis. Normality of the distribution of the data was assessed using visual inspection, Kolmogorov-Smirnov and Shapiro-Wilk tests and then parametric and non-parametric tests were employed. Accordingly, either one-way repeated measures analysis of variance or related samples of Friedman's Two-Way Analysis of Variance were used for paired data. Bonferroni correction was used where appropriate. Chi-squared tests were applied for categorical data and reported as frequencies and proportions (as percentages). Statistical significance was set at <0.05. However, as interim analyses were carried out one year from the beginning of recruitment,[42,43] the alpha spending function of Lan and DeMets approaches[44,45] was used to control the number of Type I errors.

Ethics and Registration

Ethical approval was obtained and sought from the Regional Research Ethics Committee London (Research Ethics Committee Reference: 17/LO/1457), and the declaration of Helsinki was conformed to. The Trial was registered at the ClinicalTrials.gov (NCT03392753) and sponsored by Imperial College London (17HH4084).

Results

There were 392 participants screened, of whom 225 were ineligible or declined to participate. The common reason for declining participation was dislike or inability to attend follow-up appointments, dislike for randomisation, preference for a different intervention, or preference for the treating clinician decision. A total of 167 participants consented and underwent randomisation. Four participants did not receive allocated intervention and were included in the intention to treat analysis. Covid-19 has a profound impact on the number and proportion of participants who attended follow-up appointment as shown in the study Consort Diagram (Figure 1).

Baseline Characteristics

Baseline patient characteristics are summarised in Table 1 and were comparable in both groups. Table 2 summarises characteristics of the veins treated. Overall, 92.8% of the truncal veins treated were GSVs. The median treated truncal vein diameter was comparable in both groups. However, the median procedure duration for GSVs was significantly shorter for MOCA than for the CAE group (MOCA 17min (IQR:14.3–20.3), vs CAE 22.7min (IQR: 17.5–27.2), Mann-Whitney U test, p=.001). There was no difference in proportion of adjunctive treatment.

Primary outcome (pain score)

Maximum Pain Score Post-truncal Treatment

Overall, the median maximum pain score experienced during truncal treatment was 23mm (IQR 10–44) on a VAS and 3 (IQR: 2–5) on the 10-point number scale. Distributions of the maximum pain scores for MOCA and CAE were similar. The median maximum pain scores measured by VAS for MOCA, and CAE were 24mm (IQR: 11.5–44.7mm) and 20mm (IQR: 9–42mm; p=0.230), respectively. As measured on a 10-point number scale, median for MOCA was 4 (IQR: 2–5) compared to 3 for CAE (IQR: 2–4; p=0.179) (Figure 2). There was a statistically significant, strong positive correlation between VAS and number scale, $r = 0.783$, $p < 0.001$.

Most patients experienced maximum pain for seconds (83.7%), including in both NTNT groups (p=0.616).

“Average” pain Score Post-truncal Treatment

The overall median “average” pain score experienced at the end of truncal treatment was 10.5mm (IQR 3–25) on a VAS, and 3 (IQR: 3–4) on the 10-point number scale.

Distributions of the “average” pain scores for MOCA and CAE were similar. The median “average” pain score measured on VAS for MOCA was 8mm (IQR: 3–22mm) and 11mm (IQR: 4–27mm) for CAE ($p = 0.257$). On the number scale, MOCA scored 4 (IQR: 2–5), compared to 3 for CAE (IQR: 2–4) ($p = 0.657$) (Figure 2). There was a statistically significant, strong positive correlation between VAS and number scale for “average” pain, $r = 0.681$, $p < 0.001$.

Secondary Outcomes

Table 3. summaries all secondary outcomes.

10 Day Postoperative Pain Scores

The overall median pain score reported in the ten-days postoperatively was 9.75 mm (IQR 2.9–16.75) on a VAS. The median pain score for MOCA was 10.5mm (IQR: 3–16mm) and CAE 7mm (IQR: 2.5–19mm). This was not statistically significantly different ($p = 0.847$) (eFigure 1 in the Supplement).

Quality of life

- **Disease specific quality of life – AVVQ and CIVIQ-14**

There were no significant differences in disease specific QoL scores between the two treatment groups over the follow-up period. The AVVQ score in both groups improved significantly by the third and sixth months, and these improvements were preserved to the 12th month ($p <0.001$). Post hoc analysis revealed statistically significant reduction in AVVQ scores from baseline (median = 14.14) to 3-months (median = 4.76; $p < 0.001$), to 6 months (median = 5.01; $p < 0.001$) and to 12 months (median = 4.76; $p < 0.001$), but not at 2 weeks. Similarly, CIVIQ-14 scores were also statistically significant improved at follow-up ($p <0.001$, Friedman). Post hoc analysis showed statistically significant differences in CIVIQ-14 scores from baseline (median = 19.64) to 2-weeks

(median = 12.50; p = 0.028), 3 months (median = 5.35; p < 0.001), 6 months (median = 5.35; p < 0.001) and to 12 months (median = 5.35; p < 0.001) (eFigure 2 in the Supplement).

- **General quality of life - EQ-5D and EQ- VAS**

Both groups showed significant improvement at 6-month follow up, which was maintained to 12 months follow up in the EQ-3D VAS (p = <0.001). Significant improvements were seen in EQ-5D at 3-month follow-up and sustained to 12 months (p = <0.001). Between treatment groups, no significant difference was seen eFigure 3 in the Supplement.

Clinical Disease Severity – VCSS and VDS

Patients in both groups demonstrated significant improvement in the VCSS (eFigure 4 in the Supplement) and VDS, which was maintained to 12-month follow-up ((VCSS, p <0.001; VDS, p = <0.001)) with no significant difference between groups.

Other Secondary Outcomes

Rreturn to normal activities and work was similar for both groups (p=0.543 and 0.359, respectively) (eFigure 5 in the Supplement). The degree of ecchymosis was also similar for both groups (p= 0.270). Both groups were equally compliant with post-op compression (p=0.533) (eFigure 5 in the Supplement) and the occlusion rate at 12 months was also equivalent (p=0.943).

Adjunctive Treatments

Adjunctive treatment of the varicosities, in addition to truncal ablation, was performed in 47.1% of patients (25.3% foam sclerotherapy and 74.7% ambulatory phlebectomy). Overall, the median maximum pain score experienced at the end of adjunctive treatment was 23 mm (IQR 7.25–42.7) on a VAS and 5 (IQR: 2–6) on number scale, and for “average” pain score 18.5 mm (IQR 6.25–36.7) on a VAS, and 3 (IQR: 2–5) on number scale. Patients who had CAE and ambulatory phlebectomy experienced slightly higher pain score, but this was not significantly different. eTable 3 in the Supplement shows maximum and “average” pain score for those had ambulatory phlebectomy or foam sclerotherapy.

Complications

No major complications of DVT or pulmonary embolus (PE) were reported. Four patients (all treated with CAE and adjunctive procedures) developed minor complications - three superficial thrombophlebitis (SVT) and one thrombus extension (endovenous glue-induced thrombosis - EGIT).[46]

The first SVT case was a patient on extended VTE prophylaxis post-procedure. Treatment was GSV CAE ablation and foam sclerotherapy (below knee, 10 ml) for his varicosities. 3 months after his intervention, the patient presented with calf pain. DUS identified chronic occlusion of the treated veins without DVT, and no treatment was required. The other two cases of SVTs developed in patients had treated for GSV incompetence and ambulatory phlebectomy for their varicosities. The SVTs developed in the truncal vein which were resolved without treatment.

One thrombus extension to the level of the common femoral vein occurred (EGIT-1) developed in an 80-year-old gentleman treated for GSV incompetence at 6 weeks. Although, the patient was asymptomatic, he was treated with anticoagulation. Repeat DUS confirmed no thrombus in the common femoral vein and the anticoagulation was stopped.

Discussion

The treatment of superficial venous insufficiency in patients with symptomatic varicose veins improves QoL. The primary outcome of this study was pain score after truncal ablations as measured by VAS. Our findings showed that maximum and “average” pain score were low and similar between the MOCA group and the CAE group. There was no statistically significant difference between treatment groups in pain experienced in the ten days postoperative, return to normal activities or work, ecchymosis score and occlusion rates. The median clinical and QoL scores significantly improved in both groups after treatment with no difference between the groups. Previous studies support the results of our study, demonstrating lower pain scores following NTNTs when compared to ETAs, both RFA[20–23,47,48] and EVLA[23–25]. In agreement with established

ETA techniques, a statistically significant and clinically relevant improvement in the clinical and QoL scores post treatment were reported in systematic reviews and meta-analysis[49,50].

The complete occlusion rates at 3-, 6- and 12-months follow up visits were equivalent for both techniques; however, the number of patients who had post-intervention duplex ultrasound scanning were low as the ongoing Covid-19 pandemic has affected follow-up visits. The overall complete occlusion rates observed are consistent with the literature.

The duration of procedure was significantly longer in patient treated with CAE. The reason for this is that the IFU of this technique requires waiting for 3 minutes for the first 4 cm of vein. Post-procedural compression is not required following CAE; however, patient in both groups were provided with stockings to treat them similarly.

There were no major complications such as DVT or PE in either group in our study. However, superficial thrombophlebitis and thrombus extensions were observed in patients treated with CAE, but only the EGIT-1 required any treatment.

This study shows no difference in outcomes following MOCA or CAE, and previous studies have demonstrated that NTNTs have similar outcomes to ETAs. This would indicate that the main determinant of which interventions to use would be surgeon and patent preference and the cost-effectiveness of each technique. This is especially important as the Covid-19 pandemic has significantly ravaged many health systems around the world and only limited resources would be made available to treat benign, but quality of life affecting conditions like varicose veins. Current list price for MOCA devices is approximately £375 and for CAE devices utilised in this study is £640. This suggests that with similar QoL outcomes and occlusion rates, but a shorter procedural time and lower device cost; MOCA is likely to be more cost-effective than CAE if assessed formally.[51]

Strengths and Limitations

Strengths of this study is that it was based on a prospective randomised clinical trial; with prespecified outcome measures in the published study protocol. However, there were a few limitations in our study. The first limitation was a lack of interventional blinding due to the different device techniques, though this was mitigated was by blinded follow-up assessments. Secondly,

because of Covid-19, approximately 41% of patients were lost to follow-up or dropped out at 12 months. However, the proportion did not differ between dropouts and non-dropouts, and this limitation was controlled by conducting intention to treat analysis and the primary outcome was recorded on day zero. This would suggest that the confidence in the primary outcome should be strong. Finally, although both groups were assessed for a pain score of 10 days post-operatively, the use of analgesia was not reported.

Conclusion

This was the first RCT comparing both two different NTNT techniques directly in treating truncal veins insufficiency. The results demonstrated that both techniques were similar in terms of peri-procedural pain score. Further well-designed RCTs with longer-term follow-up would be needed to assess longer term efficacy and cost-effectiveness of using NTNTs techniques in treatment of saphenous veins reflux.

Article Information

Corresponding Author:

Prof Alun H. Davies, Section of Vascular Surgery, Department of Surgery and Cancer, Imperial College London, 4N12A, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, United Kingdom. Email: a.h.davies@imperial.ac.uk.

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Author Affiliations: Department of Surgery and Cancer, Imperial College London, London, United Kingdom (Belramman, Bootun, Lane, Davies); Singapore General Hospital and Sengkang General Hospital, Singapore (Tang)

Author Contributions: Dr Belramman and Bootun had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Bootun, Lane and Davies participated in the design of the study

Acquisition, analysis, or interpretation of data: All authors

Drafting of the manuscript: Belramman

Statistical analysis: Belramman, Bootun, Lane

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Additional Contributions:

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FIGURE LEGENDS

Figure 1. Study Consort Diagram

Figure 2. Maximum and average pain score post-truncal treatment for mechanochemical ablation (MOCA) and cyanoacrylate adhesive injection (CAE)

Panel A. Visual Analogue Scale

Panel B. A 10-Point Number Scale

604 Table 1. Baseline Characteristics of the Study Participants

Characteristics	MOCA Group (n=83)	CAE Group (n=84)	P-value
Age — yr. (mean (± SD))	57 (± 16)	55 (± 15)	.657[a]
Sex — no. (%)			
Female	53 (63.9)	46 (54.8)	.232[b]
Height in meters (mean (± SD))	1.70 (± 0.18)	1.69 (± 0.17)	.837[a]
Weight in Kg (mean (± SD))	76.56 (± 18)	75.77 (± 23)	.825[a]
BMI (mean (± SD)) (kg/m2)	27.8 (± 7)	27.0 (± 6.5)	.587[a]
Smoker — no. (%)	13 (16.9)	10 (13)	.498[b]
Hypertension — no. (%)	20 (25.3)	17 (21)	.516[b]
Clinical CEAP Class–no. **(%)**			
C2	25 (31.3)	23 (29.5)	.850[b]
C3	19 (23.8)	22 (28.2)	
C4	27 (33.8)	27 (34.6)	
C5	3 (3.8)	1 (1.3)	
C6	6 (7.5)	5 (6.4)	
Clinical severity scoring– (median (IQR))			
VCSS	4 (3–6)	5 (3–7)	.189[c]
VDS	1 (1–2)	1 (1–2)	.771[c]
Generic QOL– (median (IQR))			
EQ-VAS	80 (70–90)	80 (70–88)	.180[c]
EQ-5D	0.73 (0.65–0.77)	0.69 (0.62–0.78)	.950[c]
Disease-Specific QOL– (median (IQR))			
AVVQ	14 (8.3–22.1)	13 (9.1–23.6)	.768[c]
CIVIQ-14	19 (6.24–41)	19 (8.9–37.5)	.544[c]

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BMI: body mass index; CEAP: clinical etiology anatomy pathology; VCSS: venous clinical severity score; VDS: venous disability score; EQ-5D: Euroqol 5 Domain 3 Level; EQ-VAS:EuroQol's visual analogue scale; AVVQ: Aberdeen varicose vein questionnaire; CIVIQ-14: chronic venous insufficiency quality of life questionnaire. MOCA: Mechanochemical ablation; CAE: cyanoacrylate adhesive injection; IQR: interquartile range; SD: standard deviation; a: Student t-test; b: X2 test; c: Mann-Whitney U test.

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Table 1. Characteristics of the veins treated

Characteristics	MOCA Group (n=83)	CAE Group (n=84)	P-value
Leg treated— **no. (%)**			
Right	36 (47.4)	40 (52.6)	.582[b]
Truncal veins treated			
GSV — no. (%)	75 (48.4)	80 (51.6)	.222[b]
Length of GSV treated cm (mean (± SD))	42.1 (±14)	39 (±13.5)	.177[a]
Cannulated level — (%)			
Above knee	17.2	17.1	.966[b]
Knee	20.3	18.6	
Below knee	62.5	64.3	
GSV diameter (median (IQR))	5 (4–6)	6 (4.5–7)	.061[c]
Procedure duration, minutes (median (IQR))	17 (14.3–20.3)	22.7 (17.5–27.2)	.001[c]
Volume of sclerosant used (ml) (range)	6 (5–9)	—	
Volume of glue used (ml) (range)	—	1.4 (1.1–1.6)	
Adjunctive Treatment			
carried out— no. (%)	29 (43.9) *	37 (56.1)	.216[b]
AP — no. (%)	25 (49)	26 (51)	.169[b]
FS — no. (%)	5 (31.2)	11(68.8)	
SSV — no. (%)	8 (66.7)	4 (33.3)	.222[b]
Length of SSV treated cm (mean (± SD))	28.7 (±13)	17 (±4.9)	.141[a]
SSV diameter (median (IQR))	5 (4.25–6.7)	4.75 (4.12–6.12)	.061[c]
Procedure duration, minutes (median (IQR))	14.6 (10–19)	14.8 (9.7–18)	1.000[c]
Volume of sclerosant used ml (range)	5 (4–7)	—	NA
Volume of glue used (ml) (range)	—	0.6 –1	NA
Adjunctive Treatment			
carried out— no. (%)	4(57.1)	3 (42.9) *	.293[b]
AP — no. (%)	3 (60)	2 (40)	.163[b]
FS — no. (%)	1 (33.3)	2 (66.7)	

*GSV: great saphenous vein; SSV: small saphenous vein; MOCA: Mechanochemical ablation; CAE: cyanoacrylate adhesive injection; AP: ambulatory phlebectomy; FS: foam sclerotherapy; NA: not applicable; IQR: interquartile range; SD: standard deviation; a: Student t-test; b: X^2 test; c: Mann-Whitney U test. * Means patients had both ambulatory phlebectomy and foam sclerotherapy procedure*

625 *Table 2. Summaries Secondary Outcomes*

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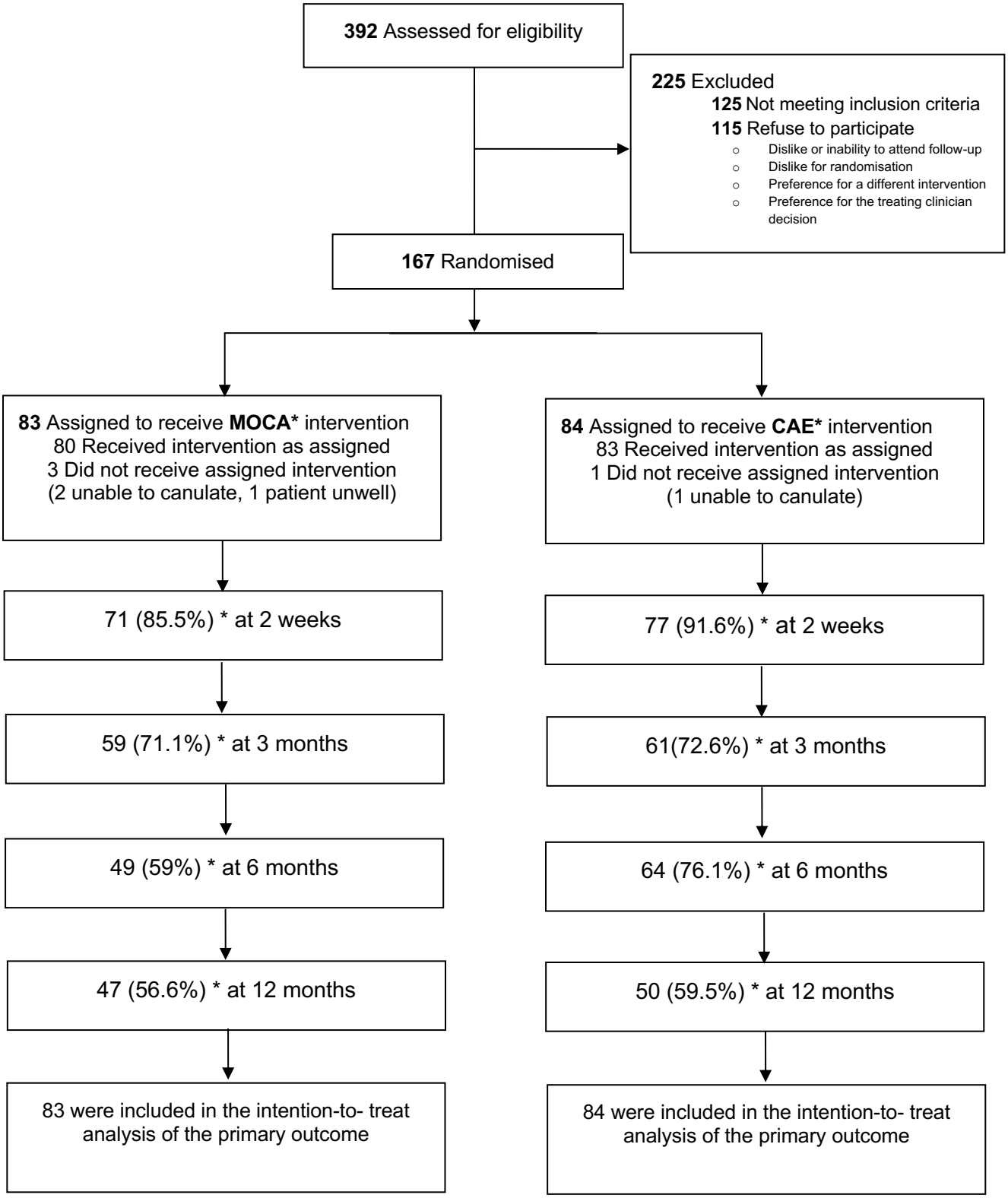
Secondary outcomes	MOCA Group	CAE Group	P-value
10 days postoperative pain score– (VAS (median (IQR))	10.5mm (3–16)	7mm (2.5–19)	.847[c]
Clinical severity scoring– (median (IQR))			
VCSS			
Baseline	4 (3–6)	5 (3–7)	.189[c]
2 wk	3 (1–4)	3 (1–6)	.500[c]
3 mo	2 (1–4)	2 (1–4)	.728[c]
6 mo	1 (1–3)	2 (1–3)	.069[c]
12 mo	2 (1–3)	2 (1–3)	.434[c]
Generic QOL– (median (IQR))			
EQ-VAS			
Baseline	80 (70–90)	80 (70–80.7)	.180[c]
2 wk	85 (70–94)	85 (71.5–95)	.862[c]
3 mo	85 (80–90)	83 (72.5–90)	.357[c]
6 mo	85 (80–90)	90 (80–90)	.588[c]
12 mo	90 (80-92)	90 (80-90)	.691[c]
EQ-5D			
Baseline	0.73 (0.65–0.77)	0.69 (0.62–0.78)	.950[c]
2 wk	0.76 (0.69–1)	0.77 (0.69-1)	.466[c]
3 mo	1 (0.72–1)	0.78 (0.76–1)	.889[c]
6 mo	1 (0.76–1)	0.79 (0.69–1))	.109[c]
12 mo	1 (0.74–1)	1 (0.73–1)	.848[c]
Disease-Specific QOL– (median (IQR))			
AVVQ			
Baseline	14.1 (8.3–22.1)	13.9 9.1–23.68)	.768[c]
2 wk	13.2 (7.7–17.7)	11.0 (5.2–20.0)	.660c
3 mo	5.5 (2.0–13.8)	4.2 (1.7-12.9)	.432[c]
6 mo	4.0 (1.7–9.2)	6.9 (1.6–13.4)	.256[c]
12 mo	4.0(0.0–11.9)	5.9 (1.4–13.4)	.412[c]
CIVIQ-14			
Baseline	19.6 (6.2–41.0)	19.6 (8.9–37.5)	.544[c]
2 wk	12.5 (3.5–30.5)	14.2 (3.5-28.5)	.532[c]
3 mo	5.3 (0.00–14.5)	5.3 (0.89–16.9)	.666[c]
6 mo	5.3 (0.00–14.2)	5.3 (0.00–21.42)	.541[c]
12 mo	3.5 (0.00–20.0)	7.1(0.75–21.4)	.191[c]
Compliance with wearing compression– (median (IQR))	7 (4–10)	8.5 (4–10)	.533[c]
Time to return to normal activities– (median (IQR))	2 (1–3)	2 (1–4)	.543[c]
Time to return to work– (median (IQR))	2.5 (1–7)	4 (2–7)	.359[c]
Technical success of truncal ablation (complete occlusion)— no. (%)			
3 months: 98 (58.7%) *			

Complete Occluded	39 (88.6)	45 (83.3)	.451[b]
Proximal Occluded	2 (4.5)	6 (11.1)	
Distal Occluded	3 (6.8)	2 (3.7)	
Open	0 (0.0)	1(1.9)	
6 months: 91 (54.5%) *			
Complete Occluded	38 (84.4)	39 (84.8)	.924[b]
Proximal Occluded	3 (6.7)	4 (8.7)	
Distal Occluded	2 (4.4)	2 (4.3)	
Open	2 (4.4)	1 (2.2)	
12 months: 67 (40.1%) *			
Complete Occluded	29 (87.9)	31 (91.2)	.943[b]
Proximal Occluded	1 (3)	1 (2.9)	
Distal Occluded	2 (6.1)	1 (2.9)	
Open	1 (3)	1 (2.9)	
Ecchymosis– no. (%)			
<25%	53 (89.8)	59 (83.1)	0.270[b]
25%+	6 (10.2)	12 (16.9)	

*VAS: visual analogue scale; VCSS: venous clinical severity score; EQ-5D: Euroqol 5 Domain 3 Level; EQ-VAS:EuroQol's visual analog scale; AVVQ: Aberdeen varicose vein questionnaire; CIVIQ-14: chronic venous insufficiency quality of life questionnaire; MOCA: Mechanochemical ablation; CAE: Cyanoacrylate adhesive injection; IQR: interquartile range; SD: standard deviation; b: X^2 test; c: Mann-Whitney U test.*means the total (%) pf patients had scan*

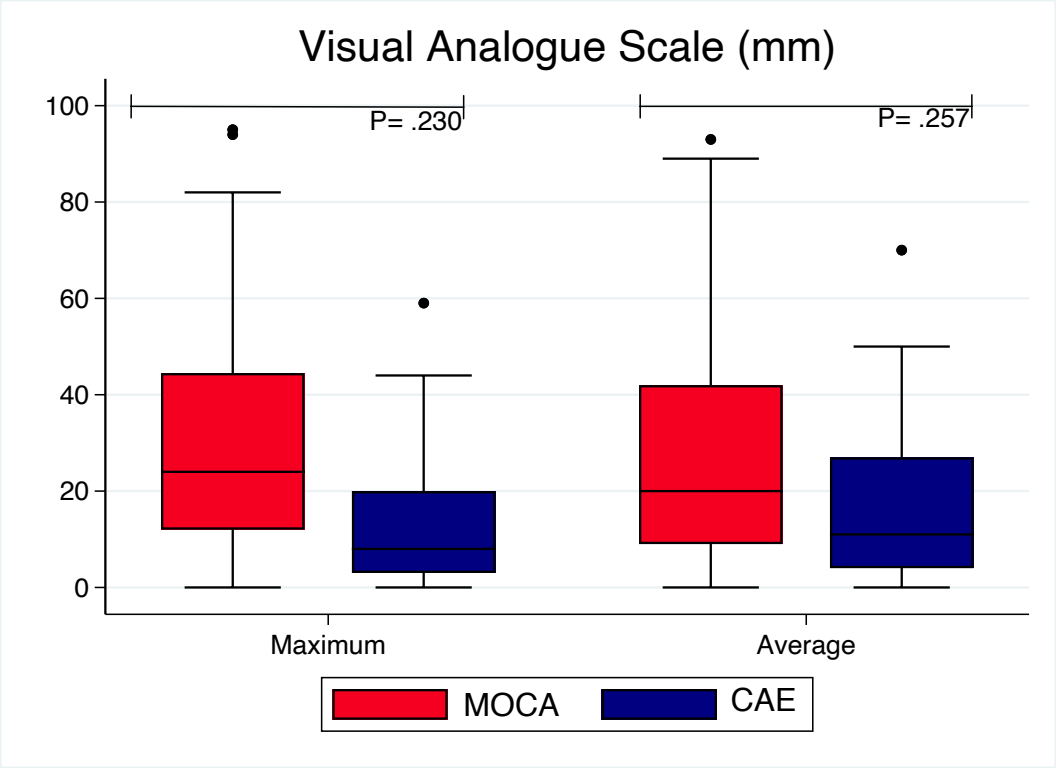
Figure 1. Study Consort Diagram


392 Assessed for eligibility
225 Excluded
125 Not meeting inclusion criteria
115 Refuse to participate
Dislike or inability to attend follow-up
Dislike for randomisation
Preference for a different intervention
Preference for the treating clinician decision
167 Randomised
83 Assigned to receive MOCA* intervention
80 Received intervention as assigned
3 Did not receive assigned intervention
(2 unable to canulate, 1 patient unwell)
84 Assigned to receive CAE* intervention
83 Received intervention as assigned
1 Did not receive assigned intervention
(1 unable to canulate)
71 (85.5%) * at 2 weeks
77 (91.6%) * at 2 weeks
59 (71.1%) * at 3 months
61(72.6%) * at 3 months
49 (59%) * at 6 months
64 (76.1%) * at 6 months
47 (56.6%) * at 12 months
50 (59.5%) * at 12 months
83 were included in the intention-to- treat analysis of the primary outcome
84 were included in the intention-to- treat analysis of the primary outcome

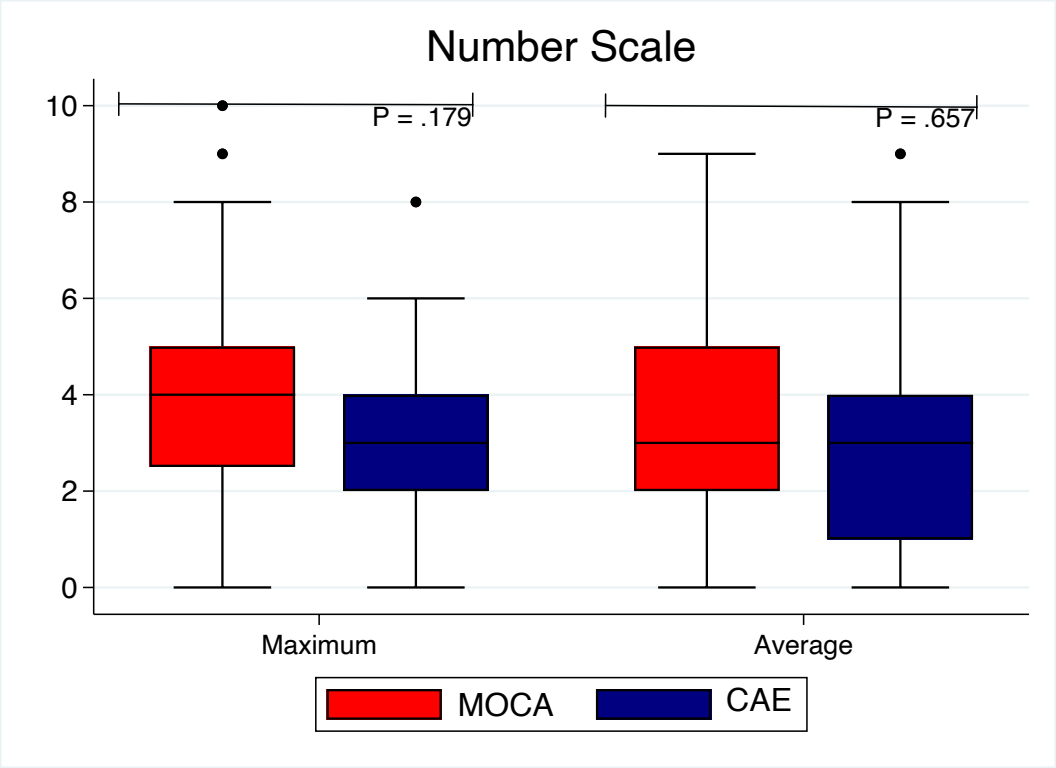
**MOCA: Mechanochemical ablation; CAE: Cyanoacrylate adhesive injection*

** Means the number and percent of patients who returned for each follow-up*

(a) – visual analogue scale


Visual Analogue Scale (mm)
100
80
60
40
20
0
P= .230
P= .257
Maximum
Average
MOCA
CAE

(b) – a 10-point number scale


Number Scale
10
8
6
4
2
0
P = .179
P = .657
Maximum
Average
MOCA
CAE