Macroscopic and Histologic Analysis of Vessel Wall Reaction After Mechanochemical Endovenous Ablation Using the ClariVein OC Device in an Animal Model

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WHAT THIS PAPER ADDS
This study describes the effects of mechanochemical endovenous ablation and its separate components on vessel wall histology in an animal model, further elucidating the mechanism of action.

Objective/Background: Mechanochemical endovenous ablation (MOCA) has been developed as a tumescentless technique to ablate saphenous veins and to avoid heat induced complications and post-procedural pain. The mechanism of action of MOCA is poorly understood. The present experiments were conducted to determine the effect of MOCA on vein wall injury and sclerosis in an animal model.

Methods: A total of 36 lateral saphenous veins (LSVs) were treated in 18 goats according to the human protocol. Veins from nine goats were evaluated 45 min after the procedure, while in the remaining nine, the treated veins were evaluated 6 weeks later. All treated veins were divided equally over three treatment groups: (i) MOCA, (ii) mechanical ablation without the sclerosant, and (iii) liquid sclerotherapy alone. The histological effects of treatment on the vein wall were systematically evaluated.

Results: The average diameter of the LSV was 4.0 ± 0.5 mm. Technical success was achieved in all but one LSV (35/36; 97%), with a median procedure time of 14 min (range 9–22 min). In the acute group, histological examination showed that mechanical ablation (alone or MOCA) induced severe injury to the endothelium in 82% but no damage to other layers of the vein wall. Mechanical ablation led to vasoconstriction. After 6 weeks follow-up, four of six MOCA treated veins were occluded. The occluded segments consisted mainly of fibrotic lesions possibly evolved from organised thrombus. No occlusions were observed after sclerotherapy or mechanical treatment alone. No major complications occurred during procedures or follow-up.

Conclusion: MOCA is associated with an increased occlusion rate compared with its separated components of mechanical ablation or sclerotherapy. The occlusion consists of cellular fibrotic material likely to be evolved from organised thrombus with fibrotic alterations to the surrounding media and adventitia. This study underlines the hypothesis that the additive use of MOCA increases the effectiveness of sclerosants alone by inducing endothelial damage and probably venous constriction.

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Article history: Received 22 June 2016, Accepted 25 November 2016, Available online 23 December 2016

Keywords: Mechanochemical ablation, Saphenous vein, Sclerotherapy, Varicose veins, Varicose veins therapy

INTRODUCTION
Varicose veins of the lower limbs are a common diagnosis, with a prevalence of up to 21% in the adult population, associated with physical impairment and decreased general and disease specific quality of life.1–3 Without treatment venous pathology has a tendency to progress over time.4 For more than a century, surgical high ligation, with or without stripping or compression therapy, was the only available treatment option for superficial venous insufficiency. The introduction of minimally invasive ablation techniques in recent decades has revolutionised the treatment of varicose veins. As a result, endovenous laser or radiofrequency ablation became the new standard of care owing to excellent occlusion rates in both the great and small saphenous vein (GSV and SSV, respectively).5,6
However, the need for tumescent anaesthesia, the risk of heat induced nerve injury, especially in the SSV and below knee GSV, and post-procedural pain are considered disadvantages to both of these endothermal techniques. To eliminate these cons, a growing interest in non-thermal techniques has developed in recent years.

Mechanochemical endovenous ablation (MOCA) is a non-thermal technique that combines endovenous mechanical injury to the vein wall with simultaneous infusion of a liquid sclerosant. Even though MOCA has been proven to be safe for the treatment of GSV and SSV insufficiency, with increasing data available on long-term results, the precise working mechanism and effect on the vein wall remain unknown. To date, experimental histological studies on MOCA are sparse.7–9 The goal of this study was to elucidate the mechanism of action of MOCA by analyzing the effects of its separate components on vessel wall histology in 18 goats.

MATERIALS AND METHODS

Study design

The study included 18 female dairy goats. Half of the goats (nine goats/18 veins) were enrolled into an acute experiment to assess direct effects of the MOCA treatment and its separate components. The remaining nine animals (18 veins) were treated within the 6 week follow-up protocol. The following experimental groups (six treated veins each) were created (Fig. 1): (1) acute experiment—mechanochemical ablation (ClariVein® + 2% Aethoxysklerol®); (2) acute experiment—liquid sclerotherapy (2% Aethoxysklerol); (3) acute experiment—mechanoablation (ClariVein without Aethoxysklerol); (4) follow-up experiment—mechanochemical ablation (ClariVein + 2% Aethoxysklerol); (5) follow-up experiment—liquid sclerotherapy (2% Aethoxysklerol); (6) follow-up experiment—mechanoablation (ClariVein without Aethoxysklerol).

The experiments were approved by the Committee on Animal Experiments (DEC), Utrecht, The Netherlands (Protocol No.: 2012.II.12.185). All procedures were performed by an endovascular specialist with extensive experience with MOCA (>50 procedures) and were conducted in accordance with good laboratory practice and international guidelines in animal research, under guidance of licensed biotechnicians at the animal laboratory of the Experimental Cardiology Department, University Medical Centre Utrecht, the Netherlands.

Animals

After a pilot study was conducted to prove the feasibility of the study protocol, a total of 18 female dairy goats were included and allocated to the different experimental groups. The sample size of the study groups is in line with previous international publications in this field.7,10 The fully grown animals were obtained from a local, qualified supplier. All animals were given normal chow without supplements, and water was freely available. The animals were housed in pairs, except for pre-procedure and post-procedure days, when isolation was maintained to protect the animals.

Experimental procedures

All animals were treated under general anaesthesia and oxygenated with a mechanical respirator. The animal was placed in the lateral supine position on the operating table. The hind legs were shaved, the skin was disinfected with iodine, and sterile draping was applied. A small transverse skin incision at the level of the ankle was made to visualise the distal lateral saphenous vein (LSV) and to insert an introducer sheath (Fig. 2). The LSV was chosen because of similarity to the human saphenous vein regarding diameter and length. The 2.67-F ClariVein occlusion catheter (OC; Vascular Insights, Madison, CT, USA) was introduced via a 5-F introducer sheath, and the tip was positioned approximately 25 cm from insertion into the vein.

The goats were equally divided into the six groups, as stated above, and once the allocation was determined, changing the procedure was no longer possible. In groups 1 and 4, the treatment was in line with current human treatment.11 In short, the ClariVein OC was used at maximum rotations per minute (3500 rpm), and after activation for 7 s proximally without infusion or withdrawal, the device was pulled back 1 cm every 7 s. Aethoxysklerol 2% (Kreussler Pharma, Wiesbaden, Germany) was administered simultaneously through the ClariVein OC. The dosage and infusion rate were chosen according to the dosing table made available by the manufacturer.

In groups 2 and 5, the treatment consisted of liquid sclerotherapy alone. The sclerosant was delivered over 25 cm using a ClariVein catheter, without activation of the motor, with a similar dosage and infusion rate as in MOCA.

In groups 3 and 6, the treatment consisted of the mechanically induced damage without additional sclerosant.
Venous explantation

In the acute experiments, a pressure bandage was applied at the puncture site to control bleeding. The treated LSV was harvested between 30 and 45 min after the procedure was finished. The veins were surgically exposed over the total length of treatment. The exposed vein was studied macroscopically for occlusion or any complication (perforation, rupture, or vein wall hematoma). Proximally and distally the vein was ligated with a Vicryl 3-0 suture (Johnson & Johnson, New Brunswick, NJ, USA). Long ends of the suture were used for identification of the proximal end. Large side branches were ligated with a similar suture or with a titanium clip. The veins were fixed in formaldehyde solution 4% for 48 h before further histological processing. After the veins were harvested, the animals in the acute experiment were killed directly with a lethal overdose of potassium.

In goats randomised to the follow-up experiments, the puncture site was closed with a Prolene 6-0 suture (Johnson & Johnson). The skin was closed with Monocryl 3-0 (Johnson & Johnson). After monitored recovery, the animals were placed in group housing for 6 weeks. All follow-up animals were administered Augmentin (10 mg/kg i.v.; GlaxoSmithKline, London, UK) before treatment and Depomycin (1 mL/kg i.m.; Intervet, Boxmeer, the Netherlands) at the end of the procedure. No anticoagulants or platelet aggregation inhibitors were administered.

At 6 weeks of follow-up, general anaesthesia was initiated similar to the first procedure. The hind legs were studied for ecchymosis, wound infection, and discoloration. After inspection, the treated veins were explanted, as described above, studied macroscopically, and stored in 4% formalin. Thereafter, the animals were killed with intravenous potassium.

Experimental outcomes

The acute group was designed to assess the appearance and severity of the damage inflicted by the treatment. Macroscopically, the vein was inspected for perforations and surrounding hematoma. Microscopically, the degree of intimal damage and injury to other layers of the vein wall was evaluated. The vein wall thickness was measured to quantify vasoconstriction.

In the 6 week follow-up group, the veins were macroscopically and microscopically studied to assess venous occlusion (anatomical success). Microscopically, the veins were further analysed to describe the histology and components of the occluded segments.

Histological analysis

The treated LSVs were fixed in formalin 4%. All veins were segmented into 5 mm pieces every 2 cm starting 1 cm from the proximal end (1 cm, 3 cm, 5 cm, etc.) and processed.
into standard paraffin blocks. Slides were made of 4 μm thick sections and stained with hematoxylin and eosin for general observations and with Elastin van Gieson for microscopic evaluation and assessment of fibrosis. α-Smooth muscle actin (α-SMA) immunostains were used to assess vein medial damage, and quantitatively scored with the use of cellSens (Olympus Lifesciences, Tokyo, Japan) in all sections.

In the acute experiments, the intimal layer and the entire vein wall were assessed for damage. To visualise the endothelial cells, von Willebrand factor and ERG (ETS related gene) immunostains were performed. The percentage of the circumference with injured or absent endothelium was measured and categorised as mild (<10% damage), moderate (20–50%), and severe (>50%). The section of each vein with the highest degree of injury was scored, in which the circumference of endothelium was measured and divided by the total circumference of the lumen of the vein. To score the injury, this percentage was deducted from 100%. To measure possible venous constriction, a ratio between diameter and vein wall thickness was calculated. The mean of the vein wall thickness measured on each quadrant of the vein was divided by the radius of the vein. Total occlusion or remaining lumen area and area of intimal hyperplasia and the aspect of the vein wall were assessed at 6 weeks. Additional α-SMA immunostain and Perl’s iron stain were performed to further study the components of intimal lesions in selected slides.

**Statistical analysis**

Final analysis was performed on the nine acute goats (18 veins) and nine goats with 6 weeks of follow-up (18 veins) separately. Mean ± SD data are presented. Medians (range) are used to present numeric data. Chi-square tests to compare categorical variables and Kruskal–Wallis tests were used to compare continuous variables. SPSS 21.0 (IBM, Armonk, NY, USA) was used for all analyses.

**RESULTS**

**Procedure**

The goats weighed, on average, 59 ± 7 kg. The average diameter of the LSV at the level of introduction was 4.0 ± 0.5 mm. The median skin to skin treatment duration was 14 min (range 9–22 min). Cannulating and treating the LSV according to plan was feasible in all but one hind leg (technical success rate 97%). The unsuccessful procedure was in a vein with the smallest diameter of all (2 mm) and was planned for mechanoablation without sclerosant in an acute experiment (group 3). After reviewing this case, no replacement for the vein was deemed necessary. In all remaining acute experiments, harvesting the vein was feasible within the designated time of 30–45 min after treatment. No other peri-operative problems or complications were noted. No complications were observed during follow-up, especially no signs of deep venous thrombosis or wound infection.

A pilot study of two animals was first conducted to evaluate the feasibility of the study protocol. This pilot study revealed no technical difficulties and showed that MOCA treatment could be executed as planned. Because the initial protocol was feasible and no changes were made to surgical procedures, the samples of these two animals were included in the analysis of group 1.

**Macroscopic evaluation**

All treated veins in the acute experiments were surgically exposed. No hematoma or perforation of the vein wall was observed (Fig. 3A). All veins were compressible and filled with blood. No thrombus or occlusion was observed. The diameter varied between and within the veins (range 1.5–9 mm).

The wounds in all follow-up animals healed without signs of infection or local hematoma. Hyperpigmentation of the overlying skin was seen in three hind legs (one after MOCA and two after liquid sclerotherapy). The most distinct cases were present in a leg treated with liquid sclerotherapy (Fig. 3B). No ecchymosis over the treated trajectory was noted.

All veins treated with liquid sclerotherapy or mechanoablation (groups 5 and 6) were patent and compressible over the entire length. No macroscopic signs of perforation or total vein destruction were present. Of six veins treated with MOCA (group 4), four were macroscopically occluded, and fibrotic, though non-compressible, and no efflux of blood was seen (Fig. 3C). Some of the smaller side branches of this part of the LSV were macroscopically occluded over
the first millimeters. A major side branch was present in all animals a few centimeters above the puncture zone. Distal to this major side branch, all LSVs were patent. The remaining two veins treated with MOCA (group 4) showed no macroscopic changes. The veins were patent and compressible over their entire length.

**Histological evaluation**

In the acute experiments, no histological evidence of damage beyond the endothelial layer of the vessel wall was found in any of the treatment groups. In 82% (nine of 11) of the veins treated with MOCA and mechanical action (groups 1 and 3), at least one segment showed severe endothelial injury versus 17% (one of six) in the veins treated with sclerotherapy (group 2). The endothelial damage differed greatly within the veins: segments with (nearly) total endothelial abrasion and segments with totally intact endothelium were seen within single veins (Fig. 4). Veins with intact venous valves were seen in all acute groups.

Quantitative measurement of α-SMA staining in the media showed no significant differences between the treatment groups (p = .654). In the groups treated with mechanical ablation or MOCA, the vein wall thickness and the vein wall to vein radius ratio was increased compared with Aethoxysklerol, indicating venous constriction. The absolute measurements are reported in Table 1.

In the follow-up experiments, occlusion was only seen in veins treated with MOCA, of which total occlusion was observed in four of six veins (Table 2). The veins with total occlusion showed a cellular fibrotic lesion with α-SMA-positive myofibroblasts and microvessels. The observed fibrosis extended in the medial and adventitial layers but showed no signs of earlier perforation of the vein wall. Abundant iron pigment was observed within the lesions, suggesting that these have evolved from organised thrombus (Fig. 5). One segment in one of these veins showed a 50% stenosis, showing intimal hyperplasia consisting of loose connective tissue with myofibroblasts, a few deposits of iron pigment, and the presence of neovascularisation. The medial layer of this section showed no fibrotic alterations. Elastica van Gieson staining showed an increase of fibrosis in the media/ adventitia of totally occluded veins, which was not present in the non-occluded veins. The two remaining MOCA treated veins were open, with limited intimal hyperplasia of no more than 20% of the luminal area. Quantitative measurement showed a significant decrease in α-SMA positive area in the media of MOCA treated veins compared with mechanical or Aethoxysklerol-treated veins (p = .001; Fig. 6). The open segments within the MOCA group showed higher percentages of α-SMA areas than occluded segments in the MOCA group (p < .001).

As also reported in the macroscopic evaluation, only the segments proximal to the large side branch were occluded. In line with the macroscopic data, no occlusions were seen in groups 5 and 6. In one of six veins treated with

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**Figure 4.** Histology of acute experiment: (A, B) mechanical treatment. (A) Venous constriction with reduction of the lumen (Elastica van Gieson stain). (B) Endothelial damage with loss of endothelial cells. Endothelial cells are stained red and indicated with arrow (ETS related gene immunostain). (C, D) Aethoxysklerol treatment. (C) No venous constriction with preservation of the lumen (Elastica van Gieson stain). (D) No loss of endothelial cells (ERG immunostain).
Aethoxysklerol, limited intimal thickening was noted of up to 20% of the vein lumen. The remaining five veins were fully open. The occlusion rate in veins treated with MOCA was higher than in the other two treatment groups ($p = .036$). No histological signs of damage or fibrosis to other layers of the vein walls in the non-occluded veins, including the two non-occluded veins treated with MOCA, was observed. The ClariVein OC got stuck in two veins several times during treatment, and debris was tangled around the tip of the device. One vein was in group 4 (MOCA) and was totally occluded at 6 weeks follow-up, the other vein was in group 6 (mechanical only) and was fully patent at 6 weeks, with no signs of vein wall damage on histological examination.

**DISCUSSION**

The present study shows the effects of MOCA and its separate components in an acute and follow-up animal experiment. The experiments revealed that the mechanical action inflicts damage to the endothelium without signs of injury to the other layers of the vein wall. A significant narrowing of the veins was observed after MOCA or mechanical ablation compared with sclerotherapy. After 6 weeks follow-up, the results of MOCA were superior to mechanical ablation only and sclerotherapy: occlusion in four of six veins treated with MOCA was observed versus no occlusions in the veins treated with mechanical action or Aethoxysklerol separately.

The results of this study confirm the hypothesis that the ClariVein leads to venous occlusion by inflicting mechanical injury to the endothelial barrier, permitting the liquid sclerosant to induce an increased chemical reaction to the deeper layers of the vein wall. In the acute experiment severe endothelial injury was seen in 82% (nine of 11) of veins treated with MOCA or solely mechanical action, significantly more than after sclerotherapy. In line with results of an earlier small ex vivo study, there was a large spread in degree of injury within a single vein. This is an interesting finding to discuss, because this could be the cause of partial recanalisation, which is relatively frequently seen in humans and is usually without clinical consequences. Increasing endothelium injury might be the key to further optimising treatment results. Decreasing the speed of pull-back of the ClariVein might lead to more injury by prolonged exposure to the mechanical action and, thus, potentially induce more vasoconstriction. Evaluation of techniques to increase endothelial damage and its effect on anatomical success could be relevant subjects for future studies.

Another important finding of this study is the observation that veins were significantly constricted after MOCA and solely mechanical treatment than after sclerotherapy alone. This might be induced by direct contact of the “stirring wire” with the vessel wall or by shear stress of whirling intraluminal fluid. This narrowing might be a contributor to the overall effect in MOCA by further increasing the effect

### Table 1. Histologic aspects of veins in the acute experiments.

<table>
<thead>
<tr>
<th>Aspect lumen</th>
<th>MOCA ($n = 6$)</th>
<th>Mechanical ($n = 5$)</th>
<th>Sclerotherapy ($n = 6$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor/moderate</td>
<td>2 (33)</td>
<td>0 (0)</td>
<td>5 (83)</td>
</tr>
<tr>
<td>Severe (&gt;50%)</td>
<td>4 (67)</td>
<td>5 (100)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Wall thickness (µm)</td>
<td>376 (127–426)</td>
<td>277 (206–383)</td>
<td>170 (85–379)</td>
</tr>
<tr>
<td>Vein diameter (mm)</td>
<td>2.5 (1.8–4.9)</td>
<td>2.9 (1.4–4.0)</td>
<td>4.0 (1.8–7.7)</td>
</tr>
<tr>
<td>Wall to radius ratio</td>
<td>0.31 (0.05–0.44)</td>
<td>0.25 (0.10–0.40)</td>
<td>0.10 (0.03–0.42)</td>
</tr>
<tr>
<td>$\alpha$-SMA $^b$</td>
<td>80 (67–88)</td>
<td>80 (51–92)</td>
<td>79 (62–87)</td>
</tr>
</tbody>
</table>

Note. Categorical data are presented as n (%), and continuous data are reported as mean ± SD or median (range). MOCA = mechanochemical endovenous ablation; $\alpha$-SMA = smooth muscle actin.

$^a$ Limited intimal hyperplasia up to 20% may be present.

$^b$ Percentage of total media area (range).

### Table 2. Histologic aspects of veins in the follow-up experiments.

<table>
<thead>
<tr>
<th>Aspect lumen</th>
<th>MOCA ($n = 6$)</th>
<th>Mechanical ($n = 6$)</th>
<th>Aethoxysklerol 2% ($n = 6$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up 6 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occlusion</td>
<td>4 (67)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Open $^a$</td>
<td>2 (33)</td>
<td>6 (100)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Vessel diameter (mm)</td>
<td>3.2 (1.7–4.8)</td>
<td>4.0 (2.0–5.5)</td>
<td>4.7 (3.3–6.0)</td>
</tr>
<tr>
<td>Lumen diameter (mm)</td>
<td>1.1 (0–4.4)</td>
<td>3.6 (1.7–5.1)</td>
<td>4.5 (1.7–5.8)</td>
</tr>
<tr>
<td>Lumen area (mm²)</td>
<td>1.2 (0–11.9)</td>
<td>6.7 (2.3–15.2)</td>
<td>14.9 (0.8–18.6)</td>
</tr>
<tr>
<td>Intimal hyperplasia</td>
<td>5 (83)</td>
<td>0 (0)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Intimal hyperplasia area (mm²)</td>
<td>1.1 (0.0–5.9)</td>
<td>0.0 (0.0–0.1)</td>
<td>0.01 (0.0–0.7)</td>
</tr>
<tr>
<td>$\alpha$-SMA $^b$</td>
<td>64 (29–88)</td>
<td>80 (66–94)</td>
<td>80 (67–90)</td>
</tr>
</tbody>
</table>

Note. Categorical data are presented as n (%) and continuous variables as median (range). MOCA = mechanochemical endovenous ablation; $\alpha$-SMA = smooth muscle actin.

$^a$ Limited intimal hyperplasia up to 20% may be present.

$^b$ Percentage of total media area (range).
Figure 5. Histology of total occlusion after mechanochemical endovenous ablation: (A, B) Hematoxylin and eosin stain showing cellular fibrotic lesion, ingrowth of microvessels and presence of iron pigment. (B, C) Elastica van Gieson stain confirming the presence of connective tissue in the lesion (purple). (D, E) Perl’s iron stain shows abundant presence of iron pigment, suggesting an organised thrombus. (G, H) α-Smooth muscle actin stain (red) shows the smooth muscle cells in the media and the myofibroblasts in the occlusive lesion.
of sclerosant on the vein wall. Vasoconstriction will result in the sclerosant reaching a higher concentration in the vein as a result of a decreased amount of intraluminal blood and, possibly, stasis. Furthermore, vasoconstriction will theoretically limit the washout of liquid sclerosant and thereby lead to prolonged exposure. As recently published, prolonging the exposure to liquid sclerosant leads to increased chemically induced injury to the vein wall.14

In contrast to histological studies with endovenous laser ablation in which acute and total destruction of venous wall is seen,10 these results suggest that all occlusions seemed to originate from organised thrombus with fibrotic alterations to the surrounding media and adventitia. This might also give insight into the reason for recanalisation of initially MOCA occluded veins, especially when neovascularisation arises within these occlusive lesions. This phenomenon is seen in almost all clinical cohort studies published to date.

Compared with the anatomical success of 88.2–96.7% occlusion rates in human cohort studies,11–13,15–17 the occlusion rate in this animal study is less than expected. This leads to discussion of whether the current model is adequate to evaluate the working mechanism of MOCA. Even when the potential factors of influence on the anatomical success rate are evaluated the reason remains unclear. The procedure was performed exactly as the standard procedure in clinical practice. To avoid bias due to experience, the procedures were performed by a dedicated team with vast experience in MOCA. Furthermore, the concentration and dosage of Aethoxysklerol was determined according to the human dosing table.

Furthermore, the goat as the model to induce and study venous damage may be questioned. The main reason this animal model was chosen is that previous experiments in endothermal ablation and MOCA used goats,7,10 and the size of the LSV was another major reason: with an average diameter of 4 ± 0.5 mm, the veins are within the lower range of varicose veins included in human studies.11 In contrast to the current study, the occlusion rate in the study form Tal et al. was 100%.7 There are two important differences compared with that study: (i) sodium tetradecyl sulfate 1.5% was used instead of Aethoxysklerol (polidocanol) 2%; and (ii) compression stockings were applied. Although sodium tetradecyl sulfate (trademarks: Sotradecol or Fibrovein) has been shown to be a more potent sclerosant than polidocanol in an in vitro experiment,18 no differences in anatomical success were observed in humans.

Similar to the present study, Tal et al. described no occlusion following treatment with only mechanical ablation or sclerotherapy.7 Finally, it is important to appreciate that the results from the discussed study described only selected data of a larger experiment (11 of 18 goats).7

Only one aspect differs between this study or the clinical setting and the present experiments: the MOCA procedure is directly followed by the use of compression stockings for at least the first 24 h.11–13 For practical reasons and animal welfare, it was not possible to apply stockings during follow-up. Compression therapy might be a beneficial addition measure in MOCA.

Finally, even though this study gives an important insight into the tissue reaction to MOCA and its separate components, significant data could not be retrieved on endpoints to draw indisputable conclusions owing to the small sample size.

CONCLUSIONS

MOCA is associated with an increased occlusion rate compared with its separated components of mechanical ablation or sclerotherapy. However, MOCA in the animal model resulted in occlusion in only two thirds of the animals. The occlusion consists of cellular fibrotic material likely to be evolved from organised thrombus with fibrotic alterations to the surrounding media and adventitia. This study underlines the hypothesis that the additive use of MOCA increases the effectiveness of sclerosants alone by inducing endothelial damage and probably vasoconstriction.
CONFLICT OF INTEREST

D.B., M.M.J.P.R., and J.P.P.M.V. have been speakers for Vascular Insights LLC.

FUNDING

These studies were funded by Varysta, an independent foundation for vascular research. Varysta received an unrestricted research grant from Vascular Insights LLC.

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