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Endovenous Laser Ablation: The Role of Intraluminal Blood

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Abstract *Objective:* In this histological study, the role of the intraluminal blood during endovenous laser ablation was assessed.

Methods: In 12 goats, 24 lateral saphenous veins were treated with a 1500-nm diode laser. Four goats were treated in an anti-Trendelenburg position (group 1). The next four goats were treated in a Trendelenburg position (group 2) and the remaining four goats in the Trendelenburg position with additional injection of tumescent liquid (group 3). Postoperatively, the veins were removed after 1 week and sent for histological examination. We measured the number of perforations. Vein wall necrosis and the perivenous tissue destruction were quantified using a graded scale.

Results: The 'calculated total vein wall destruction' was significantly higher in the third group (81.83%), as compared with groups one (61.25%) ($p < 0.001$) and two (65.92%) ($p < 0.001$). All three groups showed a significant difference in the perivenous tissue destruction scale ($p < 0.001$) with the lowest score occurring in the third group. Vein wall perforations were significantly more frequent in groups one and two as compared with the third group (T -test respectively $p < 0.001$, $p = 0.02$).

Conclusion: A higher intraluminal blood volume results in reduced total vein wall destruction. Injection of tumescent liquid prevents the perivenous tissue destruction and minimises the number of perforations.

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Endovenous laser ablation (EVLA) is a very popular minimally invasive alternative to surgical vein stripping in the treatment of saphenous vein reflux. After catheterising the saphenous vein and introducing a laser fibre into the lumen, light energy is delivered within the vein. This energy is absorbed by the intraluminal blood, water or the vein wall. The aim of this technique is to irreversibly obliterate the treated vein. Long-term occlusion rates in saphenous veins in between 87% and 100% have been reported.^{1–4} These endovenous lasers are commonly classified into two groups: one in which there is a higher absorption coefficient for oxyhaemoglobin^{5–8} (810–940–980-nm lasers) and a second one in which the energy is preferentially absorbed by water^{9–12} (1320–1470–1500-nm diode laser). In all used wavelengths, the optical extinction is very similar for blood and for water.^{13,14} Only the energy is 5–7 times more selective absorbed at the higher wavelengths.¹² So conclusions about the role of the intraluminal blood using a 1500 nm diode laser also account for the use of lower-wavelengths lasers.

Many studies have been based on the assumption that during EVLA, the vein is filled with blood. In the light of clinical experience, the presence of blood inside the vein has a number of consequences.^{15–17}

- Blood around the fibre tip reduces the transmission of light to the biological target of EVLA, the venous wall.¹⁸ Since thermal damage to the inner vein wall (tunica intima) is required to achieve the tissue alterations necessary for permanent vein occlusion, the presence of blood greatly impairs the effect of the laser on the vessel wall. If the laser light energy is entirely absorbed by the blood, the initial success rate will be mainly due to a thrombotic effect; but thrombus dissolution will then lead to recanalisation, as clearly demonstrated by Proebstle et al.¹⁹
- The presence of blood can generate steam bubbles. The formation of these steam bubbles has been confirmed by Proebstle et al. who have observed that they were generated in haemolytic blood by 810-, 940- and 980-nm diode lasers, whereas no bubbles were produced in normal saline or plasma.²⁰ This mechanism is now, however, considered to be of secondary importance to the efficacy of EVLA.^{21,22}
- Last, but not least, the presence of blood induces carbonisation at the fibre tip and often melting of the glass fibre tip. This phenomenon implies fibre tip temperatures in excess of 1200 °C. This melting point of the glass fibre tip has been observed by Fan and Rox-Anderson.²² The partial destruction of the tip compromises beam homogeneity leading to an unpredictable pattern of energy distribution inside the vein. Furthermore, the carbon layer that rapidly forms at the tip absorbs most of the light energy and converts it into heat, radically altering the laser/tissue interaction process.

Variability in the amount of blood within the vein leads to inconsistent results. In our experience, the vein lumen is emptied of its blood by using leg elevation (Trendelenburg positioning) and perisaphenous subcutaneous tumescent saline solution infiltration. This solution containing local anaesthetic serves three purposes. First, the vein itself and

the surrounding tissues are anaesthetised. Second, the fluid around the vein helps to protect the surrounding tissues from any collateral injury from the heat of the laser. Third, the fluid exerts compression around the vein and induces spasm. This helps to empty the vein of its contents.

Until now, although it is assumed that the intraluminal blood can alter the efficacy of EVLA, no histological studies can be identified concerning the role of blood during *in vivo* EVLA. The objective of this histological trial is to assess the consequences of the presence of the intraluminal blood.

Materials and Methods

Materials and techniques

Our investigation was approved by the ethics committee for animal experiments at the Catholic University of Leuven, Belgium. Goat saphenous veins were used since the lateral saphenous vein has a mean diameter of 4–6 mm in the supine position, which is comparable to that of human veins.

Using 12 goats, 24 lateral saphenous veins were treated with EVLA. The goats were treated under general anaesthesia. Under ultrasound control (Mindray M5 ultrasound, Shenzhen, China), access was achieved by puncture of the distal part of the lateral saphenous vein. A sheath was introduced and a 600- μm tulip fibre (Tobrix, Waalre, the Netherlands) was placed near the saphenofemoral junction. This tulip fibre consists of a hollow tube, fixed to the laser fibre. This tube has tulip-shaped self-expandable blades at its distal end and is made of stainless steel. When the blades expand, they push away the vein wall and thus centre the fibre tip intraluminal.²³ The reason for using this tulip fibre was to avoid direct contact between the fibre tip and the vein wall (see discussion). We divided the sample into three distinct groups with different amounts of intravenous blood. Four goats (eight veins) were treated in an anti-Trendelenburg position (group one), which was in order to maximise the amount of intraluminal blood. The next four goats were treated in a Trendelenburg position (group two) and the remnant four goats in Trendelenburg position with additional injection of tumescent liquid around the target vein (group three). This tumescent liquid is physiological saline (at 36 °C). Injection was performed under ultrasound control and the target vein was surrounded by the liquid. On average, 90 ml was injected around the veins, equivalent to 5.8 ml cm⁻¹. Veins were treated with a 1500-nm diode laser (Inter-Medic, Barcelona, Spain), using a continuous pullback protocol. Power was set to 5 W and pullback speed was adjusted to deliver a linear endovenous energy density (LEED)²⁴ between 45 and 50 J cm⁻¹.

Postoperatively, all the veins were completely surgically removed, including perivenous tissue, 1 week after treatment and sent for histological examination. About 14 sections of each vein were taken at random. The pathologists measured both vein wall necrosis and the perivenous tissue destruction, as described below. All the scoring has been done by one pathologist, who was blind to the study group. The other pathologist assisted, as a second opinion, in scoring in a limited number of sections.

Measurement of vein wall necrosis

Each vein wall is divided into three layers: the intima, the media and the adventitia. For each layer, the circumferential necrosis was measured and expressed as a percentage of the total circumference (Fig. 1). For each section, these three measured percentages were added together and divided by three. The obtained result is proposed as the 'total vein wall necrosis score' and varies from 0 to 100.

Perivenous tissue destruction scale (PVTD) (Fig. 2)

The lateral saphenous vein in a goat is surrounded by a fascia. Perivenous tissue destruction was measured at three different points at the edge of the vein, located 120° apart. The distance between the vein wall and the surrounding fascia was divided into three equal layers. The extent of necrosis was graded according to the following scale: 0 = no necrosis, 1 = necrosis. If any extrafascial necrosis was seen, an additional score of 2 was added. Extra fascial necrosis correlates with more significant perivenous tissue destruction that justifies the additional score. Therefore, in one position the maximal score is 5.

Consequently, if the necrosis was seen in all three positions, the maximum necrosis score would be equal to 15.

Measurements of perivenous temperature

The temperature in the perivenous tissue was measured using thermocouples (thermocouple type K,TJC100-CASS-M050E-150 Omega Engineering Limited, Manchester, UK). Four needles were inserted around the target vein, this from distal to proximal. The needle tip of the thermocouples was located in the immediate proximity of the vein wall. Their position was checked by perioperative ultrasound. The thermocouples were connected to a 10-channel 22-bit DAS system (Omega Engineering, Manchester, UK) and the temperatures curves were controlled in real time using OMB-DAQ-SW-PLUS software (Omega Engineering) on a Laptop (MacBook Pro, Apple Inc, California, USA). The temperature was measured during fibre withdrawal to determine the maximum temperature for the three groups.

Statistical evaluation

Statistical analysis was performed using SPSS 16.0 (Statistical Package for the Social Sciences). We used the Spearman correlation test for correlation analysis. Inter-group variances for unpaired continuous and ordinal data were evaluated non-parametrically using the Mann–Whitney *U* test for goat clinical data analysis and the Student's *T*-test for histological score analysis. A significance α -level of 0.05 was used.

Results

Goats' clinical data

Twelve goats were treated according to the protocol described above. The mean diameter of the veins was 0.45 cm (SD: 0.07) measured in the supine position. The treated vein segments had on average a length of 15.6 cm (SD: 3.8) and there was no significant difference between the groups. The used energy (LEED and fluence) was not different in the three groups (Table 1). After catheterisation and tumescent injection in the third group, the diameter of the veins was reduced due to spasm. Before treatment (after catheterisation, and in case injection of the tumescence liquid) the average measured diameter of the veins was for groups 1, 2 and 3, respectively: 0.41 cm (SD: 0.13), 0.37 cm (SD: 0.11) and 0.20 cm (SD: 0.09). We found a significantly higher diameter reduction in the third group as compared to groups one and two (Mann–Whitney *U*, $p = 0.001$).

Temperature measurements

The observed temperature increase around the treated vein during fibre pullback was very variable. Some thermocouples showed no temperature increase, while others showed a steep climb to a maximum varying between 36 and 102 °C. We could not find any significant difference between the groups.

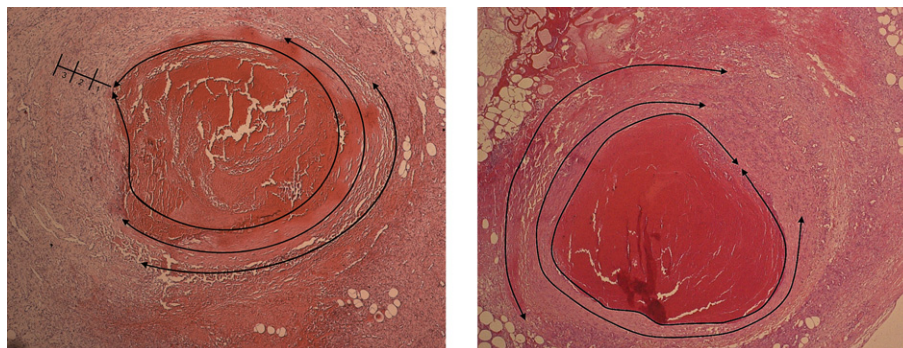


Figure 1 Measurement of the vein wall destruction: from the 3 layers the necrose is measured and expressed as a percentage of the total circumference.

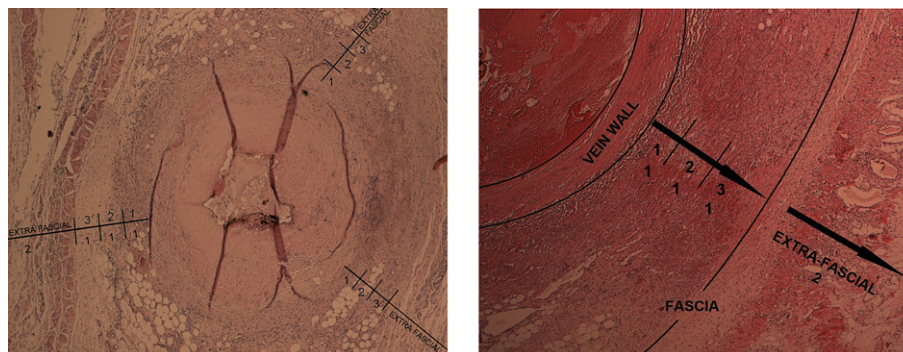


Figure 2 Perivenous Tissue Destruction scale (PVTD): the perivenous destruction is measured at three points. The distance between the edge of the outer vein wall and the surrounding fascia is divided into three equal parts. An additional measurement of necrosis was done at the extrafascial tissue.

Histological results

All veins were harvested 1 week after treatment and sent for histological examination. A total of 329 sections of the veins ($n = 24$) were made.

Several 'perforations' (Fig. 3) of the treated veins were noted. These were significantly more frequent in groups one and two compared to the third group (T -test respectively $p < 0.001$, $p = 0.02$). The difference between groups one and two was marginally significant ($p = 0.04$) (Table 2).

In the vast majority of all sections, a homogeneous endothelial destruction was noted. In group one, this 'intimal destruction' encompassed an average of 85.77% of the circumference. In groups 2 and 3, the percentages were 87.73% and 97.96% of the circumference, respectively. Again, we found a statistical significant difference between the third group and the other groups ($p < 0.001$). Major parts of the vein wall were destroyed and the muscle cells were necrotic. Some sections showed vacuolisation of the muscular layer (Fig. 4). When we look at the 'calculated total vein wall destruction' a significantly higher percentage of vein wall destruction in the third group (81.83%) was noted, as compared with groups 1 (61.25%) ($p < 0.001$) and 2 (65.92%) ($p < 0.001$).

We could not find any significant difference in total vein wall destruction between groups 1 and 2 ($p = 0.23$).

Around the treated veins, we observed a necro-inflammatory process of new small vessels with migration of fibroblasts and phagocytes, as previously described.^{18,23}

Some perivenous structures also showed necrosis and were infiltrated by this newly formed inflammatory tissue. Interestingly, this inflammatory tissue preferentially infiltrates the partly destroyed tissues. Even perivenous co-axial veins or nerves can be damaged (Figs. 5 and 6). This perivenous tissue destruction was found to be significantly greater in group two. All three groups show a significant difference in the PVT scale ($p < 0.001$) with a lowest score in the third group (PVT = 5.83).

Discussion

EVLA of the incompetent saphenous vein is safe and effective. Nevertheless, discussions are still continuing about the way of acting and especially about the role of the intraluminal blood. Proebstle stated that the intraluminal blood has a key role in energy absorption, resulting in the formation of steam bubbles, which can heat up the vein wall.^{8,20} Clinical studies have shown, however, that emptying the vein of its contents results in a significantly higher occlusion rate.^{15,16} Using a bare fibre allows a direct contact between the fibre tip and the vein wall resulting in ulcerations and perforations, due to the convection of heat in the vein wall.^{18,22,23}

This direct contact results in an uneven vein wall destruction^{18,24} and more perivenous tissue damage.²³ To avoid these ulcerations and direct heat convection in the vein wall, we used the tulip fibre in this trial.

Table 1 Goats clinical data.

	Position	Mean diameter	MDAC	Length	RIBV/cm length	LEED	Fluence (after catheterisation)
Group 1 ($n = 8$)	Anti-Trendelenburg	0.47 cm (SD = 0.09)	0.41 cm (SD = 0.13)	15 cm (SD = 3.1)	0.12 cm ³ (SD = 0.09)	44.67 J/cm (SD = 3.5)	37.11 J/cm ² (SD = 11.6)
Group 2 ($n = 8$)	Trendelenburg	0.44 cm (SD = 0.08)	0.37 cm (SD = 0.11)	16.3 cm (SD = 3.0)	0.07 cm ³ (SD = 0.08)	44.19 J/cm (SD = 4.8)	38.86 J/cm ² (SD = 10.1)
Group 3 ($n = 8$)	Trendelenburg + tumesence	0.44 cm (SD = 0.04)	0.20 cm (SD = 0.09)	15.5 cm (SD = 3.8)	0.00 cm ³ (SD = 0.02)	45.97 J/cm (SD = 4.9)	72.25 J/cm ² (SD = 7.7)

MDAC: mean diameter of the veins after catheterisation, positioning and liquid injection (group 3) RIBV: remnant intraluminal blood volume: volume of blood calculated using MDAC, length and withdrawing the catheter volume.

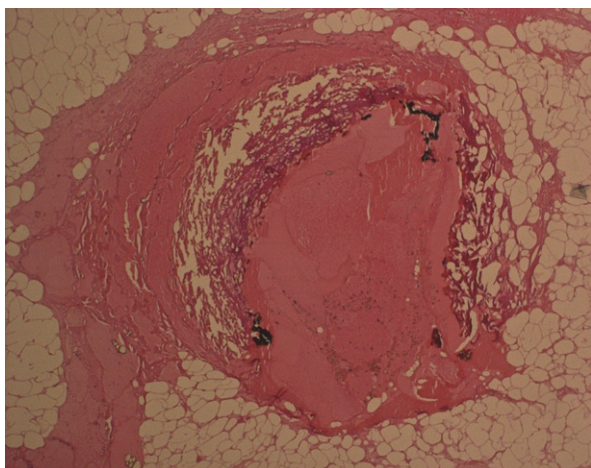


Figure 3 Perforation of the treated vein, complete transmural vein wall necrosis (vein 12, group 2).

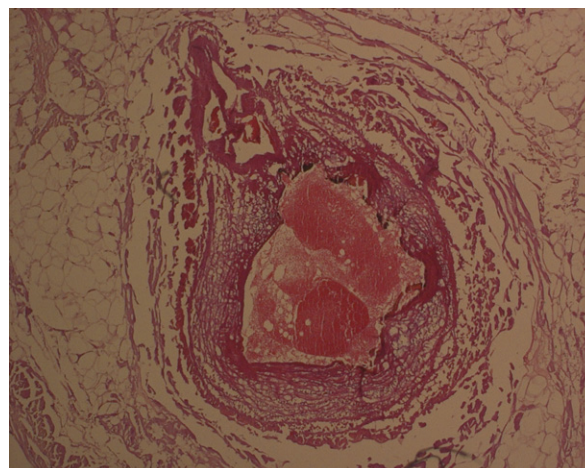


Figure 4 Vacuolisation of the muscular layer of the vein wall (vein 13, group 2).

Nevertheless, we did find some perforations in the treated veins. Some of the perforations identified may have been due to the injection of tumescent fluid and the punctures used to position the thermocouples.

We did not find the common carbonised tracts, ulcerations and small perforations like we did in veins treated with a bare fibre (direct contact).^{18,23} Here, the morphology was different showing vacuolisation of the vein wall and in some cases a complete implosion of the vein (Fig. 7).

A probable explanation of the origin of perforations is the fact that the delivered energy in using the 1500-nm laser was too high for these goat veins. The optical extinction coefficient at this wavelength is 5–7 times higher for blood and for water as compared to the more commonly used 980-nm diode laser.¹² In terms of volume, the energy deposited per unit of volume is increased by a factor 43 (calculated by S. Mordon using a Monte-Carlo program).^{25,26} The same energy acts on a volume 43 times smaller and so exposes a risk of overdose and thus of perforation. We found many vacuoles in the muscular layer (Fig. 4), which is the result of intense thermal destruction. If this thermal destruction becomes too intense, a perforation or a bursting (Figs. 3 and

7) of the vein wall will be the result. The maximum temperatures measured near the vein wall reached in excess of 100 °C. These measurements, however, were rather exceptional. Conversely, the tumescent liquid around the vein acts as a ‘heat sink’ to protect the perivenous tissues. However, it also limits the temperature rise in the vein wall and possibly prevents perforations in that way. This may explain why we saw only a limited number of perforations (5/109 sections) in the third group.

The temperature measurement did not differ significantly between the three groups, but there was a wide range of measurements. This was due to the position of the thermocouples. The thermocouples used were very thin and very difficult to localise under ultrasound control. The thermocouples also had to be fixed to the skin because they moved easily. If the thermocouples are not always positioned at exactly the same distance from the vein wall, then comparison between the various groups is impossible.

We removed all the veins 1 week after treatment because the extent of vein wall destruction and perivenous tissue destruction cannot be assessed in veins harvested immediately after treatment, but only in samples removed later.^{18,23} Absorption is the primary event that allows

Table 2 Histological destruction data of the three groups. Group1: Anti-Trendelenburg position, Group 2: Trendelenburg position, Group 3: Trendelenburg position + Tumescence.

	Perforation	Intimal destruction	Media destruction	Adventitial destruction	Total vein wall destruction	PVDS:/15
Group 1 (n = 110)	n = 27	85.77% (SD = 26.32)	60.50% (SD = 33.68)	37.48% (SD = 38.36)	61.25% (SD = 29.25)	7.17 (SD = 2.63)
Group 2 (n = 110)	n = 15	87.73% (SD = 19.75)	64.23 (SD = 31.35)	45.83% (SD = 43.57)	65.92% (SD = 29.46)	8.70 (SD = 1.51)
Group 3 (n = 109)	n = 5	97.98% (SD = 8.25)	82.94% (SD = 25.65)	64.59% (SD = 39.89)	81.83% (SD = 22.24)	5.83 (SD = 1.15)
P-value (T-test)	p* = 0.04 p** < 0.001 p*** = 0.02	p* = 0.54 p** < 0.001 p*** < 0.001	p* = 0.40 p** < 0.001 p*** < 0.001	p* = 0.13 p** < 0.001 p*** < 0.001	p* = 0.23 p** < 0.001 p*** < 0.001	p* < 0.001 p** < 0.001 p*** < 0.001

PVDS: perivenous tissue destruction scale. p*: comparison between group 1 and group 2; p**: comparison between group 1 and group 3; p***: comparison between group 2 and group 3.

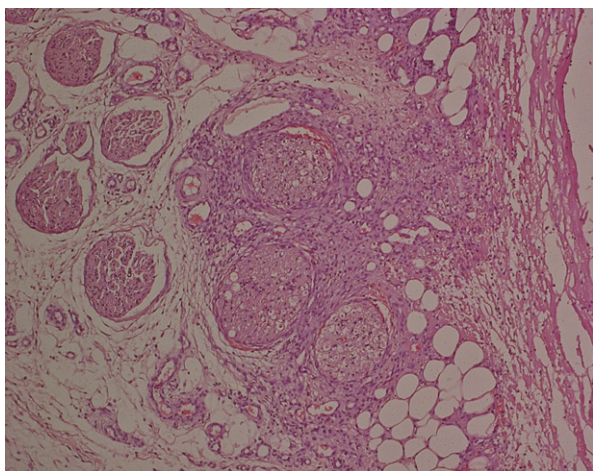


Figure 5 Perivenous nerve destruction with formation of the necro-inflammatory tissue infiltrating the nerve (vein 2; group 1).

a laser or other light source to cause a potentially therapeutic (or damaging) effect on a tissue. If the temperature rises above 42 °C, protein denaturation begins. Due to the transformation of light energy into thermal energy, the temperature in and around the treated veins rises.^{27,28} The vein wall cells are heated, their intracellular proteins denature and the cells become necrotic. This cannot be detected histologically until sufficient time has elapsed to allow inflammatory and tissue repair processes to begin. If the veins are removed several weeks after treatment, then the tissues are diffusely infiltrated by necro-inflammatory tissue and the exact border of necrotic tissue is often difficult to establish. The process of perivenous tissue destruction at that time may be in regression due to the healing process.²³

When we measured the destruction of the vein wall, we found a significantly higher intimal destruction in the third group. Since residual islands of endothelial cells can promote recanalisation,¹⁸ a higher percentage of circumferential endothelial destruction will minimise that risk. After a successful EVLA, the treated vein will show an

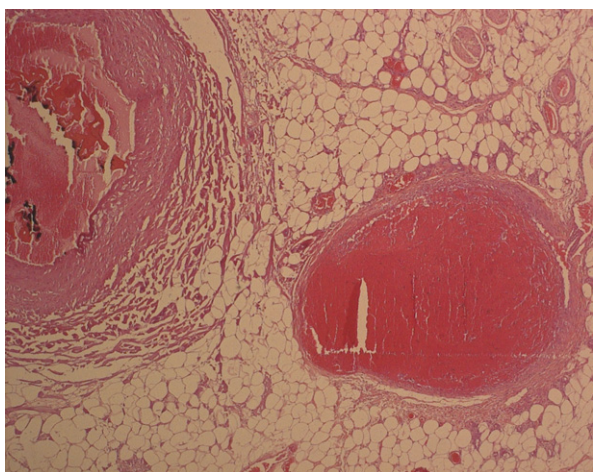


Figure 6 Partial vein wall destruction of a collateral vein at a distance of 2 mm from the target vein (vein 14, group 2).

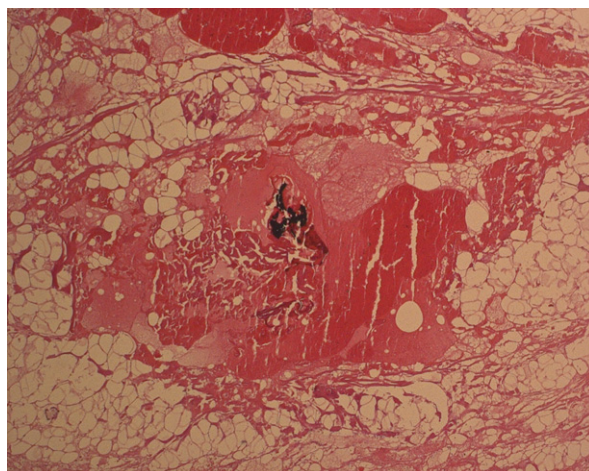


Figure 7 Complete disintegration of the vein wall after EVLA (vein 12, group 2).

important shrinkage and evolves into a fibrotic cord.¹² This fibrotic process^{18,23,29} is initiated by the formation of an inflammatory tissue surrounding the vein and an infiltration of fibroblasts and macrophages. This cell migration results in resolving the necrosis and transforms it into fibrotic tissue. A higher amount of media and adventitial vein wall destruction, as we noticed in the third group, will probably lead to a more important shrinkage of the treated veins.

We did find a slight but significant correlation between the remaining intraluminal blood volume (RIBV) (Table 2) and the total vein wall destruction (Pearson correlation r : 0.306, $p < 0.01$): the lower the RIBV, the higher the vein wall destruction. This can be explained by the layer of carbonised blood around the fibre tip, which hinders the even distribution of energy to the vein wall. A higher volume of intraluminal blood will absorb a proportionally high amount of delivered light energy, limiting the amount of energy that can reach the vein wall. This also accounts for the highest PVTD score being achieved by group two, compared to group one. More energy reaches and passes the vein wall, leading to perivenous tissue destruction. This perivenous tissue destruction could clearly be minimised by injecting the tumescent liquid around the target vein. It acts as a heat sink for the energy delivered intraluminally, allowing a higher 'calculated total vein wall destruction', preventing vein wall perforations and minimising the perivenous tissue destruction. The injection of tumescent liquid had a significantly higher influence on the vein diameter, compared to the Trendelenburg position alone (Mann–Whitney U ; $p = 0.001$). This resulted in a significantly higher fluence (after catheterisation and tumescent injection) and a higher 'calculated total vein wall destruction' (T -test; $p < 0.001$). The injection of tumescence minimised the perivenous tissue destruction (T -test: $p < 0.001$) and prevented most of the perforations ($p = 0.02$).

The lateral saphenous vein in goats has been used as a venous model in the previous work in this field.^{18,23,30} These are not varicose veins and the thickness of the vein wall is therefore somewhat lower than the thickness of human varicose veins. Whilst this is a useful model, it does not replicate human varicose saphenous veins.

The histological scoring in this trial was carried out by independent pathologists. The results obtained are sometimes approximate, because the measured destruction was sometimes unevenly distributed and sometimes the borders were difficult to establish.

Conclusion

The amount of intraluminal blood during EVLA should be minimised as much as possible. A higher intraluminal blood volume results in reduced total vein wall destruction. The injection of tumescent liquid lowers the amount of intraluminal blood, resulting in an increased total vein wall destruction. Its functions as a heat sink and, in this way, prevents perivenous tissue destruction and vein wall perforations.

Acknowledgements

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Conflict of Interest

There is no conflict of interest.

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