

ARE NON-THERMAL, NON-TUMESCENT TECHNIQUES MORE RECOMMENDED? ENDOVENOUS TREATMENT OF SAPHENOUS VEINS REFLUX – METHODS AND RESULTS OVERVIEW AND DISCUSSION

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ABSTRACT

Chronic venous disease is one of the biggest health problems of today's world. The consequences of the progression of venous disorders can lead to severe acute complications like superficial venous thrombosis, deep vein thrombosis, and pulmonary embolism, as well as chronic venous ulcers. The costs of the treatment of these conditions are still growing.

The development of minimally invasive techniques has led to huge progress in the treatment of chronic venous disease. There are many modalities in the phlebological armamentarium, which can be chosen to eliminate axial reflux that is responsible for the progression of disease in the majority of cases. Various groups of techniques can be used: thermal and tumescent procedures, non-thermal tumescent options, or non-thermal non-tumescent treatment. In recent years special interest has been directed towards non-thermal, non-tumescent modalities, following suggestions that these procedures would create the same effects as thermal-tumescent ones, but are less invasive and give the patient a better outcome and quality of life. The review of recently published studies did not confirm this theory in general; however, some superiority of these options is present. Thus, further investigations and trials on this issue are highly recommended. Currently there is not enough strong evidence to promote non-thermal, non-tumescent techniques over other endovenous modalities.

Key words: chronic venous disease, endovenous treatment, clinical outcome.

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INTRODUCTION

Chronic venous disease manifests in clinical symptoms like pain, feeling of heaviness of legs, cramps, and itching. These complaints are often related to incompetency of the axial veins of the superficial system like the great saphenous vein (GSV), small saphenous vein (SSV), or anterior accessory saphenous vein (AASV). Elimination of the reflux in these vessels is not only essential for the improvement of symptoms but also can prevent acute complications of venous disease like superficial venous thrombosis, deep vein thrombosis, and pulmonary embolism. Elimination of varicosities also diminishes the possibility of acute bleeding in the case of varicose vein injury.

Because conservative treatment with medical compression stockings and venoactive drugs is not recommended as the only possibility and is not popular, especially amongst young and active patients, interventional options have gained a lot of popularity in developed health care systems. In the last decade, the highest interest of patients and phlebologists has been directed to minimally invasive, endovenous techniques. The major advantages of them are the possibility to perform the pro-

cedure without general or spinal anaesthesia and immediate recovery and return to work time.

Endovenous modalities of the treatment of axial reflux in chronic venous disease (CVD) have been present in phlebological armamentarium for many years. They include thermal and tumescent (TT) procedures like laser ablation (EVLA), radiofrequency (RF), or steam (SVS), and non-thermal tumescent (NTT) options like long-catheter foam sclerotherapy or non-thermal non-tumescent (NTNT) treatment, which include mechano-chemical ablation (MOCA) and glue (CA).

Some of the thermal and tumescent procedures were introduced to phlebology over 15 years ago, like RF and laser (first results in 1999) [1, 2]. They have strong recommendations for use, and well-known complications and limitations. So now the debate is not about whether they should be used, or even what the indications are for them, but rather how to avoid the side effects connected with the treatment and eliminate even mild and insignificant complications. Since international guidelines clearly indicate that laser and radiofrequency are the methods of choice in axial reflux elimination [3, 4], these procedures have been

used as a comparator to surgical treatment [5-7]. Following the results of such trials, newer minimally invasive modalities of eliminating of venous reflux have been assessed and compared to EVLA or RF. Nevertheless, the latest of these are still being developed and changed, giving new perspectives for usage and revealing better results.

METHODS OVERVIEW

Endovenous thermal ablation (EVTA)

Endovenous laser ablation (EVLA) seems to be the most widespread modality of EVTA [8]. The first studies describing the results of EVLA reported the use of a haemoglobin targeting wavelength of 810 nm, subsequently followed by longer wavelengths – 940, 980, and 1064 nm. A trigger to look for other options was the conception of using water as a chromophore for laser light, and this thought led to development of generators producing higher wavelengths that target the vein wall instead of blood (1320, 1470, 1500, 1920, or 2100 nm). Although the results of studies comparing efficacy and safety of laser procedures performed using two different groups of generators are not fully consistent, there are some papers advocating application of water-absorbing waves to reduce pain and bruising [9-12].

Another important factor influencing the results of EVLA is fibre type. The possibility of vein wall injury and subsequent perforation caused by direct contact of the fibre with the endothelium has led to the development of many types of fibre tips, which are more commonly used now instead of a bare tip fibre: radial or bi-radial, spherical, covered, or tulip tipped catheters [13-15]. Due to the spherical or radial shape of the laser beam or by covering the energy-emitting part of the fibre, the delivered energy is diffused and energy density is lowered, so the possibility of perforation of the wall is essentially eliminated. Upon the results of recent papers, it seems that the EVLA procedures connecting longer wavelength generators with new fibres are safer and more efficient [16-18].

Radiofrequency ablation (RF) is a method similar to EVLA, which was introduced to the endovenous treatment in 1999 as the Closure Plus (VNUS) system being the first FDA-approved method of thermal ablation [19]. As the low pullback speed made the procedure duration too long, in 2007 it was replaced by the RF segmental system – Closure Fast with a 7-cm therapeutic distal tip. To treat shorter segments of veins, a 3-cm heating probe was introduced in 2012. The results of the RF treatment are similar to those using laser [20, 21]. The other conception using radiofrequency is bipolar thermotherapy utilising blood and vein wall as a conductor, which is heated (RFITT).

Steam ablation (SVS) is the most recently introduced method of EVTA. Currently there are two systems available – Steam Vein Sclerosis[®] and VBox System. The meth-

od allows truncal reflux treatment and can be used to ablate tributaries and malformations. Although there are very few publications on steam ablation, and the worldwide experience is limited, preliminary results are promising, showing non-inferiority to other thermal procedures [22-24].

Mechano-chemical ablation (MOCA)

Mechano-chemical ablation is one of NTNT methods of abolishing the reflux in saphenous veins. The first used MOCA device was ClariVein[®]. Apart from minimal local anaesthesia at the puncture site, the system does not require any additional analgesia. Although the results of MOCA procedures are promising and comparable to TT ones, it should be remembered that only one saphenous vein can be closed within 24 hours because of the dose limitation of the sclerosing agent [25].

Another MOCA modality is the Flebogriif[™] system, which utilises specific expendable hooks to scratch the intima prior to sclerosant injection. Scarification should result in better vein constriction and direct contact between the vessel wall and injected foam. Although only preliminary results have been published, they are promising [26].

Glue ablation (cyanoacrylate ablation – CA)

The most recent development of NTNT saphenous vein ablation is glue. Primarily cyanoacrylate glue (Medtronic VenaSeal[™]) was introduced and researched as a method compared to TT methods. Several studies revealed good results after up to three years of follow-up [27, 28]. Recently, other medical adhesives have also been introduced to abolish venous reflux, like Biolas VariClose[®] or Invamed VenaBlock[®] treatment systems. There are some technical details that differ between the systems, like glue viscosity (which is lower for VariClose[®]), the patterns of application (interrupted or continuous), the catheter type, or tip positioning at the saphenofemoral junction. The first results of VariClose[®] procedures are promising [29], but longer follow-up data are still lacking. In contrast to foam sclerotherapy or MOCA, there is no limitation of dosage while using CA, hence even four saphenous veins can be treated in one session. As opposed to the majority of other ablation methods, post-procedural compression is not essential after intervention.

RESULTS OF THE ENDOVENOUS ABLATION TECHNIQUES – TECHNICAL SUCCESS

Early results

Laser and radiofrequency methods have been widely described because they are the oldest and most pop-

ular modalities of abolishing the saphenous vein reflux. As for 2014, 67 and 47 studies were published showing the results of EVLA and RF, respectively [30]. In a group of trials performed after 2010, which is when modern modalities have been introduced, pooled for follow-up time up to six months, the rate of occlusion of saphenous veins range between 100% and 93.3% for laser and between 100% and 86.4% for radiofrequency. Also, novel techniques have been assessed. For SVS the early success rate varies from 65% to 95%, whereas in the most recently published reviews, the pooled anatomic success for MOCA and CA was 94.7% and 94.8% at six months, respectively [31]. These data indicate very good short-term results of all modalities of endovenous ablation. There is also a suggestion, revealed by recent publications, that NTNT methods are more effective compared to TT methods. This conclusion must be revised by further investigations, especially describing longer periods of follow-up and larger cohorts of patients.

Mid-term results

For TT methods many studies with mid-term follow-up have proven the durability of EVTA. The rate of closure of saphenous veins after such procedures are still higher than 90% in the majority of trials. The Varico-2 study showed 96.2 % and 96.6% of closed trunks after 60 months for RF and EVLA, respectively [32].

It seems undebatable that SVS and NTNT methods are becoming more interesting, so some studies have been conducted to assess their efficacy and to compare them to TT. The LAST trial showed non-inferiority of technical success rate while performing steam ablation compared to EVLA – 92% vs. 96% of closed saphenous veins after one year of observation ($p = 0.331$) [33]. The VeClose Study, which was performed to compare glue ablation (VenaSeal™) with RF modality revealed 94.4% of closed saphenous veins in a cyanoacrylate group vs. 91.9% in an RF group after 36 months of follow-up [34]. Another mid-term study, the eSCOPE trial, showed that three years after VenaSeal™ procedure 88.5% of saphenous veins were free from recanalisation [35], whereas Almeida *et al.* reported 94.7% of successfully closed GSV trunks 36 months after cyanoacrylate ablation [36]. For the treatment with n-butyl cyanoacrylate derivative, similar results have been published showing 94.1% of closed veins after 30 months of follow-up [37]. There are not so many studies analysing mid-term outcomes of MOCA. One of them was performed to assess the ClariVein® device to abolish SSV reflux. The closure rate after one year was 94% [38], and for GSV the clinical success rate was 93% [39]. Mirrandola reported a success rate of 89% after 36 months [40], whereas Witte *et al.* – 87% [41] while using MOCA to treat incompetent superficial veins.

Long-term results

The assessment of long-term results of TT methods can be used only for RF and EVLA because they have been the only modalities present in the phlebological armamentarium for more than 10 years. There are some studies showing good rates of closure of saphenous trunks. The ELA-FOS study evaluated the durability of laser treatment after 66 to 110 months (mean 88) of follow-up and showed partial recanalisation in only 3.4% and total recanalisation in 5.1% of treated veins [42]. Also, RF procedure results seem to be stable for longer periods after the procedure. Proebstle *et al.* reported a high occlusion rate of 91.9% of treated veins after five years of follow-up [43], while the study of the longest observation time after EVTA showed a rate of 88.1% of technical success 15 years after RF VNUS closure [44].

Foam sclerotherapy

The oldest modality of endovenous treatment of axial reflux is ultrasound-guided foam sclerotherapy (UGFS). This method has had a well-established place in phlebology although the majority of trials show worse results of UGFS compared to TT or novel NTNT techniques. Occlusion rate at one year ranges between 51 and 75% [45-48] and is significantly lower at five years, up to 23% of closed veins in van der Velden *et al.* RCT [49]. Despite worse technical results, clinical outcomes of foam therapy measured by CIVIQ or EQ-5D do not differ from EVTA, especially at one year, thus making UGFS still an attractive method, particularly considering the cost-effectiveness of the therapy.

RESULTS OF THE ENDOVENOUS ABLATION TECHNIQUES – CLINICAL OUTCOME

It is essential for the clinician physician to assess the results of the procedures first of all from the patient's perspective. It means that we should compare health-related quality of life after the treatment, not only technical and anatomical findings. Because there are many factors influencing the clinical outcome, reliable assessment is complicated. It is especially difficult for EVTA, because many different devices and modifications of treatment have been used for more than 15 years of the history of endovenous thermal ablation. For example, the bare fibre tip combined with laser generators producing 810 nm wavelength should not be compared with contemporary implemented equipment, similarly it is not advisable to check VNUS against the Closure Fast system. Hence the NTNT are not so varied, and their results' comparison is more reliable inside each group.

The analysis of patients' quality of life after EVTA reveals improvement compared to open surgery in short-term, mid-term, and long-term follow-up [7, 45, 50]. In

short- and mid-term time after the procedure, the rate of clinical complications is also very low for NTNT [51], even the intra- and postprocedural pain seems to be lower for MOCA and CA than for EVTA. Other minor and major complication rates, time to return to work, and normal activity do not differ significantly [36, 52-56].

Simultaneously, clinical outcomes must be evaluated considering the recurrence rates. The precise assessment is then more accurate when longer follow-up periods are taken into account. Thus, only EVTA modalities can be measured because they are unique methods that have been used long enough to be compared to open surgery. The results of mid-term and long-term trials reveal the same recurrence rates of varicosity after EVTA compared to open surgery – high ligation and stripping (46.6% and 54.6%, respectively) [57]. According to recent trials the resources of recurrences are better established and it is suspected that same-site recurrence is more often expected after EVTA procedures compared to open surgery, while the relief of venous symptoms, changes of CEAP stages, and quality of life are equally improved [58, 59]. The most frequently found cause of recurrent disease is neovascularisation and incompetency of thigh perforators after surgery or refluxing groin tributaries for EVTA. That is why some modifications of EVLA technique are proposed, like laser GSV crossectomy, i.e. ablation starting at the saphenofemoral junction [60, 61]. This method is suspected to be more efficient in preventing reflux augmentation from coming into the groin tributaries, especially to AASV, and forming varicosity. If AASV is visible, but not refluxing at the time of primary procedure, it is estimated that this vessel can be a source of recurrence in 55% of cases [62]. Thus, a very meticulous postprocedural patient control strategy is mandatory and elimination of detected reflux from the junction required. In cases when reflux is present in AASV at the time of primary procedure, it is proposed that it be eliminated simultaneously by the same technique that is planned for GSV ablation.

CONCLUSIONS

It is clearly visible that the development of endovenous techniques used in chronic venous disease has created a new perspective in phlebology. The treatment can be easier, faster, and – what is most important for the patient – safer and more effective. As an evident reduction of complications and improvement of quality of life of the patients after the procedures can be reached by all endovenous methods, it is crucial to adjust the proper mode of therapy to the specific patient and type of disease. Each minimally invasive way is valuable unless used by a skilled and qualified specialist. The differences of effectiveness among the modalities are very small and require further investigations and well-designed trials without any commercial bias. It is crucial to wait for long follow-up assessment of the newest techniques to be able

to compare them to the older ones. Currently it is not clear that non-tumescent non-thermal modalities should be chosen as a first option in the treatment to eliminate saphenous reflux.

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