


Original Research

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Trend Analysis for the Treatment of Incompetent GSV

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Authors' contributions

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the [Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors](#). Indeed, all the authors have actively participated in the redaction, the revision of the manuscript, and provided approval for this final revised version.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Abbreviations

CAC – cyanoacrylate adhesive closure
CVD – chronic venous disease
EVLA – endovenous laser ablation
EVTA – endovenous thermal ablation
GSV – great saphenous vein
SFJ – saphenofemoral junction
RFA – radiofrequency ablation
MOCA – mechanochemical ablation
UGFS – ultrasound guided foam sclerotherapy
QOL – quality of life

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ABSTRACT



Purpose: Chronic venous disease (CVD) has an excellent socioeconomic impact. Treatment modalities of CVD are evolving fields that could be derived from the disease's progressive nature.

Materials and methods: After a wide literature search in Google Scholar (Publish and Perish software), extracted data was analyzed by VOSviewer software, creating network and overlay visualizations.

Results: CVD has been investigated intensively in the literature from the beginning of the 21st century. Studies aimed to understand the mechanism of CVD in the early 2000s. Later, the focus of scientific interest was moved to novel procedures. Researchers were motivated to explore the reasons for technical failures and recurrences of endovenous thermal ablation (EVTA) procedures and open surgery to treat saphenous incompetence. Less invasive procedures replaced invasive open surgery. The search for novel tissue sealants showed a thin centralized network. Papers were dated from 2010. Therefore, this is a very recent source of evidence. There were meeting points for some components of tissue sealants. Biomaterials for novel tissue adhesion are under development and investigation. The efficacy and safe application in humans is the focus of research.

Conclusion: Researchers widely investigate CVD. An evolution from invasive open surgery (stripping) through EVTA to non-thermal ablation procedures could be discovered in the literature. There could be some versatile options for replacing cyanoacrylate in the future, but there are no clear paths to reach that point in scientific literature yet.

Keywords: Incompetent Saphenous Vein, Varicose Vein, Tissue Adhesive, Tissue Sealant, Tissue Glue.

1. INTRODUCTION

1.1. Rationale

According to recent evidence from Vein Consult Program, Edinburgh Vein Study, and Bonn Vein Study, CVD is age-dependent and affects 2-40% of the adult population resulting in a great socioeconomic impact [1-4]. A large proportion of leg ulcers develop from CVD [5-6]. For decades, the open surgical approach (high ligation of SFJ and GSV stripping) was the gold standard treatment of GSV incompetence which was replaced by less invasive but more efficient therapeutic modalities such as thermal ablation procedures. The most widespread methods are EVLA and RFA [7-11]. In the last decade, non-thermal ablations or chemical procedures, due to their less invasive features, are jeopardizing the hegemony of thermal ablation procedures such as UGFS, MOCA, and endovenous glue ablation as CAC [12-15]. Only the last one seems to be a real challenger for EVTA regarding efficacy and safety [16-21]. But what should vascular surgeons expect in the future? Will cyanoacrylate glue be replaced? Are there eligible bioadhesives for saphenous vein ablation? Objective. The purpose of this study is to seek a potential connection between bioadhesives and varicose vein treatment in the future. The aim of this review, including trend analysis and future forecasting, is to address these questions.

2. METHODS

2.1. Study design

This overview includes trend analysis and future forecasting in varicose vein treatment (GSV incompetence).

2.2. Information sources, literature search, eligibility criteria, and study selection

A wide literature search was performed in Google Scholar by Publish and Perish software (version 7.32) developed by Anne-Wil Harzing [22]. All studies were assessed up to the 27th of May in 2021. First, papers were collected with the keywords of 'varicose vein,' 'incompetent saphenous,' and 'saphenous incompetence.' The next search was performed with the keywords of 'varicose vein,' 'endovenous ablation,' 'Bioadhesive,' 'bio glue,' 'tissue adhesive,' and 'tissue glue' were the keywords for the last search. All studies were automatically selected without filters up to a limit of 1000 publications internally defined by the software. The corresponding author was responsible for the literature search and study selection. All other reviewers helped interpret the data and write this article.

2.3. Data collection, data items, and bias

There were no variables defined to seek. Papers were included if the main topic was connected with the actual keywords regardless of the type and bias of the paper. The presence or absence of keywords was considered during the publication search because this overview focuses only on surgical trends in the treatment of varicose veins and novel tissue sealants.

2.4. Summary measures and synthesis of results

VOS viewer software (version 1.6.16) developed by Nees Jan van Eck and Ludo Waltman at Leiden University's Centre for Science and Technology Studies was applied to perform network and overlay visualizations and detect potential connections between publications. Title and abstract field content were taken into account. Binary counting was applied. Structured abstract labels and copyright statements were ignored. A minimal number of term occurrences was defined as 10 (default setting). The relevance score was calculated by the VOS viewer, which was the basis for selection. The default choice was to select 60% of the most relevant terms. Network and overlay visualizations were created.

3. RESULTS

3.1. Study selection and preparation for analysis

The assessed papers are available in Supplement 1. 185 of the 5243 terms met the threshold by an occurrence for the first search. According to relevance, the number of terms to be selected was 111 out of 185, according to relevance. During the next search, 165 from the 5070 terms reached the defined limit, and 99 were chosen for analysis. Of 3333 terms, 56 met the threshold of occurrence for the last search, and 34 of them were included in the final assessment. Irrelevant terms were excluded manually (only 'et al.' for the second search). The search process is shown on the flow chart (Figure 1).

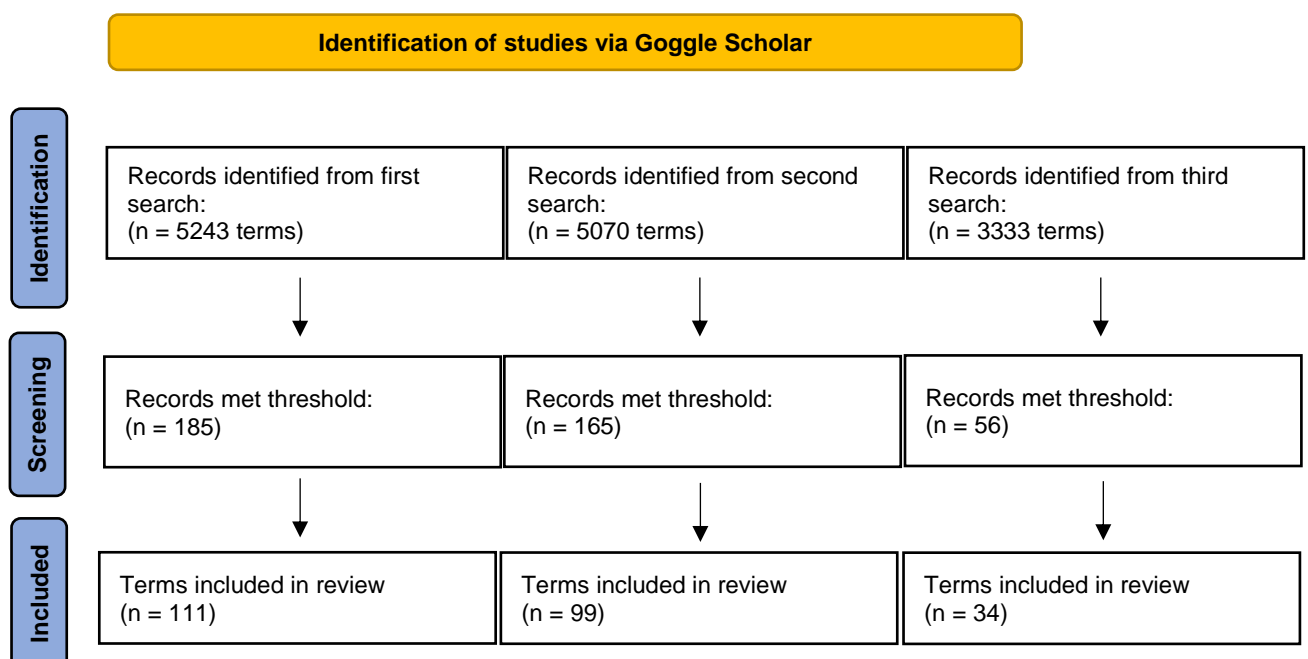


Figure 1: Flow chart of search process.

3.2. Results of analysis

The first search demonstrated that CVD had been investigated intensively in the literature from the beginning of the 21st century (Figures 2 and 3). The aim of the studies was to understand the mechanism of CVD (valvular incompetence in GSV, connection between recurrence and neovascularization, and the role of deep and perforator veins) in the early 2000s. Later, the focus of scientific interest was moved to novel procedures such as EVLA, CAC, and foam sclerotherapy for varicose vein treatment based on GSV incompetence. CAC and QOL also represented a subfield of interest.

The second search (Figures 4 and 5) showed that researchers were motivated to explore the reasons for technical failures and recurrences of EVTA procedures and open surgery in treating GSV and SSV incompetence around the end of the first decade of the 21st century. In trials, invasive open surgery was replaced by EVLA, RFA, and UGFS. Later, non-thermal ablation techniques gained more and more popularity. First was UGFS, and it evolved into MOCA.

The last search was a surprise (Figures 6 and 7). The visualization showed only a thin centralized network around the keywords 'tissue' and 'treatment effect.' Papers were dated from 2010. Therefore, this is a very recent source of evidence. There were meeting points for glutaraldehyde, a polymerization agent for many tissue sealants such as bio glue, and for mussel, which is a basis for bioinspired adhesives. Biomaterials for novel tissue adhesion are under development and investigation. The efficacy and safe application in humans is the focus of research.

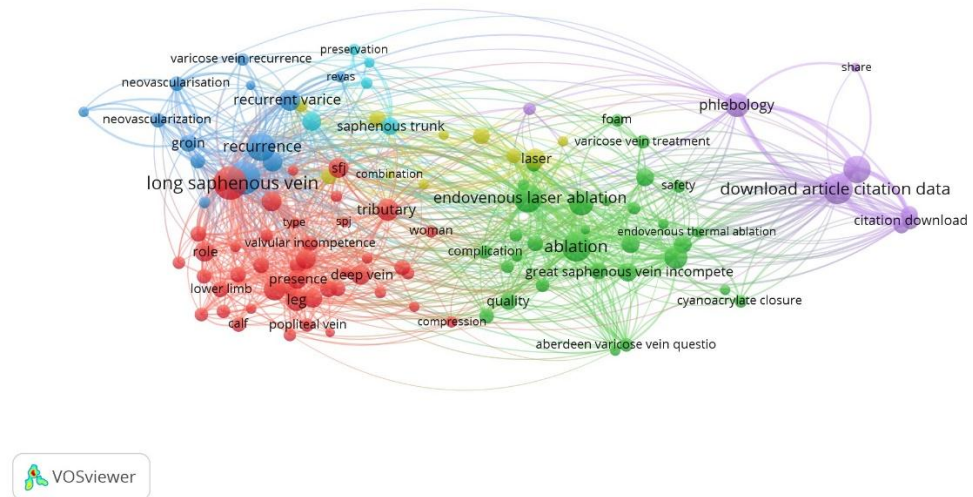


Figure 2: Network analysis of the first search.

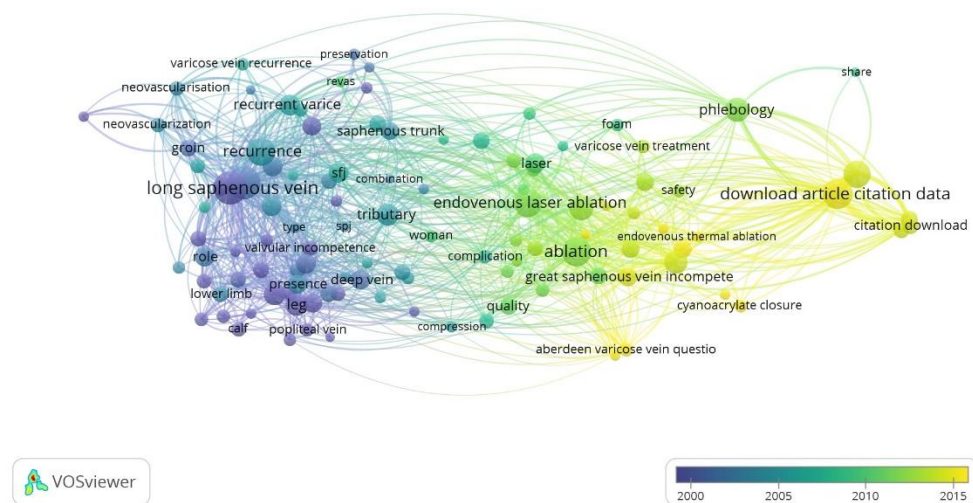


Figure 3: Overlay visualization of the first search.

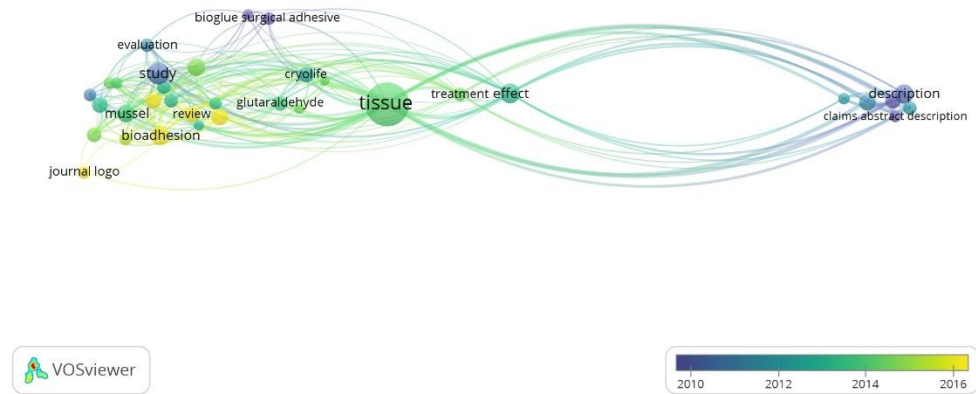


Figure 7: Overlay visualization of the third search.

4. DISCUSSION

4.1. In general

CVD resulting in limb swelling, itching, varicose veins, and leg ulcers have a tremendous socio-economic impact. CVD treatment modalities, especially saphenous reflux, have been evolving fields since the beginning of this century. This could be derived from the progressive nature of the disease and the lack of a "gold standard" technique. This may not be true because recommendations for treating GSV incompetence are always available, but recent evidence of evolving procedures (more efficient, less invasive) overwrite previous guidelines. Nowadays, endovenous glue seems the most appropriate option due to its non-invasive nature and high efficacy in GSV reflux treatment.

4.2. Interpretation of results

It is essential to understand that CVD is a chronic progressive disease. The evolution of treatment was described well by the literature. Madelung and Narath introduced invasive open surgery in the 19th century [23]. It was revolutionized by Smetana-knife and Müller-hook (further developed by Váradi) [23]. In terms of less invasivity, liquid and foam sclerotherapy (applied simultaneously or sequentially) replaced such methods in tributary elimination [23]. Stripping was introduced by Keller and Mayo in the first decade of the 20th century and was less invasive than previous surgical attempts to remove GSV [23]. It was later modified by Babcock and Oesch [23]. Cryostripping was an alternate to wire-stripping [23]. The first endovenous thermal ablation method was cryosclerotherapy, developed by Milleret and LePivert in the 1980s [24], and it was forgotten before the era of EVTA. EVLA, RFA, and UGFS were introduced at the end of the 20th century and brought a real revolution in varicose vein treatment [25-32]. Nowadays, International, European and American guidelines suggest EVTA (EVLA and RFA) as the primary choice in GSV incompetence treatment. Steam ablation, MOCA, and CAC are under evaluation due to a lack of long-term results. Non-thermal ablation methods are good alternates to EVTA [33-35].

4.3. Possible future direction

There is an escalating need to develop more sophisticated tissue sealants that could provide many advantages over classical surgical efforts for tissue adhesion in wound closure and hemostasis. The perfect agent is tissue-specific and biocompatible. It offers controllable polymerization, adhesion, and cohesive sealing strength [36,37]. Natural (fibrin, albumin, and gelatin) and synthetic (cyanoacrylate, polyethylene-glycol, polyurethane, catechol, and methacrylic anhydride) polymer-based adhesives are known now [36,37]. There is no "gold standard" tissue sealant for different applications (hemostasis, wound closure, anastomosis strengthening, closure of veins and arterial defects, meniscus repair, dural closure) [37]. Some of the adhesives are commercially available, but there are efforts for evolving new agents due to the drawbacks of traditional products.

Fibrin sealants have been in use for decades. These adhesives are composed of concentrated fibrinogen cryoprecipitate, factor XIII, and thrombin (this component - starter solution - contains calcium and antifibrinolytic agent). Fibrin sealants are non-toxic and provide good hemostasis, but they have weak and short-lasting adhesion due to complete absorption, and there is a risk for infectious disease transmission, allergic reactions, and coagulopathy due to antibody formation and embolization [36,37].

Crosslinked albumin adhesives are also commercially used. Two trademarks are composed of bovine albumin, and one product is manufactured from human albumin. These agents provide a good and rapid hemostatic effect due to mechanical sealing. The polyaldehyde or

glutaraldehyde component means the risk of cytotoxicity. The use of human albumin represents a concern of immunogenicity [36,37].

Gelatin-based glues have been in use since the 1960s. A polymerizing agent is also a type of aldehyde for commercially available products. These are low-toxic adhesives providing high bonding capability. There are novel chemical or photo-crosslinking gelatin sealants combined with other agents (alginate, kaolin with montmorillonite, xanthene dye, and ruthenium) under development [36].

Polyethylene glycol is a synthetic sealant. It provides good polymerization properties if adequate functional groups are applied. Hydrophilicity decreases the potential effect of these biocompatible adhesives in wet conditions [37]. Polyurethane adhesives provide improved biocompatibility due to isocyanate modification. However, carcinogenicity and toxicity are great concerns [37].

Cyanoacrylate is a cheap sealant providing a rapid and strong adhesion by a strong film due to the exothermic polymerization of cyanoacrylate molecules. Toxic degradation products (cyanoacrylate compounds and formaldehyde), besides limited strength in wet conditions, are the major drawbacks of this adhesive. [36,37].

Because of previous concerns about commercially available sealants, there are great efforts in the development of promising new glues. Natural-based biopolymers have human or animal origins which could lead to disease transmission and immune reactions [37]. Cithosan, a fungal and anthropoid polysaccharide, is a source of novel sealants that have promising haemostatic properties, providing stronger tissue adhesion than fibrin sealants. Researchers try to combine cithosan-based adhesives with other glue types to increase mechanical properties, solubility, and biosafety [37]. Aldehyde-linked dextran may be another tissue sealant with favorable hemostatic effects [37]. Biopolymers made of plants (photoactivatable Rose Bengal, Genipin) are promising agents for wound closure, especially in combination with other sealants [37].

Future research is directed towards evolving synthetic free radical polymerization agents. The process could be geared up by crosslinking initiators. Polymerization is induced by external light, heat, or ultrasound. Polymethyl methacrylate is a commercially available adhesive used in dental and spinal surgery. Allergic reactions represent a potential risk for this sealant. There are some promising products based on methacrylate combined with recombinant human tropoelastin or glycerol and sebacate acid. These polymers act well in wet conditions [37].

There are efforts to develop novel biomimetic adhesives mimicking mussel foot proteins. The catechol component of L-dihydroxy-phenylalanine has adhesive properties. Multiple covalent crosslinking results in a strong, cohesive effect. Tests showed good biocompatibility, strong adhesion, and instant hemostasis. Combinations of polyethylene glycol and dihydroxy-phenylalanine are another future direction to develop modified adhesive hydrogels [37].

Living glues are based on the biofilm formation of bacteria. *Bacillus subtilis* is the focus of genetic engineering. It produces biofilms under control in different locations, which can be a basis for a potential sealant for medical purposes [36].

The criteria for a novel desired biosealant are biocompatibility, appropriate wet bonding capabilities, biodegradation, good tension strength, and low cost.

4.4. Limitations

This work was based neither on a systematic review nor on a meta-analysis, and the authors did not analyze bias because it was not the aim to describe the present efficacy of known and widespread procedures or forecast any secure scientific direction.

5. CONCLUSION

CVD is widely investigated by researchers. An evolution from invasive open surgery (stripping) through EVTA to non-thermal ablation procedures could be discovered in the literature. There could be some versatile options for replacing cyanoacrylate in the future, but there are no clear paths to reach that point in scientific literature yet.

REFERENCES

- [1] Wrona M, Jöckel KH, Pannier F, Bock E, Hoffmann B, Rabe E. Association of Venous Disorders with Leg Symptoms: Results from the Bonn Vein Study I. *Eur J Vasc Endovasc Surg.* 2015;50(3):360-7. DOI: [10.1016/j.ejvs.2015.05.013](https://doi.org/10.1016/j.ejvs.2015.05.013)
- [2] Robertson LA, Evans CJ, Lee AJ, Allan PL, Ruckley CV, Fowkes FG. Incidence and risk factors for venous reflux in the general population: Edinburgh Vein Study. *Eur J Vasc Endovasc Surg.* 2014;48(2):208-14. DOI: [10.1016/j.ejvs.2014.05.017](https://doi.org/10.1016/j.ejvs.2014.05.017)
- [3] Lattimer CR. CVD: a condition of underestimated severity. *Int Angiol.* 2014;33(3):222-8. Available from: <https://pubmed.ncbi.nlm.nih.gov/24732585/>
- [4] Rabe E, Guex JJ, Puskas A, Scuderi A, Fernandez Quesada F. The VCP Coordinators. Epidemiology of chronic venous disorders in geographically diverse populations: results from

- the Vein Consult Program. *Int Angiol.* 2012;31(2):105-15. Available from: <https://pubmed.ncbi.nlm.nih.gov/22466974/>
- [5] Margolis DJ, Bilker W, Santanna J, Baumgarten M. Venous leg ulcer: incidence and prevalence in the elderly. *J Am Acad Dermatol.* 2002; 46: 381-6. DOI: [10.1067/mjd.2002.121739](https://doi.org/10.1067/mjd.2002.121739)
- [6] Marston WA. Evaluation of varicose veins: what do the clinical signs and symptoms reveal about the underlying disease and need for intervention? *Semin Vasc Surg.* 2010;23(2):78-84. DOI: [10.1053/j.semvascsurg.2010.01.003](https://doi.org/10.1053/j.semvascsurg.2010.01.003)
- [7] Antani MR, Dattilo JB. *Varicose Veins.* PubMed. Treasure Island (FL): StatPearls Publishing; 2020. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470194/> .
- [8] Rabe E, Pannier F. What is evidence-based in the treatment of chronic venous insufficiency? *Internist (Berl).* 2020;61(12):1230-1237. DOI: [10.1007/s00108-020-00899-6](https://doi.org/10.1007/s00108-020-00899-6)
- [9] Vuylsteke ME, Klitfod L, Mansilha A. Endovenous ablation. *Int Angiol.* 2019;38(1):22-38. DOI: [10.23736/S0392-9590.18.04047-6](https://doi.org/10.23736/S0392-9590.18.04047-6)
- [10] Oliveira RÁ, Mazzucca ACP, Pachito DV, Riera R, Baptista-Silva JCDC. Evidence for varicose vein treatment: an overview of systematic reviews. *Sao Paulo Med J.* Jul-Aug 2018;136(4):324-332. DOI: [10.1590/1516-3180.2018.0003240418](https://doi.org/10.1590/1516-3180.2018.0003240418)
- [11] van den Bos RR, Proebstle TM. The state of the art of endothermal ablation. *Lasers Med Sci.* 2014 Mar;29(2):387-92. DOI: [10.1007/s10103-013-1448-5](https://doi.org/10.1007/s10103-013-1448-5)
- [12] Kolluri R. Interventions for Varicose Veins: Beyond Ablation. *Curr Treat Options Cardiovasc Med.* 2016;18(7):43. DOI: [10.1007/s11936-016-0467-5](https://doi.org/10.1007/s11936-016-0467-5)
- [13] Bootun R, Lane TR, Davies AH. The advent of non-thermal, non-tumescent techniques for treatment of varicose veins. *Phlebology.* 2016;31(1):5-14. DOI: [10.1177/0268355515593186](https://doi.org/10.1177/0268355515593186)
- [14] Whiteley MS. Glue, steam and Clarivein--Best practice techniques and evidence. *Phlebology.* 2015;30(2 Suppl):24-8. DOI: [10.1177/0268355515591447](https://doi.org/10.1177/0268355515591447)
- [15] McHugh SM, Leahy AL. What next after thermal ablation for varicose veins: non-thermal ablation? *Surgeon.* 2014;12(5):237-8. DOI: [10.1016/j.surge.2014.06.003](https://doi.org/10.1016/j.surge.2014.06.003)
- [16] Tang TY, Yap CJQ, Chan SL, Soon SXY, Yap HY, Lee SQW, Choke ETC, Chong TT. Early results of an Asian prospective multicenter VenaSeal real-world postmarket evaluation to investigate the efficacy and safety of cyanoacrylate endovenous ablation for varicose veins. *J Vasc Surg Venous Lymphat Disord.* 2021;9(2):335-345.e2. DOI: [10.1016/j.jvsv.2020.03.020](https://doi.org/10.1016/j.jvsv.2020.03.020)
- [17] Morrison N, Gibson K, Vasquez M, Weiss R, Jones A. Five-year extension study of patients from a randomized clinical trial (VeClose) comparing cyanoacrylate closure versus radiofrequency ablation for the treatment of incompetent great saphenous veins. *J Vasc Surg Venous Lymphat Disord.* 2020;8(6):978-989. DOI: [10.1016/j.jvsv.2019.12.080](https://doi.org/10.1016/j.jvsv.2019.12.080)
- [18] Kolluri R, Chung J, Kim S, Nath N, Bhalla BB, Jain T, Zygmunt J, Davies A. Network meta-analysis to compare VenaSeal with other superficial venous therapies for chronic venous insufficiency. *J Vasc Surg Venous Lymphat Disord.* 2020;8(3):472-481.e3. DOI: [10.1016/j.jvsv.2019.12.061](https://doi.org/10.1016/j.jvsv.2019.12.061)
- [19] Parsi K, Roberts S, Kang M, Benson S, Baker L, Berman I, Bester LJ, Connor DE, Dinnen P, Grace J, Stirling A, Ibrahim N, Lekich C, Lim A, Matar L, Nadkarni S, Paraskevas P, Rogan C, Thibault PK, Thibault S, van Rij A, Yang A. Cyanoacrylate closure for peripheral veins: Consensus document of the Australasian College of Phlebology. *Phlebology.* 2020;35(3):153-175. DOI: [10.1177/0268355519864755](https://doi.org/10.1177/0268355519864755)
- [20] Morrison N, Gibson K, Vasquez M, Weiss R, Cher D, Madsen M, Jones A. VeClose trial 12-month outcomes of cyanoacrylate closure versus radiofrequency ablation for incompetent great saphenous veins. *J Vasc Surg Venous Lymphat Disord.* 2017;5(3):321-330. DOI: [10.1016/j.jvsv.2016.12.005](https://doi.org/10.1016/j.jvsv.2016.12.005)
- [21] Vos CG, Ünlü Ç, Bosma J, van Vlijmen CJ, de Nie AJ, Schreve MA. A systematic review and meta-analysis of two novel techniques of nonthermal endovenous ablation of the great saphenous vein. *J Vasc Surg Venous Lymphat Disord.* 2017 Nov;5(6):880-896. DOI: [10.1016/j.jvsv.2017.05.022](https://doi.org/10.1016/j.jvsv.2017.05.022). Epub 2017 Jul 21. PMID: 29037363 Review. *J Vasc Surg Venous Lymphat Disord.* 2017;5(6):880-896. DOI: [10.1016/j.jvsv.2017.05.022](https://doi.org/10.1016/j.jvsv.2017.05.022)
- [22] Harzing AW. Publish or Perish. 2016. Available from <https://harzing.com/resources/publish-or-perish>
- [23] Bihari I. Az alsó végtagi varicositas műtéti eltávolításának módszerei. *Érbetegségek.* 1999;6(2):55-66. DOI: [10.1556/650.2018.31262](https://doi.org/10.1556/650.2018.31262)
- [24] Milleret R., Le Pivert P. Cryosclerosis of the saphenous veins in varicose reflux in the obese and elderly. *Phlebologie.* 198;34(4):601-5. <https://pubmed.ncbi.nlm.nih.gov/7335776/>
- [25] Weiss RA, Weiss MA. Controlled radiofrequency endovenous occlusion using a unique radiofrequency catheter under duplex guidance to eliminate saphenous varicose vein reflux: a 2-year follow-up. *Dermatol Surg.* 2002;28(1):38-42. DOI: [10.1046/j.1524-4725.2002.01188.x](https://doi.org/10.1046/j.1524-4725.2002.01188.x)
- [26] Goldman MP, Amiry S. Closure of the greater saphenous vein with endoluminal radiofrequency thermal heating of the vein wall in combination with ambulatory phlebectomy: 50 patients with more than 6-month follow-up. *Dermatol Surg.* 2002;28(1):29-31. DOI: [10.1046/j.1524-4725.2002.01187.x](https://doi.org/10.1046/j.1524-4725.2002.01187.x)
- [27] Weiss RA. Comparison of endovenous radiofrequency versus 810 nm diode laser occlusion of large veins in an animal model. *Dermatol Surg.* 2002;28(1):56-61. DOI: [10.1097/00042728-200201000-00013](https://doi.org/10.1097/00042728-200201000-00013)
- [28] Min RJ, Zimmet SE, Isaacs MN, Forrestal MD. Endovenous laser treatment of the incompetent greater saphenous vein. *J Vasc Interv Radiol.* 2001;12(10):1167-71. DOI: [10.1016/S1051-0443\(07\)61674-1](https://doi.org/10.1016/S1051-0443(07)61674-1)

- [29] Navarro L, Min RJ, Boné C. Endovenous laser: a new minimally invasive method of treatment for varicose veins--preliminary observations using an 810 nm diode laser. *Dermatol Surg.* 2001;27(2):117-22. DOI: [10.1046/j.1524-4725.2001.00134.x](https://doi.org/10.1046/j.1524-4725.2001.00134.x)
- [30] Goldman MP. Closure of the greater saphenous vein with endoluminal radiofrequency thermal heating of the vein wall in combination with ambulatory phlebectomy: preliminary 6-month follow-up. *Dermatol Surg.* 2000;26(5):452-6.
- [31] Kanter A. Clinical determinants of ultrasound-guided sclerotherapy. Part II: In search of the ideal injectate volume. *Dermatol Surg.* 1998;24(1):136-8; discussion 138-40. DOI: [10.1016/S1076-0512\(98\)00457-9](https://doi.org/10.1016/S1076-0512(98)00457-9)
- [32] Kanter A. Clinical determinants of ultrasound-guided sclerotherapy outcome. Part I: The effects of age, gender, and vein size. *Dermatol Surg.* 1998;24(1):131-5. DOI: [10.1016/S1076-0512\(97\)00456-1](https://doi.org/10.1016/S1076-0512(97)00456-1)
- [33] Nicolaides A, Kakkos S, Bækgaard N, Comerota A, de Maeseneer M, Eklof B, et al. Management of chronic venous disorders of the lower limbs. Guidelines According to Scientific Evidence. Part II. *Int Angiol.* 2020;39(3):175-240. DOI: [10.23736/S0392-9590.20.04388-6](https://doi.org/10.23736/S0392-9590.20.04388-6)
- [34] Wittens C, Davies AH, Bækgaard N, Broholm R, Cavezzi A, Chastanet S, et al. Editor's Choice - Management of Chronic Venous Disease: Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg.* 2015;49(6):678-737. DOI: [10.1016/j.ejvs.2015.02.007](https://doi.org/10.1016/j.ejvs.2015.02.007)
- [35] Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, Gloviczki ML, et al. Society for Vascular Surgery; American Venous Forum. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg.* 2011;53(5 Suppl):2S-48S. DOI: [10.1016/j.jvs.2011.01.079](https://doi.org/10.1016/j.jvs.2011.01.079)
- [36] Gillman N, Lloyd D, Bindra R, Ruan R, Zheng M. Surgical applications of intracorporal tissue adhesive agents: current evidence and future development. *Expert Rev Med Devices.* 2020;17(5):443-460. DOI: [10.1080/17434440.2020.1743682](https://doi.org/10.1080/17434440.2020.1743682)
- [37] Bao Z, Gao M, Sun Y, Nian R, Xian M. The recent progress of tissue adhesives in design strategies, adhesive mechanism and applications. *Mater Sci Eng C Mater Biol Appl.* 2020;111:110796. DOI: [10.1016/j.msec.2020.110796](https://doi.org/10.1016/j.msec.2020.110796)