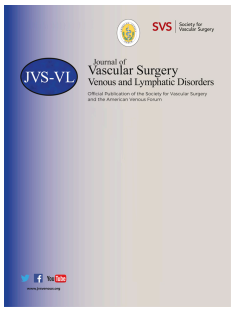
Journal Pre-proof



The 2022 Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society Clinical Practice Guidelines for the Management of Varicose Veins of the Lower Extremities.

Peter Gloviczki, MD, Peter F. Lawrence, MD, Suman M. Wasan, MD, Mark H. Meissner, MD, Jose Almeida, MD, Kellie Brown, MD, Ruth L. Bush, MD, JD, MPH, Michael Di Iorio, MD, John Fish, MD, Eri Fukaya, MD, Monika L. Gloviczki, MD, PhD, Anil Hingorani, MD, Arjun Jayaraj, MD, Raghu Kolluri, MD, M. Hassan Murad, MD, MPH, Andrea T. Obi, MD, Kathleen J. Ozsvath, MD, Michael J. Singh, MD, Satish Vayuvegula, MD, Harold J. Welch, MD

PII: S2213-333X(22)00417-6

DOI: https://doi.org/10.1016/j.jvsv.2022.09.004

Reference: JVSV 1497

To appear in: *Journal of Vascular Surgery: Venous and Lymphatic Disorders*

Received Date: 9 September 2022

Accepted Date: 23 September 2022

Please cite this article as: P. Gloviczki, P.F. Lawrence, S.M. Wasan, M.H. Meissner, J. Almeida, K. Brown, R.L. Bush, M. Di Iorio, J. Fish, E. Fukaya, M.L. Gloviczki, A. Hingorani, A. Jayaraj, R. Kolluri, M.H. Murad, A.T. Obi, K.J. Ozsvath, M.J. Singh, S. Vayuvegula, H.J. Welch, The 2022 Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society Clinical Practice Guidelines for the Management of Varicose Veins of the Lower Extremities., *Journal of Vascular Surgery: Venous and Lymphatic Disorders* (2022), doi: https://doi.org/10.1016/j.jvsv.2022.09.004.

The 2022 Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society Clinical Practice Guidelines for the Management of Varicose Veins of the Lower Extremities.

Part I. Duplex Scanning and Treatment of Superficial Truncal Reflux.

Endorsed by the Society for Vascular Medicine and the International Union of Phlebology.

Peter Gloviczki, MD,*[a] Peter F. Lawrence, MD,*[b] Suman M. Wasan, MD,*[c] Mark H. Meissner, MD,[d] Jose Almeida, MD,[e] Kellie Brown, MD,[f] Ruth L. Bush, MD, JD, MPH,[g] Michael Di Iorio, MD,[h] John Fish, MD,[i] Eri Fukaya, MD,[j] Monika L. Gloviczki, MD, PhD,[k] Anil Hingorani, MD,[l] Arjun Jayaraj, MD,[m] Raghu Kolluri, MD,[n] M. Hassan Murad, MD, MPH,[o] Andrea T. Obi, MD,[p] Kathleen J. Ozsvath, MD,[q] Michael J. Singh, MD,[r] Satish Vayuvegula, MD,[s] Harold J. Welch, MD,[t]

Rochester, MN, Los Angeles, CA, Raleigh, NC, Seattle, WA, Miami, FL, Milwaukee, WI, Temple, TX, Columbus, OH, Austin, TX, Toledo, OH, Stanford, CA, Scottsdale, AZ, New York, NY, Jackson, MS, Columbus, OH, Rochester, MN, Ann Arbor, MI, Albany, NY, Pittsburgh, PA, Plano, TX, Hyannis, MA

* Co-Primary Authors and Co-Chairs of the Writing Committee

From the Division of Vascular and Endovascular Surgery, Mayo Clinic, Rochester[a];
the Division of Vascular and Endovascular Surgery, Department of Surgery, University of California, Los Angeles[b]; the UNC, Chapel Hill Department of Medicine and Rex Vascular Specialists, UNC Health, Raleigh[c], University of Washington, Seattle[d], the University of Miami Miller School of Medicine, Miami[e], the Medical College of Wisconsin, Milwaukee[f], Central Texas VA Healthcare System and Texas A & M University College of Medicine[g], Temple, South Austin Vein Center, Austin[h] the Department of Medicine, University of Toledo, Jobst Vascular Institute, Toledo[i], Division of Vascular Surgery, Stanford University, Stanford[j], Scottsdale, AZ[k], NYU Brooklyn Medical Center, New York[l], RANE Center for Venous and Lymphatic Diseases, Jackson[m], Heart and Vascular Service, OhioHealth Riverside Methodist Hospital, Columbus, Ohio[n] the Evidence-Based Practice Research Program, the Robert D. and Patricia E. Kern Center for, the Science of Health Care Delivery, Rochester[o], the University of Michigan, Ann Arbor[p] Vascular Associates, St Peters Health Partners, Albany, [q], The University of Pittsburgh Medical center, Pittsburgh[r] Vein Clinics of America, Plano[s], the Vascular Care Group, Hyannis.[t]

Short title: SVS/AVF/AVLS Clinical Practice Guidelines for Management of Varicose Vein

Conflict of Interest Disclosures: JA has no conflicts of interest.

KB has no conflicts of interest.

RB has no conflicts of interest.

MD has no conflicts of interest.

JF is a paid speaker for Janssen Pharmaceuticals.

EF has no conflicts of interest.

MG has been paid a consulting fee by VitasuppportMD company and is on their Advisory Board.

PG has no conflicts of interest.

AH has no conflicts of interest.

AJ has no conflicts of interest.

RK is a paid consultant for Abbott, Auxetics, Avail Medsystems, Boston Scientific, Inari, Medtronic, Penumbra, Prairie Education and Research Co-operative, Philips SurModics, and Syntactx.

PL has no conflicts of interest.

MM has no conflicts of interest.

MHM was funded by SVS to conduct systematic reviews and provide methodology expertise.

AO is a PI for preclinical research grants funded by Medtronic and SurModics.

KO is an IAC board member, is a speaker/US course host for Medtronic, and is a speaker for Boston Scientific.

SV has no conflicts of interest.

SW has no conflicts of interest.

HW has no conflicts of interest.

DOC Statement:

Independent peer review and oversight has been provided by the members of the SVS Document Oversight Committee (Marc Schermerhorn, Chair, Britt Tonnessen, Vice Chair, Mohammad Eslami, Raul Guzman, Peter Henke, Vikram Kashyap, Ahmed Kayssi, Chris Kwolek, Erika Mitchell, Patrick Muck, William Robinson, Evan Ryer, Palma Shaw, Chris Smolock, Brant Ullery, Chandu Vemuri, Greg Westin, and Karen Woo).

Abstract

The Society for Vascular Surgery (SVS), the American Venous Forum (AVF) and the American Vein and Lymphatic Society (AVLS) collaborated to update the 2011 SVS/AVF clinical practice guidelines and provide new evidence-based recommendations on critical issues affecting the care of patients with varicose veins. Each recommendation is based on a recent, independent systematic review and meta-analysis of the diagnostic tests and treatments options for patients with lower extremity varicose veins. Part I. of the guidelines includes evidence-based recommendations on the evaluation of CEAP (Clinical Class, Etiology, Anatomy, Pathology) Class 2 varicose vein patients with duplex scanning and other diagnostic tests, on open surgical treatment (ligation and stripping) versus endovenous ablation techniques, on thermal versus non-thermal ablations of the superficial truncal veins and on the management of incompetent perforating veins in CEAP Class 2 disease. We also made recommendations on the concomitant vs staged treatment of varicose tributaries using phlebectomy, liquid or foam sclerotherapy (with physician compounded foam or commercially prepared polidocanol endovenous microfoam) in patients who undergo ablation of incompetent superficial truncal veins.

Keywords: Guidelines; Varicose veins; Venous insufficiency; Endovascular; Endovenous; Laser; Radiofrequency; Ablation; Cyanoacrylate; Sclerotherapy, Mechanico-chemical Ablation; Polidocanol Endovenous Microfoam.

Abbreviations: AAGSV, Anterior accessory great saphenous vein; AVLS, American Vein and Lymphatic Society; ACCP , American College of Chest Physicians; AK, above the knee; ASVAL, ablation sélective des varices sous anesthésie locale (ie, ambulatory selective varicose

vein ablation under local anesthesia); AVF, American Venous Forum; AVVQ, Aberdeen Varicose Vein Questionnaire; BK, below the knee; CAGR, Compound Annual Growth Rate; CHIVA, cure conservatrice et hémodynamique de l'insuffisance veineuse en ambulatoire (ie, ambulatory conservative hemodynamic treatment of varicose veins); ambulatory conservative hemodynamic treatment of varicose veins); CI, confidence interval; CIVIQ, Chronic Venous Insufficiency Quality of life questionnaire; CT, computed tomography; CVI, chronic venous insufficiency; CVD, chronic venous disease; DU, duplex ultrasound; DVT, deep venous thrombosis; EVLA, endovenous laser ablation; FDA, U.S. Food and Drug Administration; FS, foam sclerotherapy; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; GSV, great saphenous vein; HHD, hand-held continuous-wave Doppler; HL&S, high ligation and stripping; ICP, intermittent compression pump; IPV, incompetent perforating vein; IVC, inferior vena cava; IVUS, intravascular ultrasonography; MR, magnetic resonance; ms, millisecond; OR, odds ratio; PAGSV, posterior accessory great saphenous vein; PCD, point-of-care portable color Doppler ultrasound; PE, pulmonary embolism; PEM, polidocanol endovenous microfoam; PIN, perforate invaginate (stripping); PRO, patient-reported outcome; PTFE, polytetrafluoroethylene; QALY, quality-adjusted life-year; QoL, quality of life; s, second; RCT, randomized controlled trial; REVAS, recurrent varicose veins after surgery; RF, radiofrequency; RFA, radiofrequency ablation; RR, relative risk; SEPS, subfascial endoscopic perforator surgery; SF-36, Short-Form 36-Item Health Survey; SFJ, saphenofemoral junction; SPJ, saphenopopliteal junction; SSV, small saphenous vein; STS, sodium tetradecyl sulfate; SVM, Society for Vascular Medicine; SVS, Society for Vascular Surgery; TIPP, transilluminated powered phlebectomy; TP, thigh perforator; UIP, International Union of Phlebology; US, ultrasound; VAS, visual analog scale; VCSS, Venous Clinical Severity Score; VEINES (VEnous

120 INsufficiency Epidemiological and Economic Study)-QOL/Sym, VEINES Quality of Life

121 questionnaire; VTE, venous thromboembolism

122

Summary of Recommendations

Guideline 1.

1.1. For patients with chronic venous disease of the lower extremities we recommend Duplex ultrasound scanning as the diagnostic test of choice to evaluate for venous reflux.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: B (Moderate)

Implementation remarks of recommendation 1.1:

1.1.a. Reflux is defined as a minimum value greater than 500 ms of reversed flow in the superficial truncal veins (great saphenous vein, small saphenous vein, anterior accessory great saphenous vein, posterior accessory great saphenous vein) as well as in the tibial, deep femoral, and the perforating veins. A minimum value greater than 1 sec reversed flow is diagnostic of reflux in the common femoral, femoral, and popliteal veins.

1.1.b. Axial reflux is defined as uninterrupted retrograde venous flow from the groin to the calf. Retrograde flow can be in superficial or deep veins, with or without perforating veins. Junctional reflux is limited to the saphenofemoral or saphenopopliteal junction. Segmental reflux occurs in a portion of a superficial or deep truncal vein.

1.1.c. A definition of "pathologic" perforating veins in patients with varicose veins (CEAP Clinical Class C2) includes those with an outward flow duration of $\geq$500 ms and a diameter of $\geq$3.5 mm on Duplex ultrasound.

1.2.1. We recommend that evaluation of reflux with Duplex ultrasound be performed in an Intersocietal Accreditation Commission (IAC) or American College of Radiology (ACR) accredited vascular laboratory by a credentialed ultrasonographer, with the patient standing whenever possible. Sitting or reverse Trendelenburg position may be used if the patient cannot stand.

Level of recommendation: Ungraded good practice statement.

1.2.2. We recommend that for evaluation of reflux with Duplex ultrasound we use either a Valsalva maneuver or distal augmentation to assess the common femoral vein and the saphenofemoral junction and distal augmentation with either manual compression or cuff deflation for evaluation of more distal segments. Superficial reflux must be traced to its source, including saphenous junctions, truncal or perforating veins or pelvic origin varicose veins. The study should be interpreted by a physician trained in venous duplex ultrasound interpretation.

Level of recommendation: Ungraded good practice statement.

1.3.1. We recommend that a complete Duplex scanning examination for venous reflux in the lower extremities include transverse grayscale images without and with transducer compression of the common femoral, the proximal, mid and distal femoral and the popliteal veins and the saphenofemoral junction, the great and the small saphenous vein.

Level of recommendation: Ungraded good practice statement.

1.3.2. We recommend that a complete Duplex scanning examination for venous reflux in the lower extremities include measurement of spectral Doppler waveform using calipers. Reflux at baseline and in response to Valsalva or distal augmentation is documented in the common femoral vein and at the saphenofemoral junction, and in response to distal augmentation in the mid-femoral and popliteal vein, in the great saphenous vein at the proximal thigh and at the knee, in the anterior accessory great saphenous vein and in the small saphenous vein, at the saphenopopliteal junction or proximal calf.

Level of recommendation: Ungraded good practice statement.

1.3.3. We recommend that a complete duplex scanning examination for venous reflux in the lower extremities include diameter measurements in patients with the leg in the dependent position, from anterior to posterior wall, at the saphenofemoral junction, in the great saphenous vein at proximal thigh and at the knee, in the anterior accessory great saphenous vein, and in the small saphenous vein at the saphenopopliteal junction or proximal calf. Images of both normal and abnormal findings should be documented in the records of the patient.

Level of recommendation: Ungraded good practice statement.

1.4. We recommend the use of the 2020 upgraded Clinical Class, Etiology, Anatomy, Pathophysiology (CEAP) for classification system for chronic venous disorders. The clinical or basic CEAP classification may be used for clinical practice, and the full CEAP classification system should be used for clinical research.

Level of recommendation: Ungraded good practice statement.

Guideline 2.

2.1.1. For patients with symptomatic varicose veins and axial reflux in the great or small saphenous vein, who are candidates for intervention, we recommend superficial venous intervention over long-term compression stockings.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: B (Moderate)

2.1.2. For patients with symptomatic varicose veins and axial reflux in the anterior accessory or posterior accessory great saphenous vein, who are candidates for intervention, we suggest superficial venous intervention over compression stockings.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

2.1.3. For patients with symptomatic varicose veins and axial reflux in the superficial truncal veins, we suggest compression therapy for primary treatment if the patient's ambulatory status and underlining medical conditions warrant a conservative approach, or if the patient prefers conservative treatment, for either a trial period or for definitive management.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

2.2.1. For patients with symptomatic varicose veins and axial reflux in the great saphenous vein, who are candidates for intervention, we recommend treatment with endovenous ablation over high ligation and stripping of the great saphenous vein because of less post-procedure pain and morbidity as well as and an earlier return to regular activity.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: B (Moderate)

2.2.2. For patients with symptomatic varicose veins and axial reflux in the small saphenous vein, who are candidates for intervention, we recommend treatment with endovenous ablation over ligation and stripping of the small saphenous vein because of less post-procedure pain and morbidity as well as an earlier return to regular activity.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: C (Low to very low))

2.2.3. For patients with symptomatic varicose veins and axial reflux in the anterior accessory or posterior accessory great saphenous vein, who are candidates for intervention, we suggest treatment with endovenous ablation, with additional phlebectomy, if needed, over ligation and stripping of the accessory great saphenous vein because of less post-procedure pain and morbidity and an earlier return to regular activity.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

2.3.1. For patients with symptomatic varicose veins and axial reflux in the great or small saphenous vein, we recommend treatment with ligation and stripping of the saphenous vein if technology or expertise in endovenous ablation is not available, or if venous anatomy precludes endovenous treatment.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: B. (Moderate)

2.3.2. For patients with symptomatic varicose veins and axial reflux in the anterior accessory or the posterior accessory great saphenous vein, we suggest treatment with ligation and stripping of the accessory great saphenous vein, with additional phlebectomy, if needed, if technology or expertise in endovenous ablations is not available, or if the venous anatomy precludes endovenous treatment.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

2.4.1. For patients with symptomatic varicose veins and axial reflux in the great saphenous vein, who place a high priority on long-term outcomes of treatment (quality of life and recurrence), we suggest treatment with endovenous laser ablation, radiofrequency ablation, high ligation and stripping over physician-compounded ultrasound guided foam sclerotherapy. Level of recommendation: Grade 2 (Weak) Quality of Evidence: B (Moderate)

2.4.2. For patients with symptomatic varicose veins and axial reflux in the small saphenous vein who place a high priority on long-term outcomes of treatment (quality of life and recurrence), we suggest treatment with laser ablation, radiofrequency ablation, ligation and stripping from the knee to the upper or mid-calf over physician-compounded ultrasound guided foam sclerotherapy. Level of recommendation: Grade 2 (Weak) Quality of Evidence: C (Low to very low)

2.4.3. For patients with symptomatic varicose veins and axial reflux in the anterior accessory or posterior accessory great saphenous vein, who place a high priority on long-term outcomes of treatment (quality of life and recurrence), we suggest treatment of the refluxing superficial trunk with endovenous laser ablation, radiofrequency ablation, high ligation and stripping, with additional phlebectomy, if needed, over physician-compounded ultrasound guided foam sclerotherapy.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Guideline 3.

3.1.1. For patients with symptomatic axial reflux of the great saphenous vein, we recommend both thermal or non-thermal ablation from the groin to below the knee, depending on the available expertise of the treating physician and the preference of the patient.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: B (Moderate)

3.1.2. For patients with symptomatic axial reflux of the small saphenous vein, we recommend both thermal or non-thermal ablation from the knee to the upper or mid-calf, depending on the available expertise of the treating physician and the preference of the patient.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: C (Low to very low)

3.1.3. For patients with symptomatic axial reflux of the anterior accessory or posterior accessory great saphenous vein we suggest either thermal or non-thermal ablation, with additional phlebectomy, if needed, depending on the available expertise of the treating physician and the preference of the patient.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Guideline 4.

4.1.1 For patients with varicose veins (CEAP Class C2), who have significant, symptomatic axial reflux of the great or small saphenous vein, we recommend against treatment of incompetent perforating veins concomitant with the initial ablation of the superficial truncal veins.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: C (Low to very low))

4.1.2. For patients with varicose veins (CEAP Class C2), who have significant, symptomatic axial reflux of the anterior accessory or posterior accessory great saphenous vein, we suggest against treatment of incompetent perforating veins concomitant with the initial ablation of the superficial truncal veins.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

4.2. For patients with varicose veins (CEAP Class C2) and persistent or recurrent symptoms following previous complete ablation of incompetent superficial truncal veins we suggest treatment of perforating vein incompetence if it is the origin of symptomatic varicose tributaries.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Guideline 5.

5.1.1. For patients with symptomatic reflux in the great or small saphenous vein and associated varicosities, we recommend ablation of the refluxing venous trunk and concomitant phlebectomy or ultrasound guided foam sclerotherapy of the varicosities with physician compounded foam or commercial polidocanol endovenous microfoam.

Level of Recommendation: Grade 1 (Strong); Quality of Evidence: C (Low to very low)

5.1.2. For patients with symptomatic reflux in the anterior accessory or posterior accessory great saphenous vein, we recommend ablation of the refluxing venous trunk and

concomitant phlebectomy or ultrasound guided foam sclerotherapy of the varicosities with physician compounded foam or commercial polidocanol endovenous microfoam.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

5.2.1. For patients with symptomatic reflux in the great or small saphenous vein, we suggest ablation of the refluxing venous trunk and staged phlebectomy or ultrasound guided foam sclerotherapy of the varicosities if there are anatomical or medical reasons. We suggest a shared decision making with the patient.

Level of Recommendation: Grade 2 (Weak); Quality of Evidence: C (Low to very low)

5.2.2. For patients with symptomatic reflux in the anterior accessory great saphenous vein or the posterior accessory great saphenous vein, we suggest ablation of the refluxing venous trunk and staged phlebectomy or ultrasound guided foam sclerotherapy of the varicosities if there are anatomical or medical reasons. We suggest a shared decision making with the patient.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

5.3. For patients with symptomatic reflux in the major superficial venous trunks and associated varicosities undergoing initial ablation alone, we recommend that patients be followed for at least 3 months to assess the need for staged phlebectomy or ultrasound guided sclerotherapy for persistent or recurrent symptoms. Longer follow-up is recommended for patients with recurrent symptoms and for patients who participate in clinical trials.

323 **Level of Recommendation: Ungraded good clinical practice**

324

Introduction

During the past two decades evaluation and minimally invasive endovenous management of varicose veins and more advanced forms of lower extremity chronic venous insufficiency has progressed. The number of endovenous procedures including thermal and non-thermal interventions has increased rapidly[1-3] and over 90% of these are performed in an office setting as outpatient procedures.[4] In the United States, between 2005 and 2014, total annual claims for venous procedures in the Medicare fee-for-service beneficiaries increased from 95,206 to 332,244, for a Compound Annual Growth Rate (CAGR) of 15%.[4] With the publication of 5-year follow-up data of multiple prospective randomized trials (RCTs),[5-13] and with ten-year follow-up of one of the RCTs,[14] long-term effectiveness of different procedures are available today to help physicians make informed decisions on treatment recommendations. The widely accepted and frequently used CEAP (Clinical presentation, Etiology, Anatomy, Pathophysiology) classification and reporting standards were recently updated [15] and a multi-society Delphi-consensus document was published on Appropriate Use Criteria (AUC) for the management of chronic venous disease.[16] Assessment of early and late results using patient reported outcomes has also improved, and the use of generic and disease specific QoL instruments has become the gold standard for outcome assessment.[17-19]

In 2011, the Society for Vascular Surgery (SVS) and the American Venous Forum (AVF) published the first evidence based guidelines on ”The care of patients with varicose veins and associated chronic venous diseases ”.[20] With the improvement of imaging studies and minimally invasive technology, methodology has also improved, enabling the reporting of guidelines that incorporate new indications, and technology. Several new venous clinical practice guidelines were published during the past decade, with updated recommendations, as new

evidence emerged. [21-27] To collect the latest evidence on evaluation and management of CEAP (Clinical Class, Etiology, Anatomy, Pathology) Class 2 varicose vein patients, the American Vein and Lymphatic Society (AVLS) joined the SVS and AVF and commissioned an independent health science group to perform a new systematic review and meta-analysis.[19] All recommendations in Part I of this clinical practice guideline are based on the scientific evidence provided by this systematic review and meta-analysis.

Methods

All treatment recommendations were made according to the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology. [28, 29] This approach has been outlined in previous SVS guideline documents[28] and includes two components, the first is to determine the quality of the evidence underlying the recommendation (A = high, B = moderate, C = low to very low), and the second is to determine the strength of the recommendation (1 = strong, 2 = weak).

The first component of the GRADE system is to determine of the quality of the evidence (A – C) as a reflection of the degree of confidence in the estimated treatment effect. Rating the quality of evidence (also called certainty of evidence) A, B and C, starts with the study design. As they are less subject to bias, randomized clinical trials occupy the highest level of evidence, while other sources of evidence such as observational studies rank lower on the hierarchy. This rating can be downgraded when: (1) randomized controlled trials (RCTs) have serious methodologic limitations such as inadequate blinding, allocation concealment, or loss to follow-up; (2) results were inconsistent among RCTs; (3) RCTs were indirectly relevant; that is, did not directly apply to the patients, interventions, or outcomes of interest; (4) results were imprecise

due to small number of studies and events, or wide confidence intervals of both benefits and harms, (5) reporting bias was likely to be present. [28, 29] For GRADE A recommendations, confidence in the treatment effect is high and further research is unlikely to change the estimate of effect while for GRADE C recommendations, further research is very likely to impact the estimate of effect.

The second component of GRADE is to determine the strength of a recommendation, which includes an assessment of the relative balance between potential benefits and harms of an intervention, patient values and preferences, and other contextual factors. The implications of a Grade 1, or strong recommendation, are that the potential benefits of an intervention clearly outweigh the potential harms and burdens; and virtually all well-informed patients would choose such an intervention, and the physician can confidently recommend the treatment without a detailed knowledge of the underlying data. In contrast, for Grade 2 or weak recommendations, the benefits and risks are more balanced or uncertain, so different patients may choose different treatment options based on their values and preference. The physician must be familiar with the underlying data before making such a recommendation and counsel patients appropriately. These guidelines use the word "recommend" for GRADE 1, strong recommendations and "suggest" for GRADE 2, weak recommendations. It should also be recognized that in most cases guidelines are developed based on studies of average patients and that deviation from the guidelines may be necessary under unusual circumstances.

The committee also made several specific technical remarks to facilitate adoption and implementation of the new updated guidelines, as well as several ungraded good practice statements.[30] Since a new systematic review of these remarks and good practice statements could not be performed, these were based on the committee's clinical expertise, knowledge of

the literature and on studies that did not meet criteria to be included in the systematic review. Some of these statements were adopted from the 2011 guidelines, if new information was not available.[20] The document uses the terminology established in the updates of the CEAP classifications,[15, 31] in the Vein Glossary,[32] the VEIN-TERM document[33] and "The 2020 appropriate use criteria for chronic lower extremity venous disease." [16] (See Supplementary Table 1.)

Evidence to decision framework

Evidence to decision framework tables that addressed decision criteria were constructed for each recommendation.[34] These tables address the balance of benefits and harms, certainty of the evidence, patient values, feasibility and acceptability of recommended actions (Supplementary Tables 2-6). Patient preferences regarding the relative importance of different aspect of their care are highly variable and must be considered in evaluating treatment approaches. In a pre-evaluation survey of 111 patients from the United Kingdom, the majority of patients (56%) were not concerned about missing work, and the importance of post-operative discomfort and risk of recurrence was variable.[35] As 80% of patients reported that their treatment decision would be influenced by the opinion of their treating physician, it is important that physician preferences be recognized and that the risks and benefits of all treatment options be discussed. Another study, which only considered the early post-operative period, found that out-of-pocket expenses were the most important factor for many to patients, followed in order by postoperative discomfort, risk of adverse events, time to return to normal activity, number of skin punctures made for tumescent anesthesia, and number of required treatment visits.[36]

Most CEAP (Clinical Class, Etiology, Anatomy, Pathology) class C2 patients with symptomatic varicose veins recognize the need for long term follow-up vein care. The panel considered mortality, venous thromboembolism, anaphylactic shock, or stroke as extremely rare but the most severe outcomes, followed by less severe outcomes such as wound complications, infection, allergy, and recurrence of varicose veins.

The recommendations in these guidelines were based on several assumptions. First, patient-centric outcomes such as QoL and recurrent varicose veins are more important than surrogate outcomes such as anatomic closure rates. Significant heterogeneity in the reporting of recurrence has been found in previous systematic reviews, with trials variously reporting overall limb recurrence versus site specific recurrence and clinical recurrence versus ultrasound recurrence.[37] As the clinical relevance of ultrasound imaged recurrence is unclear, this data should be interpreted with caution. Second, although short-term outcomes such as post-operative pain, perioperative complications, return to work and usual activities are important for many patients, superficial venous disease is a chronic disease and long-term patient outcomes were prioritized over short-term clinical outcomes. The committee elected to prioritize outcomes in the following order: 1. QoL at five years, 2. Recurrence and need for reintervention at 5 years. 3.Major and minor peri-operative adverse events, 4. Postoperative pain and return to work and usual activities. 5. Anatomic closure at five years and 6. Cost of the procedure. The guideline committee and the systematic review[19] did not include a formal cost – effectiveness analysis because almost all reported and reviewed studies were performed in the United Kingdom and other European countries, where a different cost and reimbursement system exists than in the United States. Therefore, cost effectiveness judgments in the evidence to decision tables were usually labeled as unknown.

Evidence synthesis

The guideline panel for this document (Part I.) prioritized five critical questions that were most relevant to current management of patients with varicose veins. The questions were the following: Q1: The diagnostic utility of Duplex Ultrasound (DU) in adults with varicose veins (C2-C6), Q2: High ligation and surgical stripping versus any endovenous ablation technique in patients with varicose vein and axial incompetence of the great or small saphenous vein, Q3: Thermal versus non-thermal endovenous ablation technique outcomes in patients with varicose veins and axial incompetence of the great or small saphenous vein Q4: Incompetent perforating vein ablation versus no perforator ablation in patients with simple varicose veins (CEAP class C2) with or without axial incompetence of the great or small saphenous vein Q5: Treatment of varicose tributaries with phlebectomy or sclerotherapy, concomitant with or staged after endovenous ablation of the incompetent great or small saphenous vein.

The Mayo Clinic Evidence-Based Practice Center was asked to conduct a systematic review and meta-analysis of the latest data available to address these questions.[19] For the review, comprehensive searches were conducted through December 7, 2020, using the MEDLINE, Embase, Scopus, the National Library of Medicine (PubMed) and the Cochrane databases. All recommendations of these clinical practice guidelines were based on this systematic review and meta-analysis that is published together with these guidelines.[19] Additional major studies, RCTs, Cochrane and other systematic reviews and meta-analyses, published on-line or in print before submission of these guidelines were also reviewed by the writing committee.

Guidelines

1. DIAGNOSTIC EVALUATION OF VEIN INCOMPETENCE

Guideline 1.1

For patients with chronic venous disease of the lower extremities we recommend Duplex ultrasound scanning as the diagnostic test of choice to evaluate for venous reflux

Level of recommendation: Grade 1 (Strong), Quality of Evidence: B (Moderate)

Rationale

Duplex Ultrasound (DU) is a non-invasive diagnostic test that is safe, sensitive, specific, and cost-effective to evaluate vein incompetence in patients with varicose veins. The test is objective and reproducible, but it requires technical training and experience to perform a thorough and accurate study. It also requires physician expertise to interpret a DU study. DU was recommended as the diagnostic test of choice for patients with chronic venous disease (CVD) in previous SVS/AVF guidelines and in a consensus document of the International Union of Phlebology (UIP).[20, 38, 39] The 2016 Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) panel,[40] and an earlier systematic review, [41] however, did not find sufficent evidence to support or refute the recommendations to use DU as the first line diagnostic test for CVD.

Evidence

Combining data of two prospective comparative studies,[42, 43] a recent systematic review found that using DU scanning for evaluation of chronic venous disease changed management in 10-25% of the patients, who were studied with a hand-held continuous wave Doppler (HHD). (Table 1.).[19] Mercer et al. compared HHD findings with those of DU and found that the HHD sensitivity to detect reflux was only 73% at the saphenofemoral junction (SFJ), 77% at the

485 sapheno-popliteal junction (SPJ) , and 51% for thigh perforators.[42] Treatment based on HHD
486 would have left residual sites of reflux in 24% of the cases. Rautio et al. observed that the HHD
487 sensitivity was 56% at the SFJ and only 23% at the SPJ and concluded that DU finding modified
488 the treatment decision in 9.1%. [44] Darke et al. found better HHD sensitivity at the SFJ (95%)
489 but concluded that HHD was not satisfactory for evaluation of reflux at the SPJ.[45] Another study
490 by Wills et al found HHD sensitivity of 71% at the SFJ and concluded that 29% of the limbs
491 would have had sites of reflux untreated without DU evaluation.[46] Dhillon et al. recently
492 compared HHD with point of care portable color Doppler ultrasound (PCD) in assessing venous
493 reflux.[47] Although PCD had marginally greater sensitivity than HHD and a better negative
494 predicting value above the knee, both tests had a ~30% negative predictive value. This is
495 inadequate for exclusion of significant reflux. Similar to several other studies and reviews,[48, 49]
496 the authors of this guideline recommend routine DU scanning for definitive evaluation of
497 patients for venous reflux. Table 1. summarizes the relevant PICO (patients, intervention,
498 comparator, outcome) data of five studies. [42] [43] [44] [45] [47]

499 Of other imaging modalities, descending contrast venography in some patients is useful
500 to diagnose reflux in the superficial veins.[50] Ascending venography may provide additional
501 information on the anatomy of the superficial system and in some cases it may help
502 intraoperatively to perform complete ablation of superficial veins.[51] However, in the era of high
503 resolution DU imaging and other less invasive diagnostic imaging studies, contrast venography
504 is rarely used today for preoperative evaluation of patients with varicose veins. Contrast
505 venography, intravascular ultrasound, computed tomographic and magnetic resonance imaging
506 and venography are reserved for investigation of the anatomy and function of the deep venous
507 system.[52, 53, 54] Based on evidence of the systematic review and additional data of the literature,

including the recommendations of the 2020 appropriate use criteria (AUC) of multiple vascular societies,[16] the panel strongly supported DU scanning as the current gold standard for the evaluation of reflux in patients with chronic venous disease.

Implementation remarks for guideline 1.1:

1.1.a. Reflux is defined as a minimum value greater than 500 ms of reversed flow in the superficial truncal veins (great saphenous vein, small saphenous vein, anterior accessory great saphenous vein, posterior accessory great saphenous vein) as well as in the tibial, deep femoral, and the perforating veins. A minimum value greater than 1 sec reversed flow is diagnostic of reflux in the common femoral, femoral, and popliteal veins.

Van Bemmelen et al. [55] studied the duration of reflux in the femoral, popliteal and tibial veins in 32 healthy patients in the supine and upright position, using a Valsalva's maneuver, proximal limb compression, and release of distal limb compression. The distal cuff deflation method was the most accurate and reproducible method to measure duration of reflux. The reflux times in standing patients were < 500 msecond in 95% of the patients.[55] Based on data by Labropoulos et al.[56] obtained with DU evaluation of 80 limbs of 40 healthy normal volunteers and 60 limbs of 45 patients with chronic venous disease, a minimum value for abnormally reversed venous flow (reflux) in the great and small saphenous, the tibial and deep femoral vein of over 500 ms has been adopted as the standard for degree of reflux. A similar 500 ms value was also proposed and accepted as the minimum value for patients with incompetence of other superficial truncal veins, including the anterior accessory great saphenous vein (AAGSV).[57] The minimum value for significant reflux in the femoral and popliteal vein of 1sec has also been defined in multiple

previous guidelines and consensus documents[20, 38, 39, 58] and our writing committee also accepted it as best practice statement.

1.1.b. Axial reflux is defined as uninterrupted retrograde venous flow from the groin to the calf. Retrograde flow can be in superficial or deep veins, with or without perforating veins. Junctional reflux is limited to the saphenofemoral or saphenopopliteal junction. Segmental reflux occurs in a portion of a superficial or deep truncal vein.

To define axial, junctional and segmental reflux, we adopted the terminology defined in the updates of the CEAP classification,[15, 31] in the Vein Glossary,[32] and the VEIN-TERM document (See Appendix I.).[33] "Complete axial reflux in a symtomatic patient is pathognomic, but junctional reflux alone is an indication for ablation. Conversely, a competent junction may be associated with an incompetent, pathologic GSV distal to the terminal valve and the source of varicosity in such patients can be either pelvic vein incompetence or an incompetent thigh perforating vein."

1.1.c. A definition of "pathologic" perforating veins in patients with varicose veins (CEAP Clinical Class C2) includes those with an outward flow duration of ≥500 ms and a diameter of ≥3.5 mm on Duplex ultrasound.

In patients with chronic venous disease (C2-C6), the minimal values suggested for clinically significant incompetent perforating veins were 350 ms and 500 ms.[56, 59, 60] Most guidelines and consensus documents agreed, however, to define perforating vein incompetence as those with >500ms outward flow during calf relaxation or release after distal compression.[20, 38, 39]

Labropoulos et al, reported on a 96% specificity and a 73% sensitivity of Duplex scanning in

predicting incompetence of the perforating veins in patients with a vein diameter of 3.9 mm.[61] In this study, one third of the incompetent perforators were <3.9 mm in size. Sandri et al, [62] however, found in his study that >90% of the incompetent perforators were over 3.5 mm in size. The SVS/AVF venous guidelines defined "pathologic" perforating veins as those with outward flow of >500 ms, with a diameter of ≥3.5 mm, located beneath a healed or open venous ulcer (for patients with CEAP class C5-C6).[20, 23, 38] In C4 patients incompetent perforators should be beneath areas of impending skin breakdown or areas of skin vulnerability.[38] These recommendations remain current.

Guideline 1.2

1.2.1.

We recommend that evaluation of reflux with Duplex ultrasound be performed in an Intersocietal Accreditation Commission (IAC) or **American College of Radiology (ACR) accredited vascular laboratory by a credentialed ultrasonographer, with the patient standing whenever possible. Sitting or reverse Trendelenburg position may be used if the patient cannot stand.**

Level of recommendation: Ungraded good practice statement.

1.2.2. We recommend that for evaluation of reflux with Duplex ultrasound we use either a Valsalva maneuver or distal augmentation to assess the common femoral vein and the saphenofemoral junction and distal augmentation with either manual compression or cuff deflation for evaluation of more distal segments. Superficial reflux must be traced to its source, including saphenous junctions, truncal or perforating veins or pelvic origin

varicose veins. The study should be interpreted by a physician trained in venous duplex ultrasound interpretation.

Level of recommendation: Ungraded good practice statement.

Rationale and Evidence

The technique of correct Duplex scanning to investigate venous reflux was previously described in detail. [56 60, 63] A significant part of the test should be performed with the patient in the upright position, to determine degree of reflux and venous diameter.[56] Labropoulos reported on DU results in patients in supine and standing positions. DU in 37 vein segments had reflux >500 ms in the supine position. When the study was repeated in the standing position, 22 segments (59%) showed non-significant reflux <500 ms.[56] The authors concluded that "standing allows more definitive closure of competent valves." To investigate reflux, manual compression of the thigh and calf is suggested to assess reflux. In addition, both the Valsalva technique and rapid cuff deflation have been recommended. [60] Masuda et al.[64] found that reflux in the upper thigh veins--common femoral, femoral, deep femoral, and GSV was similarly demonstrated in both normal and symptomatic states by cuff deflation and the Valsalva technique. To standardize reflux, the panel recommends the generally adopted guidelines[56, 63] of using a Valsalva maneuver or distal augmentation to assess the common femoral vein and saphenofemoral junction and either manual compression or standardized cuff deflation distal to the segment of interest to assess the more distal veins.

Guideline 1.3.

1.3.1. We recommend that a complete Duplex scanning examination for venous reflux in

the lower extremities include transverse grayscale images without and with transducer compression of the common femoral, the proximal, mid and distal femoral and the popliteal veins and the saphenofemoral junction, the great and the small saphenous vein.

Level of recommendation: Ungraded good practice statement.

1.3.2. We recommend that a complete Duplex scanning examination for venous reflux in the lower extremities include measurement of spectral Doppler waveform using calipers. Reflux at baseline and in response to Valsalva or distal augmentation is documented in the common femoral vein and at the saphenofemoral junction, and in response to distal augmentation in the mid-femoral and popliteal vein, in the great saphenous vein at the proximal thigh and at the knee, in the anterior accessory great saphenous vein and in the small saphenous vein, at the saphenopopliteal junction or proximal calf.

Level of recommendation: Ungraded good practice statement.

1.3.3. We recommend that a complete duplex scanning examination for venous reflux in the lower extremities include diameter measurements in patients with the leg in the dependent position, from anterior to posterior wall, at the saphenofemoral junction, in the great saphenous vein at proximal thigh and at the knee, in the anterior accessory great saphenous vein, and in the small saphenous vein at the saphenopopliteal junction or proximal calf. Images of both normal and abnormal findings should be documented in the records of the patient.

Level of recommendation: Ungraded good practice statement.

Rationale

To use duplex scanning for evaluation and follow-up of patients, appropriate documentation of both normal and abnormal findings in the patient's records is mandatory. A complete duplex scanning examination for chronic venous disease includes[65] visualization, compressibility, venous flow with and without augmentation, measurement of duration of reflux and measurements of vein diameter. Vein diameter should be acquired in the dependent position, in transverse, anterior wall to posterior wall measurement. Spectral Doppler waveforms with the extremity(s) in a dependent position, demonstrating baseline flow and response to distal augmentation must be recorded. If present, reflux duration of retrograde flow must be measured with calipers in the following segments: common femoral vein, saphenofemoral junction, GSV at proximal thigh and at knee, femoral vein at the mid-thigh, popliteal vein, anterior and posterior accessory great saphenous vein (when identified), SSV at saphenopopliteal junction or midcalf, if the junction is not identified. [66] Measurements of reflux in calf-veins is optional. Axial reflux is defined as uninterrupted retrograde venous flow from the groin to the calf, either to the upper calf or to the level of the ankle. Superficial reflux is confined to the superficial venous system, deep reflux is confined to the deep venous system, and combined reflux involves any combination of the three main venous systems (superficial, deep, perforating).Some authors suggest documenting the extent (length) of incompetent veins as well as the distance of the incompetent truncal vein from the skin.[67]

Evidence

Several studies investigated the association of vein diameter with reflux, clinical class and outcome of intervention in patients with varicose veins.[68-75] Kim et al evaluated 198 limbs of 99 patients and found that the diameter of the GSV in the lower thigh with reflux > 0.5 s with rapid cuff deflation in standing patients was significantly larger than that of GSVs without reflux (4.7 mm vs 4.2 mm; P < .001). The cutoff value of the GSV diameter that was associated with reflux in this study was 5 mm (P = .025). [68] Another study from Korea investigated 777 patients and found 5.05 mm to be the best positive predictive value for reflux in the GSV and 3.5 mm in the SSV. [71] Others, however, found that ablation of small (<5mm) symptomatic GSV provided clinical success in 83% of limbs at 3 months with significant improvement in venous disease severity score, with a median change of -2 (IQR, -3, -1).[65]

A retrospective study of 728 limbs of 531 patients with chronic venous disease found a positive correlation between vein diameter and reflux duration measured with DU and CEAP clinical class, venous disease clinical severity score (VCSS) and the HASTI (Heaviness, Achiness, Swelling, Throbbing, Itching) scores.[76] Several other studies provide evidence that superficial vein diameters correlate with the CEAP Class and the severity of chronic venous disease.[72-74] In a prospective observational study of 330 symptomatic varicose vein patients, vein diameter had a significant association with VCSS (P = 0·041), but no other QoL or symptom measures were related to vein diameter.[77] Mendoza et al found that measurements at the proximal thigh at 15 cm distal to the groin correlated better with reflux and they were more sensitive and specific than measurements made at the saphenofemoral junction. [72] In a study of 152 patients with varicose veins, a GSV diameter of 5.880 mm measured 5 cm distal to the saphenofemoral junction using computed tomography in patient in the supine position was the cut-off value to predict reflux (sensitivity 91.4%, specificity 81.8%). [78] The authors concluded, however, that vein diameter alone cannot be used as an absolute reference for venous reflux.

High level of evidence on treatment decisions made based on vein diameters alone, however, is still lacking. Analyzing data of 242 patients who participated in a randomized controlled trial, Attaran et al recently reported a poor correlation between the GSV diameter and baseline VCSS (R = -0.004; P = .95) and between the GSV diameter and VCSS improvement for </=36 months follow-up (R = 0.04; P = .55). [69] Gibson et al. in 91 patients also found a weak correlation between increasing GSV diameter and VCSS and no correlation between GSV diameter and QOL scores, including the CIVIQ, VEINES-QoL and VEINES-Sym. These authors concluded that using GSV diameter as the sole criterion for determining medical necessity for the treatment of GSV reflux is inappropriate.[70] To establish the minimal values for diameters of incompetent superficial truncal veins that could be used as a criterion for ablation, it is important to collect more data on patients where Duplex scan was used in the dependent position, measured in the GSV at the proximal third of the thigh.

Guideline 1.4.

We recommend the use of the 2020 upgraded Clinical Class, Etiology, Anatomy, Pathophysiology (CEAP) for classification of chronic venous disorders. The clinical or basic CEAP classification may be used for clinical practice, and the full CEAP classification system should be used for clinical research.

Level of recommendation: Ungraded good practice statement.

Rationale and Evidence

Evaluation of patients should include documentation of the clinical class of chronic venous disorder. The panel recommends using the recently updated 2020 Clinical Class, Etiology,

Anatomy, Pathophysiology (CEAP) classification system and reporting standards as a good practice statement (Table 2.). [15] Each clinical class (C0 – C6) is further characterized with a subscript, depending on the presence or absence of symptoms (S, symptomatic, A, asymptomatic), for example, $C2_A$ or $C2_S$. Symptoms include aching, pain, tightness, skin irritation, heaviness, muscle cramps, and other complaints attributable to venous dysfunction.[31] The basic CEAP classification is used for clinical practice, and the full CEAP classification system is used for clinical research. For patients with C2 disease (varicose veins), in the most recent CEAP clinical classification, recurrent varicose veins require a different diagnostic and treatment strategy. Consequently, these patients now are identified with the subscript (r) for recurrence: $C2_{r.}$ [15]

2. HIGH LIGATION AND SURGICAL STRIPPING VERSUS ENDOVENOUS ABLATION

Guideline 2.1.

2.1.1. For patients with symptomatic varicose veins and axial reflux in the great or small saphenous vein, who are candidates for intervention, we recommend superficial venous intervention over long-term compression stockings.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: B (Moderate)

2.1.4. For patients with symptomatic varicose veins and axial reflux in the anterior accessory or posterior accessory great saphenous vein, who are candidates for intervention, we suggest superficial venous intervention over compression stockings.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

2.1.5. For patients with symptomatic varicose veins and axial reflux in the superficial truncal veins, we suggest compression therapy for primary treatment if the patient's ambulatory status and underlining medical conditions warrant a conservative approach, or if the patient prefers conservative treatment, for either a trial period or for definitive management.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Rationale

Compression garments of varying strength, in addition to a healthy lifestyle, weight loss, exercise and avoiding prolonged standing or sitting, have long been recommended to patients with varicose veins to decrease pain, discomfort and swelling caused by congestion due to refluxing and dilated superficial veins.[20] Compression has been shown to decrease acute symptoms,[79] but there is no evidence that long-term compression is either curative or arrests or reverses progression of chronic venous disease. An arbitrary 3-month period of compression treatment before an intervention, often used by insurance companies before procedural authorization, has not been supported by scientific evidence.

Evidence

A recent Cochrane Review studied the effectiveness of compression stocking for patients with varicose veins.[80] Data on 1021 patients with C2-C4 disease from 13 RCTs were analyzed. A variety of compression stocking ranging from 10 to 50 mmHg were used in the studies, none reported QoL measures to assess outcome. No side effects were reported. The review concluded that "there is insufficient high-certainty evidence to determine whether or not compression

738 stockings are effective as the sole and initial treatment of varicose veins in people without healed
739 or active venous ulceration, or whether any type of stocking is superior to any other type." [80]

740 Clinical outcomes at 2 years after conservative treatment, which included lifestyle
741 modifications and compression stocking, vs surgery, that included high ligation and saphenous
742 stripping (HL&S), by Michaels et al. were reported in the randomized REACTIVE trial of 246
743 patients with varicose veins.[81] At 2 years, patients who underwent surgery to ablate the
744 superficial varicose veins had significant QoL benefit based on the SF-6D and the EQ-5D
745 scores.[81] Improvement in symptoms and venous anatomy was also significant. In this United
746 Kingdom study, surgical treatment for varicose veins offered a modest health benefit for
747 relatively little additional NHS cost relative to conservative treatment.[82]

748 An additional randomized trial including 153 patients randomized to surgery or
749 compression stockings found surgery to be associated with significant decreases in VCSS and
750 HRQol in comparison to compression therapy.[83] In addition, others have found that the majority
751 of patients to benefit from surgery even after failing to respond to compression therapy[84] and in
752 the United Kingdom, the conservative management of varicose veins was not found to be cost
753 effective .[85, 86] The consistency of the data supports a strong recommendation for surgical
754 intervention over compressions stockings alone in those who are candidates for a procedure and
755 are willing to undergo an intervention to treat symptomatic incompetent superficial truncal veins
756 and varicose tributaries. There is no evidence to support a benefit to a trial of three months
757 compression therapy before offering a surgical or endovenous intervention in most patients.

758 Based on these data, the panel adopted the previous SVS/AVF guidelines[20] and
759 recommends intervention over compression stocking alone to those who are candidates for a
760 procedure and willing to undergo an intervention to treat the symptomatic incompetent

761 superficial truncal veins and varicose tributaries. The patient's ambulatory status and any
762 underlining medical conditions must be considered in making a treatment recommendation. The
763 decision making should be shared and patients may elect to undergo a trial with compression, or
764 choose definitive treatment with compression alone.
765 .

766 **Guideline 2.2.**

767 **2.2.1. For patients with symptomatic varicose veins and axial reflux in the great saphenous**
768 **vein, who are candidates for intervention, we recommend treatment with endovenous**
769 **ablation over high ligation and stripping of the great saphenous vein because of less post-**
770 **procedure pain and morbidity as well as and an earlier return to regular activity.**

771 **Level of recommendation: Grade 1 (Strong), Quality of Evidence: B. (Moderate)**

772 **2.2.2. For patients with symptomatic varicose veins and axial reflux in the small saphenous**
773 **vein, who are candidates for intervention, we recommend treatment with endovenous**
774 **ablation over ligation and stripping of the small saphenous vein because of less post-**
775 **procedure pain and morbidity as well as an earlier return to regular activity.**

776 **Level of recommendation: Grade 1 (Strong), Quality of Evidence: C. (Low to very low))**

777 **2.2.3. For patients with symptomatic varicose veins and axial reflux in the anterior**
778 **accessory or posterior accessory great saphenous vein, who are candidates for intervention,**
779 **we suggest treatment with endovenous ablation, with additional phlebectomy, if needed,**
780 **over ligation and stripping of the accessory great saphenous vein because of less early pain**
781 **and morbidity and an earlier return to regular activity.**

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Rationale

All the treatment modalities discussed in this section can be used to successfully treat symptomatic reflux of the great saphenous vein (GSV) (Fig.1.). Surgical treatment includes high ligation of the GSV or SSV at the saphenofemoral junction (SFJ) or at the sapheno-popliteal junction (SPJ), respectively, and invagination stripping of the distal portion of the vein under general anesthesia, or under tumescent local anesthesia. Contemporary surgical and endovenous procedures are universally performed with DU assistance. Endovenous interventions, including thermal and non-thermal ablations, are minimally invasive percutaneous procedures that maybe performed in an outpatient setting. Thermal ablations can use laser technology with different types and wavelengths of laser fibers (EVLA)[87, 88] or can be performed with radiofrequency ablation (RFA),[65, 89, 90] using local tumescent anesthesia. The most frequently used devices in the United States include, among others, the VenaCure 1470-nm laser system (Angiodynamics, Waterlooville, UK) and the Closurefast RFA system (Medtronic, Minneapolis, MN).

Non-thermal (and non-tumescent) ablation include Endovenous cyanoacrylate closure (CAC) (VenaSeal; Medtronic, MN)[12, 91, 92] or VariClose Vein Sealing System (VVSS); Biolas, Ankara, Turkey,[93, 94] the MOCA procedure (mechanico-chemical ablation), using the ClariVein device (MeritMedical, South Jordan UT).[95,96-98] Ultrasound guided foam sclerotherapy (UGFS) can also be another effective method to close superficial truncal and varicose veins, using either physician prepared sodium tetradecyl sulfate or polidocanol foam made at the bedside with the Tessari technique,[99, 100] or commercially prepared polidocanol endovenous microfoam (PEM) (Varithena, Boston Scientific, Marlborough, MA).[101] The Tessari technique prepares foam at

805 the bed-side, using a three-way stopcock and two syringes, mixing air with the liquid sclerosing
806 solution to create foam. [99] Varicose tributaries and tortuous superficial truncal veins like the
807 accessory saphenous veins can be removed under local or tumescent anesthesia using ambulatory
808 phlebectomy with vein hooks or forceps through multiple small stab-wounds (mini or
809 microphlebectomy). Saphenous vein sparing operations (ASVAL, CHIVA) and cryo-stripping
810 were not analyzed in our systematic review. For evidence of effectiveness of these procedures,
811 the readers are referred to previous guidelines.[20, 27]

812 Important outcomes measures used to compare procedures performed in all studies
813 included anatomic closure, complications, time to return to normal activity, recurrence, need for
814 secondary interventions, generic and disease specific quality of life. The decision to recommend
815 minimally invasive endovenous office procedures over contemporary HL&S in this guideline
816 was made based on differences in early outcomes, including periprocedural pain and discomfort,
817 need for analgesia medications, early minor adverse events, early QoL measures and earlier
818 return to regular activities.
819
820 Evidence
821 A systematic review by Farah et al. [19] analyzed data from 30 RCTs, reported in 44 publications [5-
822 9, 13, 100, 102-137]and data of 16 observational studies[11, 138-152] that compared results of surgical
823 treatment with those of endovenous ablations, using any of the techniques. The systematic
824 review [19] found that HL&S was associated with lower likelihood of being pain free (RR. 0.39;
825 95% CI 0.29-0.54)[138, 146] and increased need for analgesia (RR. 1.83; 95% CI, 1.17-2.86)[139, 141]
826 than EVLA. In the CLASS randomized controlled trial, that compared foam, laser, and open
827 surgical treatments, Brittenden et al reported significantly fewer early adverse events after laser

828 ablations than after surgery (7% vs 1%, P<.001).[100] Successful ablation of the saphenous vein,
829 however, was less common in the foam group than in the open surgery group (P<.001). At 6
830 weeks, patients who underwent surgery had lower SF-36 scores indicating worse generic QoL
831 than those who had laser treatment. The difference was significant in bodily pain, vitality and
832 role limitations due to emotional and physical health. These differences between groups no
833 longer existed at 6 months.[100] In the systematic review, there was no difference in disease
834 specific QoL scores when HL&S was compared with RFA at one month.[19 115, 132]

835 In the EVOLVE randomized controlled trial time to return to normal activities was
836 significantly better after RFA than after HL&S (mean, 1.15 days vs mean of 3.89 days; P =.02).
837 In the RFA group, 80.5% of patients returned to routine activities of daily living within 1 day,
838 compared with 46.9% of patients in the HL&S group (P <.01).[114] In a recent RCT that compared
839 HL&S with CAC ablation of the GSV in 126 patients, closure rate was 100% in both groups at 3
840 months but the postoperative pain and ecchymosis grades were significantly lower in the CAC
841 group.

842 Both open surgical stripping and the currently available endovenous procedures are durable
843 procedures. Five-year results in the CLASS study confirmed equally improved disease specific
844 QoL in both the surgery and the laser groups and both were superior compared to those who
845 were treated with physician compounded foam.[10] Using a probabilistic cost-effectiveness model
846 iteration, this British study favored laser ablation over foam ablation. When the main outcome
847 measure was occlusion rate of the treated GSV, 5-year results were similar after HL&S and
848 EVLA (96% vs 89%), but significantly worse after UGFS (51%, P<.001).[10] A meta-analysis of
849 nine RCTs by Kheireseid et al. showed that at 5 years RFA and EVLA are as effective as surgery
850 for treating saphenous vein insufficiency. The study also concluded that the number of patients

available for analysis was too small to draw any definite conclusions.[37] Similarly, an Agency for Healthcare Research and Quality systematic review [153] found either no difference or insufficient data to support differences in important long-term patient outcomes between thermal ablation and surgery.

Guideline 2.3.

2.3.1. For patients with symptomatic varicose veins and axial reflux in the great or small saphenous vein, we recommend treatment with ligation and stripping of the saphenous vein if technology or expertise in endovenous ablation is not available, or if venous anatomy precludes endovenous treatment.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: B (Moderate)

2.3.2. For patients with symptomatic varicose veins and axial reflux in the anterior accessory or the posterior accessory great saphenous vein, we suggest treatment with ligation and stripping of the accessory great saphenous vein, with additional phlebectomy, if needed, if technology or expertise in endovenous ablation is not available, or if venous anatomy precludes endovenous treatment.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Rationale and Evidence

New technology may not be available in some health care systems, or the devices can be too expensive for patients or facilities when there is no reimbursement for the procedure provided by third party payors. In addition, aneurysmal dilation of the GSV close to the SFJ,

subcutaneous location of a truncal superficial vein above the saphenous fascia and close to the skin, and tortuosity of the GSV or the small saphenous vein (SSV) (Fig.2.) are relative anatomic contraindications to some endovenous procedures.

Although the systematic review supporting these guidelines[19] found a 2-fold greater 5 year risk of recurrent varicosities after HL&S in comparison to RFA (RR: 2.00; 95% CI: 1.22 to 3.27), this was based on a single study[7] with an intermediate risk of bias. Other reviews, based largely on the same data, found no differences in 5-year recurrence between HL&S, RFA, and EVLT.[37] Overall, contemporary high ligation and stripping, performed under tumescent anesthesia had excellent mid and long term results in multiple randomized studies,[6-11] and the committee strongly recommends performing HL&S, if technology or expertise is not available for an endovascular procedure, or if the anatomy favors surgery in patients who are appropriate candidates for an intervention.

Guideline 2.4

2.4.1. For patients with symptomatic varicose veins and axial reflux in the great saphenous vein, who place a high priority on long-term outcomes of treatment (quality of life and recurrence), we suggest treatment with endovenous laser ablation, radiofrequency ablation, high ligation and stripping over physician-compounded ultrasound guided foam sclerotherapy. Level of recommendation: Grade 2 (Weak) Quality of Evidence: B. (Moderate)

2.4.2. For patients with symptomatic varicose veins and axial reflux in the small saphenous vein who place a high priority on long-term outcomes of treatment (quality of life and recurrence), we suggest treatment with laser ablation, radiofrequency ablation, ligation

and stripping from the knee to the upper or mid-calf over physician-compounded ultrasound guided foam sclerotherapy. Level of recommendation: Grade 2 (Weak) Quality of Evidence: C. (Low to very low)

2.4.3. For patients with symptomatic varicose veins and axial reflux in the anterior accessory or posterior accessory great saphenous vein, who place a high priority on long-term outcomes of treatment (quality of life and recurrence), we suggest treatment of the refluxing superficial trunk with endovenous laser ablation, radiofrequency ablation, high ligation and stripping, with additional phlebectomy, if needed over physician-compounded ultrasound guided foam sclerotherapy.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Rationale and Evidence

This recommendation applies only on physician-compounded UGFS, when using it for ablation of a superficial truncal vein and does not address the value of UGFS in the management of tributary varicosities. The recommendation is based largely on evidence of a higher rate of recurrent varicosity, higher risk of recurrent intervention, lower rate of occlusion rate of the treated truncal vein and lower disease specific QoL at 5 years following UGFS when compared with HL&S or thermal ablations.[7, 8 10] Disease-specific QoL at five years was also better for both HL&S (−2.60; 95% CI, −3.99 to −1.22, P<.001) and EVLA (-2.86; CI, -4.49 to -1.22; P<.001) than for UGFS.[10] Data on long term effectiveness of commercial polidocanol endovenous microfoam (PEM) are currently not available, although the results of one RCT[101] and of several retrospective studies[154-156] are encouraging.

Cost-effectiveness. HL&S, EVLA, and RFA are all effective treatment strategies for symptomatic varicose veins arising from axial venous reflux, although both reimbursement and out-of-pocket costs to the patient can vary significantly, depending on insurance authorization, and out-of-pocket costs may be the most important consideration for many patients.[36] Therefore, the treating physician must be aware of the costs of different treatment options and counsel the patient accordingly.

As cost-effectiveness varies with the setting and local reimbursement system, and most data on cost comes from outside of the United States, our supporting systematic review did not evaluate cost-effectiveness. In British studies physician – compounded UGFS had the lowest initial costs, although this was partially offset by the long-term costs of reintervention and lower quality of life. [86, 157]. HL&S in the inpatient setting was the most expensive strategy. At a threshold of £20,000 ($28,000) per quality-adjusted life-year (QALY) in the United Kingdom, EVLA ranked first, followed by RFA, UGFS, HL &S, and conservative care in terms of cost-effectiveness. [86] In those patients in whom out-of-pocket costs are a dominant consideration, the treating physician must be aware of the costs of different treatment options and counsel the patient accordingly. A systematic review of the cost effectiveness of varicose vein treatment in the UK found that physician-compounded UGFS had a significantly greater reintervention rate than other procedures that all had similar reintervention rates. The cost per QALY of EVLA vs UGFS was £16,966 ($23,700) per QALY, supporting EVLA as the most cost-effective procedure. RFA was a close second while MOCA, UGFS, CAC, conservative care, and high ligation and stripping were not cost effective at current prices in the UK National Health Service. [86] A Canadian cost analysis study found that RFA would be about $110-$220 more expensive

940 than open surgery but is has fewer major and minor early complications (low level of
941 evidence).[158]
942
943 **Small Saphenous Vein.** The SSV is one of the important superficial truncal veins that requires
944 treatment if symptomatic axial reflux is document by DU (Fig.2.). Data on durability of
945 endovenous treatment of the SSV however, remains limited. The systematic review by Farah et
946 al. [19] included two RCTs, reported in three publications that compared outcomes after HL&S vs
947 EVLA of the SSV. [118, 126, 127] HL&S was associated with lower anatomic closure rates and
948 increased minor sensory disturbance at 1 month. At 2 years anatomic closure rate was still
949 superior after EVLA but there was no significant difference in clinical recurrence, sensory
950 disturbance or any quality-of-life scores between the groups.[118] The use of non-thermal
951 techniques for treatment of the SSV appear promising, since the proximity of the sural nerve may
952 result in neurologic complications following open surgery or thermal ablations.[159] [160] CAC was
953 used to treat SSV insufficiency in 163 limbs of 128 patients by Cho et al. [161] Closure rate at 2
954 years was 96.3%. No major complications, including sural nerve injury, were noted. In a
955 retrospective study results of high ligation and stripping of the SSV were compared to the
956 MOCA procedure treating isolated SSV reflux.[162] Recurrence rate at 18 months were similar in
957 the two groups. The MOCA procedure, performed in 60 limbs had less pain on the first
958 postoperative day and the patients returned to work earlier than those who had open surgery Leg
959 paresthesia occurred in 3.4 % after open surgery and in 0% after the MOCA procedure. [162]
960 Others observed more saphenous neuritis after thermal ablation. [163]
961 A systematic review by Boersma et al. [164] that included 49 articles reporting on 5 RCTs
962 and 44 cohort studies found a 58% anatomical success rate after surgery, 98.5% and 97.1%

963 success after EVLA and RFA, respectively, and a 63.3% success after physician-compounded
964 UGFS at a mean follow-up of 12.5 months (0.5-48). Neurologic complications were most
965 frequent after surgery (19.6%) and thermal ablation (EVLA: 4.8%; RFA: 9.7%). These pooled
966 data had considerable heterogeneity. The study supported thermal ablations (EVLA /RFA) for
967 SSV treatment over surgery. A Cochrane review of 3 RCTs also found that at a moderate to low
968 level of evidence EVLA resulted in higher closure rate at 6 weeks and less recurrence at 1 year
969 than open surgery. The quality of evidence was low to suggest physician-compounded UGFS
970 over surgery. Further RCTs with longer follow-up are needed to define optimal treatment of
971 SSV ablation, but the lack of neurologic injury after non-thermal ablations is promising and
972 appears to be of considerable clinical benefit.
973
974 **Anterior and Posterior Accessory Great Saphenous Vein.** Both veins are superficial truncal
975 veins that join the GSV just distal to the SFJ (Fig.1.). They may need treatment if axial
976 incompetence is confirmed in patients who have symptomatic varicose veins. The posterior
977 accessory great saphenous vein (PAGSV) is rarely of clinical significance, [165, 166] but an
978 incompetent anterior accessory great saphenous vein (AAGSV) alone or combined with GSV
979 reflux frequently contributes to varicosities and also to more advanced chronic venous
980 insufficiency. An incompetent AAGSV is a source of recurrence after GSV ablation and it also
981 carries a morbidity similar to a refluxing GSV.[167 168, 169] The incidence of superficial thrombosis
982 in one study was significantly higher in the AAGSV than the GSV (6.41% vs 2.17%, P <
983 .05).[168] Endovenous therapies for the treatment of symptomatic AAGSVs demonstrated similar
984 early outcomes than to patients with symptomatic GSV reflux.[57, 170] For standalone ablations,
985 the rVCSS scores were similar between the groups pre and post procedure; however, CIVIQ20

scores returned to pre-intervention levels in standalone ablation AAGSV patients at 6 months, suggesting that patients with symptomatic AAGSV treated with ablation also require treatment of the associated tributaries (varicosities) to achieve outcomes similar to patients who have GSV ablation.[57]

3. THERMAL ABLATION VERSUS NON-THERMAL ABLATION OF SAPHENOUS VEINS

Guideline 3.1

3.1.1.For patients with symptomatic axial reflux of the great saphenous vein, we recommend both thermal or non-thermal ablation from the groin to below the knee, depending on the available expertise of the treating physician and the preference of the patient.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: B (Moderate)

3.1.2.For patients with symptomatic axial reflux of the small saphenous vein, we recommend both thermal or non-thermal ablation from the knee to the upper or mid-calf, depending on the available expertise of the treating physician and the preference of the patient.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: C (Low to very low)

3.1.3. For patients with symptomatic axial reflux of the anterior accessory or posterior accessory great saphenous vein we suggest either thermal or non-thermal ablation, with additional phlebectomy, if needed, depending on the available expertise of the treating physician and the preference of the patient.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Rationale

Both thermal and non-thermal ablation techniques are minimally invasive, percutaneous office-based procedures. Thermal ablation (EVLA[87, 88], RFA[65, 89, 90]) requires tumescent local anesthesia that may cause pain and discomfort during the procedure. Non-thermal ablations include UGFS with physician-compounded foam using the Tessari technique[99, 100] or the use of polidocanol endovenous microfoam (Varithena) .[101] Other non-thermal ablation techniques include CAC[12, 91, 92] (using the VenaSeal (Medtronic, Minneapolis, MN) system or the Turkish Glue Kit (VariClose Vein Sealing System (VVSS); Biolas, Ankara, Turkey) and mechanical-chemical ablation, the MOCA procedures . [95 96-98] All non-thermal ablations are performed without the need for tumescent anesthesia. The heterogeneity of non-thermal techniques does not allow a direct comparison of all thermal with all non-thermal ablations.

Evidence

To compare outcomes of thermal vs non-thermal, [96, 171] techniques, a systematic review[19] analyzed data from 16 RCTs, reported in 27 publications[7, 8, 10, 12, 93, 94, 100, 123, 134-137, 172-183] as well as data from 11 comparative observational studies.[11, 151, 152, 184-191] The review found significantly higher VAS pain scores perioperatively for EVLA than for CAC or UGFS, using physician compounded foam.[173, 178, 186] Early QoL scores in some studies were also better for UGFS [100] and for the MOCA procedure[96] than for EVLA. At one year, however, EVLA was associated with higher anatomic closure rates than UGFS (RR: 1.23; 95% CI: 1.11 to 1.37, I^2=0.00%).[134, 178, 186] Compared to physician compounded UGFS, EVLA and RFA were also associated with a lower risk of recurrence (RR: 0.18; 95% CI: 0.05 to 0.59) and (RR: 0.06; 95%

CI: 0.01 to 0.44) , respectively. In the CLASS study UGFS using physician compounded foam resulted in a lower anatomic closure rate (RR: 2.91; 95% CI: 1.89 to 4.49) and increased risk of reinterventions at 1 and 5 years.[10] At 5 years, disease specific QoL was better for EVLA than for UGFS. [10] Generic quality-of-life measures were similar.[5]

A British RCT, reported by Lattimer et al found that physician-compounded UGFS was 3.15 times less expensive than EVLA (£230.24 vs £724.72) with comparable effectiveness but 56% (versus 6%) of the patients who underwent UGFS required additional treatment.[177] While the potential for reintervention is clearly higher due the higher rates of recanalization following UGFS, when performed with physician compounded foam, this technique remains an important tool because of the much lower cost and easy availability, compared to other catheter based techniques. Long term results and comparative studies with polidocanol endovenous microfoam are needed.

Early adverse events were reported to be more frequent after EVLA [93] or RFA[189] than after CAC (Table 3.). Some clinical advantages of CAC, as compared to thermal techniques, up to one year, have been demonstrated in several publications, [93, 173, 180, 189] but a prospective study by Ay et al. [151] found that QoL (CIVIQ-14) was better in a group of 70 patients who underwent RFA than in the group of 85 patients who were treated with CAC (P<.05).[151] However, RFA at 1 year was associated with an increased risk of recurrent incompetence compared to CAC (RR: 3.22; 95% CI: 1.07 to 9.64, I^2=0.00%,).[180, 189] In a systematic review Vos et al.[192] reported on pooled anatomic success for MOCA and CAC was 94.7% and 94.8% at 6 months and 94.1% and 89.0% at 1 year, respectively. In a network meta-analysis Kolluri et al. [193] compared early outcomes with VenaSeal (Medtronic, Minneapolis, MN) with outcomes after EVLA,RFA, MOCA, sclerotherapy and open surgery. At 6 months Venaseal had the highest probability of

anatomic success, it ranked first in reduction of postoperative pain score from baseline (P = .690) and was lowest in occurrence of adverse events (P = .650). Three-year occlusion rate after CAC treatment was 94.7% (95% CI, 87.9%-100%) in a prospective study by Almeida et al.[91] Allergic reaction to cyanoacrylate is rare but it has been reported[194] and those with previous hypersensitivity reactions to cyanoacrylates or patients with acute superficial thrombophlebitis or sepsis should not be treated with CAC.

The five-year extension study of the VeClose trial was recently published by Morrison et al. [12] Freedom from recanalization at 5 years in the randomized CAC and RFA groups were 91.4% and 85.2%, respectively, demonstrating noninferiority of CAC compared with RFA. Both groups showed sustained improvements in quality-of-life scores.

The MOCA procedure was also evaluated in several comparative studies and results up to 3 years have been reported.[172 96, 97, 175, 176, 195] In a RCT, Bootun et al compared intraprocedural pain scores in 60 patients who received mechanochemical ablation (ClariVein) to those of 59 patients who were treated with radiofrequency ablation (Covidien VenefitTM).[172] Both maximum and mean pain scores were significantly lower in the mechanochemical ablation group compared to the radiofrequency ablation group (19.3mm vs 34.5 mm, P<.001; 13.4mm vs. 24.4 mm P<.001). In the MARADONA RCT that randomized 213 patients, mechanochemical ablation resulted in less postoperative pain but more hyperpigmentation than RFA.[175] There were more anatomic failures reported after the MOCA procedure than after RFA, but patients in both groups had similar QoL scores at 1 and 2 years. In the LAMA trial 150 patients were randomized to EVLA or the MOCA procedure. Similar low intraprocedural pain scores (22, 9–44 vs 15, 9–29, *P* = 0.210.) were reported after both procedures. At 1year, anatomical occlusion rates after EVLA were significantly better than after MOCA (91% vs 77%, *P* = 0.020.) Both EVLA and

MOCA were highly efficacious at 2 years and both significantly improved disease severity, symptoms, and QoL. In another RCT by Tawfik et al,[183] 100 patients were randomized for laser or the MOCA procedure. MOCA was associated with better Venous Clinical Severity Score, less frequent phlebitis, and shorter time to return to work. Three-year results of an RCT, evaluating the MOCA procedure vs thermal ablation (EVLA or RFA) were reported by Vahaaho et al. [195] One hundred and seventeen patients were treated, and the occlusion rate at 3 years was significantly lower with MOCA than with either EVLA or RFA (82% vs 100%, P=.005). GSV >7mm in diameter had increased recanalization rate after MOCA.

In another study, EVLA was associated with a lower recurrent varicosity scale score than UGFS, using physician compounded foam, and RFA was associated with a lower risk of re-intervention compared with UGFS (RR: 0.44; 95% CI: 0.27 to 0.71).[196] No significant differences were found for other outcomes such as DVT, recurrent varicosity, recurrent ulceration, edema, pigmentation, or recurrent ulceration**.**

In a recent retrospective study of 1070 patients with chronic venous disease (C2-C6) that included 470 C2 patients, polidocanol endovenous microfoam (PEM) ablation (Varithena, BTG International Ltd. London, UK) was compared with EVLA, using the VenaCure 1470-nm laser system (Angiodynamics, Waterlooville, UK). Reflux was eliminated in 93.5% (514/550) and 92.8% (482/520) of the PEM and EVLA treated patients during a follow-up that averaged 3 years. There were no neurological or cardiac adverse events after PEM treatment. PEM appears to be a promising new technology but the only RCT that is currently available compared endovenous microfoam with placebo to confirm safety and early efficacy.[101]

For treatment of the incompetent below-the-knee segment of the GSV, a systematic review by Sussman et al. found that thermal ablation had a lower incidence of saphenous nerve injury

that HL &S. [197] Endovenous below-the knee thermal ablations in some studies were used with good result[198] and an RCT failed to show any nerve injury caused by below-the-knee EVLA.[199] Recent results with non-thermal ablation, however, appear promising as no saphenous or sural nerve injury was reported by Jimenez et al after ablation of 49 below-the-knee GSV and 23 SSV, using commercially prepared endovenous microfoam.[200]

In summary, both thermal and non-thermal ablation techniques are safe and effective, but we cannot recommend one technique over the others. All techniques result in improved QoLscores and good clinical effectiveness 3 to 5 years after the procedures. The early benefit of non-tumescent non-thermal procedures over thermal ablation include less pain and discomfort, but the decreased anatomic closure rates for the MOCA procedure at 3 years and for UGFS with physician compounded foam, at 5 years make them less durable treatment over thermal ablations. It should be noted however, that CAC was non-inferior to thermal ablation at 5 years in one study.[12] Prospective comparative studies with endovenous microfoam are needed to confirm long-term clinical efficacy, a decreased incidence of nerve injury and recommend PEM over other ablation techniques.

GUIDELINE 4. INCOMPETENT PERFORATING VEIN ABLATION IN PATIENTS WITH CEAP Class C2 VARICOSE VEINS

Guideline 4.1.

4.1.1 For patients with varicose veins (CEAP Class C2), who have significant, symptomatic axial reflux of the great or small saphenous vein, we recommend against treatment of

incompetent perforating veins concomitant with the initial ablation of the superficial truncal veins.

Level of recommendation: Grade 1 (Strong), Quality of Evidence: C (Low to very low))

4.1.2. For patients with varicose veins (CEAP Class C2), who have significant, symptomatic axial reflux of the anterior accessory or posterior accessory great saphenous vein, we suggest against treatment of incompetent perforating veins concomitant with the initial ablation of the superficial truncal veins.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Rationale

Patients with CEAP Class C2 varicose veins often do not have incompetent perforating veins identified by DU, even when they exist, since many vascular labs concentrate on imaging superficial truncal veins (GSV, SSV, AAGSV, PAGSV) and tributary veins. There is a large number of perforating veins in the lower extremities, and their common locations have been identified in elegant anatomic dissections.[201, 202] When perforating veins are identified during evaluation of varicose veins, they are often competent and functioning normally. However, incompetent perforating veins may also be identified in the thigh and calf when a complete lower extremity venous study is performed as part of the initial evaluation (Fig. 3.). Incompetent thigh perforator veins adjacent or connected to incompetent saphenous veins are particularly easy to identify, due to their proximity to thigh truncal veins, and these perforator veins can occasionally be the single connection between an incompetent truncal thigh vein and the deep venous system, functioning in a role similar to the SFJ.

When a venous DU identifies an incompetent thigh or calf perforator vein, in conjunction with incompetent truncal and/or tributary veins, in patients with symptomatic CEAP Class C2 disease, a decision must be made on how to proceed. Is it better to perform ablation of the superficial truncal vein alone and treat the perforator vein later, if needed, as a staged procedure? Previous guidelines recommended a combined procedure in patients with more advanced chronic venous insufficiency. [20, 38]

Evidence

The systematic review of Farah et al. [19] included two RCTs with an intermediate risk of bias to define the role of perforator ablation in varicose vein patients with CEAP Class C2 disease (Table 4.).[203, 204] The first RCT by Kianifard et al.[203] had patients with primary great saphenous varicose veins and incompetent perforator veins undergo either standard surgery (HL&S and phlebectomies) or standard surgery combined with subfascial endoscopic perforator surgery (SEPS). Of the 72 patients randomized, 38 patients underwent SEPS (71% C2 disease), and 32 did not (75% C2 disease). At one year the Short Form 36 (SF-36) scores were no different between the two groups, except for bodily pain score, which improved in the SEPS group. The AVVSQ score improved in both groups. While the VISUAL ANALOGUE SCALE (VAS) score for pain, mobility and cosmetic appearance improved in both groups at the 1-year mark ($p<0.05$), the improvement in mobility was only significant in the non-SEPS group ($p<0.05$). Follow-up duplex scans showed that IPVs in the untreated leg were significantly more frequent than in the SEPS group.

The other study was by Park et al [204] who randomized patients with C2 and C3 disease to either endovenous laser ablation of IPVs in the thigh followed by ablation of the GSV below the

incompetent perforator vein (n=34) or ablation of the GSV starting just proximal to the thigh perforator without ablation of the perforator vein (n=35). Technical success was significantly lower with ablation of the perforators (76.5%) compared to ablation of the GSV (100%) [p = .002]; however, there was no significant difference in clinical success (continued closure of treated vein) between the groups (1 week - 96.1% vs 100%, 1 month - 100% vs 97.1%, 3, 6 and 12 months - 100% for both groups). The authors also reported no significant difference in complications between the two groups at all-time intervals.

Additional studies that were not discussed in the systematic review included an RCT by Fitridge et al[205] who evaluated the hemodynamic role of calf incompetent perforating veins in patients with uncomplicated varicose veins. They studied 38 limbs in 35 patients with incompetent GSVs and one or more incompetent perforators. All limbs underwent HL&S ± phlebectomy with (Group 1, n=21) or without (Group 2, n=17) open ligation of IPV. In group 2, 9 limbs had persistent incompetent perforators, while 8 limbs had no residual incompetent perforators. Both groups demonstrated significant improvement of venous function by air plethysmography postoperatively, including venous volume, venous filling index and ejection fraction. There was no significant difference between the two groups in either preoperative or postoperative venous function. Follow-up DU could not identify previously seen incompetent perforator veins in approximately 50% of patients (8/17) who did not undergo open ligation of the incompetent perforators. This finding was explained as possible due to avulsion during surgery versus possible improvement in function after pathologic saphenous vein removal.

In a prospective cohort study, Koroglu et al [206], compared the effectiveness of endovenous laser ablation and concomitant foam sclerotherapy in two groups of patients – one with isolated saphenous vein reflux (Group 1 =36 limbs) and the second group with saphenous vein reflux and

perforator vein incompetence (Group 2 = 24 limbs); 21 of 60 limbs had C2 disease. Occlusion of incompetent perforating veins was identified in 75% postoperatively, compared to 98.6% of saphenous veins. While there was no clinically significant difference in the Venous Clinical Severity Score (VCSS) between groups, the visual analog score was more prominently decreased after treatment of isolated saphenous vein insufficiency. This study suggests that clinical outcomes are superior in patients with isolated truncal insufficiency.

Van Neer and colleagues,[207] in their prospective study of 74 limbs (55 C2) in 59 patients with primary varicose veins, evaluated the impact of HL&S to just below knee before and six months after the procedure. The authors found that reflux in the GSV below the knee persists in the main GSV trunk as well as the anterior arch and posterior arch vein tributaries post-stripping. On multivariable analysis, the authors found no significant association between presence of an incompetent perforator vein preoperatively and reflux in the GSV or its branches below the knee postoperatively, or between preoperative incompetent perforators and post-operative visible varicose veins. In addition, the diameter of the GSV below the knee and its branches decreased significantly after the short stripping of the more proximal GSV. The proportion of patients with visible varicose veins in the GSV area below the knee decreased from 70% to 16% post-stripping. The authors concluded that incompetent perforator veins are not related to the persistence of visible varicose veins below the knee nor to the persistence of below the knee GSV reflux.

The findings of these studies, including the systematic review support initial non-treatment of incompetent perforator veins in patients with C2 disease who have truncal vein reflux associated with incompetent perforator veins. The addition of perforator ablation in RCTs[203, 204] did not significantly improve hemodynamic status, clinical presentation, or QoL compared to treatment of

superficial truncal vein reflux alone. In addition, there was no statistically significant difference in anatomic closure of the GSV at 1 months and at 1 year.[19]

The clinical presentation of an incompetent thigh perforator with an incompetent distal GSV deserves special consideration. In many of these patients the SFJ and the proximal GSV are competent. A good practice appears to be to treat these patients with ablation of the distal GSV and the thigh perforator, which is the major incompetent connection with the deep system. However, a RCT by Park et al. advises saphenous vein ablation alone in these patients.[204] It should be noted, however, that the primary reason of failure of the combined procedure was technical, with inability to treat the perforators in 8 of 34 limbs (23.5%).[204] Further studies to support perforator ablation during the initial procedure in these unique situations are warranted.

4.2. For patients with varicose veins (C2) and persistent or recurrent symptoms following previous complete ablation of incompetent superficial truncal veins we suggest treatment of incompetent perforating veins if they are the origin of symptomatic varicose tributaries.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C. (Low to very low)

Rationale

Once the incompetent truncal veins have been treated in patients with CEAP 2 varicose veins, all patients should return for procedural follow-up and confirmation that the symptoms and abnormal veins have been adequately treated. For patients who have persistent symptoms, new symptoms, or residual visible varicose veins, they should be reassessed with physical exam and DU to determine the cause of the residual symptoms and whether there has been incomplete treatment of visible varicose veins. The authors of these practice guidelines recommend that all patients who

have undergone a venous intervention for varicose veins have at least one follow-up visit at approximately 3 months, when symptoms related to the procedure are likely to have resolved so that patients with residual symptoms or visible residual varicose veins be reassessed using DU of the truncal, tributary, deep, and perforator veins throughout the entire leg. This DU study should identify treated veins with both complete and incomplete closure, residual untreated tributary veins, as well as incompetent deep and perforator veins. If all intended truncal and tributary veins have been treated and yet there are persistent symptoms, other potential causes of the persistent symptoms should be considered, including residual incompetent tributary veins and incompetent perforator veins, since they could represent the origin of the symptomatic varicose veins.

Evidence

In a prospective study involving 127 limbs in 92 patients, including 58 limbs with C2 disease, van Rij and colleagues[208] performed flush ligation of the SFJ or SPJ, stripping of the great saphenous vein to the knee, and multiple stab avulsions as well as ligation of incompetent perforators that had marked reflux. Deep venous reflux was present in 68 (53.5%) limbs. After 3 years, recurrence of reflux at the SFJ and SPJ was 23% and 52%, respectively. Additionally, incompetent perforator veins progressively increased in number, with an overall clinical recurrence of 51% at 3 to 5 years. Twenty-nine of 53 limbs (55%) with a normal venous filling index after surgery had deteriorated at 3 years. The authors concluded that incomplete superficial surgery, in particular at the SFJ and SPJ, is a less frequent cause of recurrent disease, and neovascular reconnection and persistent abnormal venous function are the major contributors to disease recurrence.

In a retrospective study, Stuart et al [209] evaluated 62 limbs in 47 patients (including 47 limbs with C2-C3 disease) undergoing SFJ ligation, stripping of the GSV in the thigh, and multiple phlebectomies versus saphenopopliteal junction (SPJ) ligation and multiple phlebectomies, or both. Patients were examined before surgery and at 14 weeks. Post-intervention there was a significant reduction in the total number of limbs with incompetent perforator veins (IPV) (65% preoperatively vs 37% postoperatively, p <.01). Additionally, there was a significant reduction in incompetent perforators imaged (52% vs 28%, p < .01) as well as a reduction in median IPV diameter (4 mm [1 – 11mm], vs 3, [1 – 8mm], p < .01) after surgery. However, IPV remained in 20% limbs in which axial saphenous reflux was abolished, compared with 72% of limbs in which superficial or deep reflux remained (p <.01). The authors concluded that superficial venous surgery fails to correct perforator vein incompetence in patients with deep vein reflux and in those with persistent superficial reflux.

5. ABLATION OF THE REFLUXING SYMPTOMATIC SUPERFICIAL VENOUS TRUNK AND CONCOMITANT TREATMENT OF VARICOSE TRIBUTARIES

Guideline 5.1.

5.1.1. For patients with symptomatic reflux in the great or small saphenous vein and associated varicosities, we recommend ablation of the refluxing venous trunk and concomitant phlebectomy or ultrasound guided foam sclerotherapy of the varicosities with physician compounded foam or commercial polidocanol endovenous microfoam.

Level of Recommendation: Grade 1 (Strong); Quality of Evidence: C (Low to very low)

5.1.2. For patients with symptomatic reflux in the anterior accessory or posterior accessory great saphenous vein, we recommend ablation of the refluxing venous trunk and concomitant phlebectomy or ultrasound guided foam sclerotherapy of the varicosities with physician compounded foam or commercial polidocanol endovenous microfoam.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Rationale

In patients with both truncal vein reflux and incompetent tributaries, the decision regarding optimal treatment must involve the scientific evidence, the patient wishes and concerns, and a well-informed physician providing advice. The common scenario of calf or thigh tributaries emanating from an incompetent truncal vein treated in a single session is usually the more cost-effective approach and is associated with less total time off from work. In situations where non-saphenous varicose tributaries are also present in the leg, concomitant treatment with phlebectomy or UGFS would be more appropriate. Other situations such as transportation needs, or caregiver restraints would also favor concomitant treatment.

Evidence

Harlander-Locke et al performed a retrospective review of 1000 consecutive RFA of truncal veins (916 limbs, C2-C6).[210] Five hundred seven limbs had large (>3mm) symptomatic varicose tributaries of which 355 (70%) underwent concomitant phlebectomy. An additional 145 (25%) limbs had subsequent phlebectomy for persistent symptoms. Twenty-six limbs (5%) did not require subsequent phlebectomy because of symptom resolution. An additional 19 limbs developed new superficial varicose tributaries after saphenous ablation and underwent staged phlebectomy, and 13 patients had bilateral phlebectomies. In their cohort, 95% of limbs with

superficial tributaries greater than 3mm required stab phlebectomy, either concomitantly or subsequently.

Brown et al utilized data from the Varicose Vein Registry between 2015-2019 in 3375 C2 patients who underwent thermal ablation of the saphenous veins.[211] Patients having concomitant sclerotherapy were excluded. There were 1,013 patients in each of two groups: ablation alone or ablation with phlebectomy. The preprocedural VCSS scores were similar in both groups, but there was a higher median improvement in the VCSS in those who underwent ablation and phlebectomy. In addition, the authors looked at patient reported symptoms. Post-procedure, there was improvement in all symptoms (heaviness, achiness, throbbing, swelling, itching, appearance, pain, and impact on work), but the change in scores were higher in the ablation plus phlebectomy group vs. ablation alone group.

Conway et al in a 2020 study from the Varicose Vein module of the American Venous Registry examined 526 CEAP Clinical Class C2 patients without prior venous treatment.[212] Combined treatment (CT) in this cohort consisted of phlebectomy or sclerotherapy, and unimodal treatment (UT) was thermal ablation (RFA or laser). Change in symptom severity was assessed by pretreatment and 1-month post-treatment VCSS scores. After treatment, CT was associated with significantly lower scores on the pain component of the VCSS (0.31 for UT vs. 0.07 for CT [*P*=.0008].

From England, the AVULS Trial compared simultaneous vs. staged treatment, with the Aberdeen Varicose Vein Questionnaire (AVVQ) score as the primary outcome. [213] Both groups showed significant improvement in symptoms from baseline at 6 weeks, 6 months and at 12 months ($p<0.0001$). While there was a significant difference seen at 6 weeks, with the simultaneous group showing a 5.48-point improvement ($p=0.029$), there were no significant

differences at 6 and 12 months. When comparing the staged group who subsequently needed further treatment to the simultaneous group, there was a large significant difference at 6 weeks and 6 months. There was no more significant difference, however, at 12 months.

Guideline 5.2

5.2.1. For patients with symptomatic reflux in the great or small saphenous vein, we suggest ablation of the refluxing venous trunk and staged or ultrasound guided foam sclerotherapy of the varicosities if there are anatomical or medical reasons. We suggest a shared decision making with the patient.

Level of Recommendation: Grade 2 (Weak); Quality of Evidence: C (Low to very low)

5.2.2. For patients with symptomatic reflux in the anterior accessory great saphenous vein or the posterior accessory great saphenous vein, we suggest ablation of the refluxing venous trunk and staged phlebectomy or ultrasound guided foam sclerotherapy of the varicosities if there are anatomical or medical reasons. We suggest a shared decision making with the patient.

Level of recommendation: Grade 2 (Weak), Quality of Evidence: C (Low to very low)

Rationale

A single procedure that includes both ablation of the truncal reflux and treatment of varicose tributaries provide immediate satisfaction to patients who come for treatment of symptomatic varicose veins. There should be medical or anatomical reasons why the procedures are staged,

since it is not rare that patients with bilateral varicosities are listed for several subsequent procedures to treat truncal reflux and varicosities separately. Medical reasons for staging procedure may include extensive bilateralvaricosities, need for general anesthesia or large amount of local or tumescent anesthetic. Anatomical reaons may include patients with circumferential limb variocosities requiring changing the patient's position from supine to decubitus . In addition, in some patients who have both truncal incompetence and tributary incompetence, ablation of the truncal vein will reduce the size of the tributary vein or reduce the symptoms of heaviness and aching to an extent that no further treatment is needed. Some patients with truncal and tributary reflux may only want the discomfort from their varicose veins relieved, without a desire to eliminate visible tributaries, so ablating the truncal vein may relieve enough discomfort that a second procedure may never be necessary. During a shared decision making, patients may request a staged approach with a minimally invasive treatment of the tributaries using physician compounded foam, commercial foam, or liquid sclerotherapy as an alternative to mini-phlebectomy, which may be the only procedure approved by the patient's insurance company as a concomitant procedure. Some patients also may not have large enough symptomatic tributaries for their treatment to be covered by insurance, and therefore they may delay tributary treatment until the tributaries become larger or until they have adequate financial resources to pay for the procedure. Patients who have diffuse bilateral varicosities and bilateral saphenous incompetence can safely undergo bilateral ablations, but additional concomitant phlebectomies may be too much for the patient and/or provider. Patients who elect the staged approach must be informed that there is a distinct likelihood of needing a second procedure, whether it be mini-phlebectomy, liquid sclerotherapy, or foam sclerotherapy.

Evidence

Two studies utilizing the first-generation RF catheters examined the fate of residual varicosities after ablation alone. Monahan ablated the GSV in 54 limbs. At 6 months there was complete resolution of the varicose tributaries in 13% limbs and 28.4% of varicose veins spontaneously resolved.[214] A further 88.7% of varicose veins decreased in size an average of 34.6%. Welch [215] studied 184 limbs with GSV RF ablation. Of the 155 limbs that had successful total ablation or had only a patent segment <10 cm long, 101 limbs (65.1%) had symptom resolution and did not require further treatment by 9 months of follow up.

A systematic review by Farah et al,[19] studied outcomes in 6098 patients who were enrolled in a RCT (2 publications)[216, 217] , in two observational studies[211, 212] and in another systematic review of 8 studies.[218] The data supported better short term and better to equivalent long term outcomes in patients who underwent the combined procedure.

In a meta-analysis by Aherne et al, truncal ablation alone, without any treatment of varicose tributaries was sufficient therapy for 63.9% of those assessed. [219] Both concomitant and staged treatments were safe and effective. Improvements in early disease severity and QOL scores were better in the concomitant group. Concomitant interventions in all studies resulted in less re-interventions than staged interventions but a subgroup analysis of the RCTs alone did not identify differences in reinterventions between groups.

5.3. For patients with symptomatic reflux in the major superficial venous trunks and associated varicosities undergoing initial ablation alone, we recommend that patients be followed for at least 3 months to assess the need for staged phlebectomy or ultrasound guided sclerotherapy for persistent or recurrent symptoms. Longer follow-up is

recommended for patients with recurrent symptoms and for patients who participate in clinical trials.

Level of Recommendation: Ungraded good clinical practice

Rationale

In patients who elect a staged approach, significant time must elapse post procedure to differentiate between symptoms related to recovery from the original procedure and residual symptoms from remaining venous insufficiency. We recommend a follow-up at a minimum of three months to determine if the procedure has both resolved symptoms and eliminated visible tributary veins. Longer follow-up is recommended for patients with recurrent symptoms and for those who participate in clinical trials. In patients with residual symptoms, DU should be performed to assess the treated veins for closure, as well as assessing any remaining superficial truncal veins, tributaries, and perforator veins for size and extent of reflux. Once identified, treatment with a second procedure should use the same criteria as the initial procedure, and can range from ablation of an incompletely closed or more distal truncal vein to removal or sclerotherapy of remaining incompetent tributary veins.

Evidence

In two studies[214, 215] follow-up evaluation was performed at 3 to 6 months to fully assess potential regression of tributary varicosities, with significant regression and improvement in symptoms. Conversely, Lane and coauthors[213] in the AVULS Trial had a follow-up exam at 6 weeks to assess the need for further procedure; only 36% of patients in the staged group required further treatment. A longer observation period likely would have decreased that percentage even further.

1418

REFERENCES

1. Crawford JM, Gasparis A, Almeida J, Elias S, Wakefield T, Lal BK, et al. A review of United States endovenous ablation practice trends from the Medicare Data Utilization and Payment Database. J Vasc Surg Venous Lymphat Disord. 2019;7(4):471-9.
2. Mann M, Wang P, Schul M, Khilnani NM, Park A, Makary MA, et al. Significant physician practice variability in the utilization of endovenous thermal ablation in the 2017 Medicare population. J Vasc Surg Venous Lymphat Disord. 2019;7(6):808-16 e1.
3. Stonko DP, Dun C, Walsh C, Schul M, Blebea J, Boyle EM, et al. Evaluation of a Physician Peer-Benchmarking Intervention for Practice Variability and Costs for Endovenous Thermal Ablation. JAMA Netw Open. 2021;4(12):e2137515.
4. Prabhakar AM, Misono AS, Sheth RA, Rosenkrantz AB, Hemingway J, Hughes DR, et al. Changing Medicare Utilization of Minimally Invasive Procedures for the Treatment of Chronic Venous Insufficiency. J Vasc Interv Radiol. 2017;28(6):818-24.
5. Rasmussen L, Lawaetz M, Bjoern L, Blemings A, Eklof B. Randomized clinical trial comparing endovenous laser ablation and stripping of the great saphenous vein with clinical and duplex outcome after 5 years. J Vasc Surg. 2013;58(2):421-6.
6. Rass K, Frings N, Glowacki P, Graber S, Tilgen W, Vogt T. Same Site Recurrence is More Frequent After Endovenous Laser Ablation Compared with High Ligation and Stripping of the Great Saphenous Vein: 5 year Results of a Randomized Clinical Trial (RELACS Study). Eur J Vasc Endovasc Surg. 2015;50(5):648-56.
7. Lawaetz M, Serup J, Lawaetz B, Bjoern L, Blemings A, Eklof B, et al. Comparison of endovenous ablation techniques, foam sclerotherapy and surgical stripping for great saphenous varicose veins. Extended 5-year follow-up of a RCT. Int Angiol. 2017;36(3):281-8.
8. Vahaaho S, Halmesmaki K, Alback A, Saarinen E, Venermo M. Five-year follow-up of a randomized clinical trial comparing open surgery, foam sclerotherapy and endovenous laser ablation for great saphenous varicose veins. Br J Surg. 2018;105(6):686-91.
9. Wallace T, El-Sheikha J, Nandhra S, Leung C, Mohamed A, Harwood A, et al. Long-term outcomes of endovenous laser ablation and conventional surgery for great saphenous varicose veins. Br J Surg. 2018;105(13):1759-67.
10. Brittenden J, Cooper D, Dimitrova M, Scotland G, Cotton SC, Elders A, et al. Five-Year Outcomes of a Randomized Trial of Treatments for Varicose Veins. N Engl J Med. 2019;381(10):912-22.
11. Mousa A, El Azzazi M, Elkalla MA. Different management options for primary varicose veins in females: A prospective study. Surg Open Sci. 2019;1(1):25-33.
12. 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):978-89.
13. Gauw SA, Lawson JA, van Vlijmen-van Keulen CJ, Pronk P, Gaastra MT, Mooij MC. Five-year follow-up of a randomized, controlled trial comparing saphenofemoral ligation and stripping of the great saphenous vein with endovenous laser ablation (980 nm) using local tumescent anesthesia. J Vasc Surg. 2016;63(2):420-8.

14. Eggen CAM, Alozai T, Pronk P, Mooij MC, Gaastra MTW, Unlu C, et al. Ten-year follow-up of a randomized controlled trial comparing saphenofemoral ligation and stripping of the great saphenous vein with endovenous laser ablation (980 nm) using local tumescent anesthesia. J Vasc Surg Venous Lymphat Disord. 2021.
15. Lurie F, Passman M, Meisner M, Dalsing M, Masuda E, Welch H, et al. The 2020 update of the CEAP classification system and reporting standards. J Vasc Surg Venous Lymphat Disord. 2020;8(3):342-52.
16. Masuda E, Ozsvath K, Vossler J, Woo K, Kistner R, Lurie F, et al. The 2020 appropriate use criteria for chronic lower extremity venous disease of the American Venous Forum, the Society for Vascular Surgery, the American Vein and Lymphatic Society, and the Society of Interventional Radiology. J Vasc Surg Venous Lymphat Disord. 2020;8(4):505-25 e4.
17. Catarinella FS, Nieman FH, Wittens CH. An overview of the most commonly used venous quality of life and clinical outcome measurements. J Vasc Surg Venous Lymphat Disord. 2015;3(3):333-40.
18. Mallick S, Sarkar T, Gayen T, Naskar B, Datta A, Sarkar S. Correlation of Venous Clinical Severity Score and Venous Disability Score with Dermatology Life Quality Index in Chronic Venous Insufficiency. Indian J Dermatol. 2020;65(6):489-94.
19. Farah MH, Nayfeh T, Urtecho M, Hasan B, Amin M, Sen I, et al. A systematic review supporting the Society for Vascular Surgery, the American Venous Forum, and the American Vein and Lymphatic Society guidelines on the management of varicose veins. J Vasc Surg Venous Lymphat Disord. 2021.
20. Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, Gloviczki ML, et al. 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.
21. NICE. Varicose veins in the legs: The diagnosis and management of varicose veins2013 February 21, 2021.
22. Wittens C, Davies AH, Baekgaard 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.
23. Gloviczki P, Dalsing MC, Eklof B, Lurie F, Wakefield TW, Gloviczki ML. Handbook of Venous and Lymphatic Disorders: Guidelines of the American Venous Forum. Handbook of Venous and Lymphatic Disorders: Guidelines of the American Venous Forum. 4th Edition ed. London: CRC Press; 2017.
24. Nicolaides A, Kakkos S, Baekgaard 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 I. Int Angiol. 2018;37(3):181-254.
25. Nicolaides A, Kakkos S, Baekgaard 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.
26. Kursat Bozkurt A, Lawaetz M, Danielsson G, Lazaris AM, Pavlovic M, Olariu S, et al. European College of Phlebology guideline for truncal ablation. Phlebology. 2020;35(2):73-83.
27. De Maeseneer MG, Kakkos SK, Aherne T, Baekgaard N, Black S, Blomgren L, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2022 Clinical Practice Guidelines

on the Management of Chronic Venous Disease of the Lower Limbs. Eur J Vasc Endovasc Surg. 2022;63(2):184-267.
28. Murad MH, Montori VM, Sidawy AN, Ascher E, Meissner MH, Chaikof EL, et al. Guideline methodology of the Society for Vascular Surgery including the experience with the GRADE framework. J Vasc Surg. 2011;53(5):1375-80.
29. Murad MH, Swiglo BA, Sidawy AN, Ascher E, Montori VM. Methodology for clinical practice guidelines for the management of arteriovenous access. J Vasc Surg. 2008;48(5 Suppl):26S-30S.
30. Guyatt GH, Alonso-Coello P, Schunemann HJ, Djulbegovic B, Nothacker M, Lange S, et al. Guideline panels should seldom make good practice statements: guidance from the GRADE Working Group. J Clin Epidemiol. 2016;80:3-7.
31. Eklof B, Rutherford RB, Bergan JJ, Carpentier PH, Gloviczki P, Kistner RL, et al. Revision of the CEAP classification for chronic venous disorders: consensus statement. J Vasc Surg. 2004;40(6):1248-52.
32. Perrin M, Eklöf B, Maleti O. The Vein Glossary. J Vasc Surg Venous Lymphat Disord. 2018;6(5):e11-e217.
33. Eklof B, Perrin M, Delis KT, Rutherford RB, Gloviczki P, American Venous F, et al. Updated terminology of chronic venous disorders: the VEIN-TERM transatlantic interdisciplinary consensus document. J Vasc Surg. 2009;49(2):498-501.
34. Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ. 2016;353:i2016.
35. Shepherd AC, Gohel MS, Lim CS, Hamish M, Davies AH. The treatment of varicose veins: an investigation of patient preferences and expectations. Phlebology. 2010;25(2):54-65.
36. Pappas P, Gunnarsson C, David G. Evaluating patient preferences for thermal ablation versus nonthermal, nontumescent varicose vein treatments. J Vasc Surg Venous Lymphat Disord. 2021;9(2):383-92.
37. Kheirelseid EAH, Crowe G, Sehgal R, Liakopoulos D, Bela H, Mulkern E, et al. Systematic review and meta-analysis of randomized controlled trials evaluating long-term outcomes of endovenous management of lower extremity varicose veins. J Vasc Surg Venous Lymphat Disord. 2018;6(2):256-70.
38. O'Donnell TF, Jr., Passman MA. Clinical practice guidelines of the Society for Vascular Surgery (SVS) and the American Venous Forum (AVF)--Management of venous leg ulcers. Introduction. J Vasc Surg. 2014;60(2 Suppl):1S-2S.
39. De Maeseneer M, Pichot O, Cavezzi A, Earnshaw J, van Rij A, Lurie F, et al. Duplex ultrasound investigation of the veins of the lower limbs after treatment for varicose veins - UIP consensus document. Eur J Vasc Endovasc Surg. 2011;42(1):89-102.
40. Gloviczki P, Dalsing MC, Henke P, Lal BK, O'Donnell TF, Jr., Shortell CK, et al. Report of the Society for Vascular Surgery and the American Venous Forum on the July 20, 2016 meeting of the Medicare Evidence Development and Coverage Advisory Committee panel on lower extremity chronic venous disease. J Vasc Surg Venous Lymphat Disord. 2017;5(3):378-98.
41. Jones WS, Vemulapalli S, Parikh KS, Coeytaux RR, Crowley MJ, Raitz G, et al. Treatment Strategies for Patients with Lower Extremity Chronic Venous Disease (LECVD). Rockville (MD)2017.

42. Mercer KG, Scott DJ, Berridge DC. Preoperative duplex imaging is required before all operations for primary varicose veins. Br J Surg. 1998;85(11):1495-7.
43. Rautio T, Perala J, Wiik H, Haukipuro K, Juvonen T. Influence of preoperative duplex ultrasonography on the operative procedure for primary varicose vein surgery. . Phlebology. 2002;16:149-53.
44. Rautio T, Perala J, Biancari F, Wiik H, Ohtonen P, Haukipuro K, et al. Accuracy of hand-held Doppler in planning the operation for primary varicose veins. Eur J Vasc Endovasc Surg. 2002;24(5):450-5.
45. Darke SG, Vetrivel S, Foy DM, Smith S, Baker S. A comparison of duplex scanning and continuous wave Doppler in the assessment of primary and uncomplicated varicose veins. Eur J Vasc Endovasc Surg. 1997;14(6):457-61.
46. Wills V, Moylan D, Chambers J. The use of routine duplex scanning in the assessment of varicose veins. Aust N Z J Surg. 1998;68(1):41-4.
47. Dhillon J, Thorwald M, Chung S, Maloney G, Srivatsa S. Comparison of hand-held acoustic Doppler with point-of-care portable color Doppler ultrasound in the assessment of venous reflux disease. J Vasc Surg Venous Lymphat Disord. 2020;8(5):831-9 e2.
48. Blomgren L, Johansson G, Emanuelsson L, Dahlberg-Akerman A, Thermaenius P, Bergqvist D. Late follow-up of a randomized trial of routine duplex imaging before varicose vein surgery. Br J Surg. 2011;98(8):1112-6.
49. Cavezzi A, Labropoulos N, Partsch H, Ricci S, Caggiati A, Myers K, et al. Duplex ultrasound investigation of the veins in chronic venous disease of the lower limbs--UIP consensus document. Part II. Anatomy. Eur J Vasc Endovasc Surg. 2006;31(3):288-99.
50. Masuda EM, Kistner RL. Prospective comparison of duplex scanning and descending venography in the assessment of venous insufficiency. Am J Surg. 1992;164(3):254-9.
51. Varcoe RL, Thomas SD, Bourke V, Rubesamen NM, Lennox AF. Utility of Adjunctive Digital Subtraction Venography for the Treatment of Saphenous Vein Insufficiency. J Endovasc Ther. 2017;24(2):290-6.
52. Jayaraj A, Raju S. Three-dimensional computed tomography venogram enables accurate diagnosis and treatment of patients presenting with symptomatic chronic iliofemoral venous obstruction. J Vasc Surg Venous Lymphat Disord. 2021;9(1):73-80 e1.
53. Gagne PJ, Tahara RW, Fastabend CP, Dzieciuchowicz L, Marston W, Vedantham S, et al. Venography versus intravascular ultrasound for diagnosing and treating iliofemoral vein obstruction. J Vasc Surg Venous Lymphat Disord. 2017;5(5):678-87.
54. Schleimer K, Barbati ME, Grommes J, Hoeft K, Toonder IM, Wittens CHA, et al. Update on diagnosis and treatment strategies in patients with post-thrombotic syndrome due to chronic venous obstruction and role of endovenous recanalization. J Vasc Surg Venous Lymphat Disord. 2019;7(4):592-600.
55. van Bemmelen PS, Bedford G, Beach K, Strandness DE. Quantitative segmental evaluation of venous valvular reflux with duplex ultrasound scanning. J Vasc Surg. 1989;10(4):425-31.
56. Labropoulos N, Tiongson J, Pryor L, Tassiopoulos AK, Kang SS, Ashraf Mansour M, et al. Definition of venous reflux in lower-extremity veins. J Vasc Surg. 2003;38(4):793-8.

57. Deol ZK, Lakhanpal S, Pappas PJ. Severity of disease and treatment outcomes of anterior accessory great saphenous veins compared with the great saphenous vein. J Vasc Surg Venous Lymphat Disord. 2021.
58. De Maeseneer M. European Society for Vascular Surgery (ESVS) 2022 Clinical Practice Guidelines on the Management of Chronic Venous Disease of the Lower Limbs. European Journal of Vascular and Endovascular Surgery. 2022.
59. Dillavou ED, Harlander-Locke M, Labropoulos N, Elias S, Ozsvath KJ. Current state of the treatment of perforating veins. J Vasc Surg Venous Lymphat Disord. 2016;4(1):131-5.
60. Labropoulos N, Leon LR, Jr. Duplex evaluation of venous insufficiency. Semin Vasc Surg. 2005;18(1):5-9.
61. Labropoulos N, Mansour MA, Kang SS, Gloviczki P, Baker WH. New insights into perforator vein incompetence. Eur J Vasc Endovasc Surg. 1999;18(3):228-34.
62. Sandri JL, Barros FS, Pontes S, Jacques C, Salles-Cunha SX. Diameter-reflux relationship in perforating veins of patients with varicose veins. J Vasc Surg. 1999;30(5):867-74.
63. Malgor R, Labropoulos N. Duplex ultrasound scanning for chronic venous obstruction and valvular incompetence. In: Gloviczki P, Dalsing MC, Eklof B, Lurie F, Wakefield TW, Gloviczki ML, editors. Handbook of Venous and Lymphatic Disorders: Guidelines of the American Venous Forum. 4th Edition ed. London: CRC Press; 2017. p. 151-64.
64. Masuda EM, Kistner RL, Eklof B. Prospective study of duplex scanning for venous reflux: comparison of Valsalva and pneumatic cuff techniques in the reverse Trendelenburg and standing positions. J Vasc Surg. 1994;20(5):711-20.
65. Perrins S, Cha A, Qaqish R, Plummer D, Hsu R, Dietzek AM. Clinical and anatomic outcomes of endovenous radiofrequency ablation performed on symptomatic small-diameter great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2013;1(3):245-9.
66. Commission IA. IAC Standards and Guidelines for Vascular Testing Accreditation 2021 May 22, 2022.
67. Vitale C, D'Abate F, Froio A. Needs of standardisation in reporting a venous lower limb ultrasound exam for the assessment of varicose veins. Phlebology. 2021;36(8):665-7.
68. Kim MJ, Park PJ, Koo BH, Lee SG, Byun GY, Lee SR. Association between venous reflux and diameter of great saphenous vein in lower thigh. J Vasc Surg Venous Lymphat Disord. 2020;8(1):100-5.
69. Attaran RR, Bhalla A, Mena-Hurtado CI, Ochoa Chaar CI. Correlation between great saphenous length of treatment zone and diameter with improvement in symptoms after ablation. J Vasc Surg Venous Lymphat Disord. 2021;9(6):1443-50.
70. Gibson K, Meissner M, Wright D. Great saphenous vein diameter does not correlate with worsening quality of life scores in patients with great saphenous vein incompetence. J Vasc Surg. 2012;56(6):1634-41.
71. Joh JH, Park HC. The cutoff value of saphenous vein diameter to predict reflux. J Korean Surg Soc. 2013;85(4):169-74.
72. Mendoza E, Blattler W, Amsler F. Great saphenous vein diameter at the saphenofemoral junction and proximal thigh as parameters of venous disease class. Eur J Vasc Endovasc Surg. 2013;45(1):76-83.

73. Hamel-Desnos CM, De Maeseneer M, Josnin M, Gillet JL, Allaert FA, Group DS. Great Saphenous Vein Diameters in Phlebological Practice in France: A Report of the DIAGRAVES Study by the French Society of Phlebology. Eur J Vasc Endovasc Surg. 2019;58(1):96-103.
74. Navarro TP, Delis KT, Ribeiro AP. Clinical and hemodynamic significance of the greater saphenous vein diameter in chronic venous insufficiency. Arch Surg. 2002;137(11):1233-7.
75. Mdez-Herrero A, Gutierrez J, Camblor L, Carreno J, Llaneza J, Rguez-Olay J, et al. The relation among the diameter of the great saphenous vein, clinical state and haemodynamic pattern of the saphenofemoral junction in chronic superficial venous insufficiency. Phlebology. 2007;22(5):207-13.
76. Yang Q, Zhao Y, Chen X, Tang P, Li L, Zhao J, et al. Association between vein diameters, reflux characteristics, and clinical severity in patients with chronic venous insufficiency in Northwest China. J Vasc Surg Venous Lymphat Disord. 2021;9(2):401-8 e1.
77. Lane TRA, Varatharajan L, Fiorentino F, Shepherd AC, Zimmo L, Gohel MS, et al. Truncal varicose vein diameter and patient-reported outcome measures. Br J Surg. 2017;104(12):1648-55.
78. Choi JY, Lee JH, Kwon OJ. Association between the saphenous vein diameter and venous reflux on computed tomography venography in patients with varicose veins. PLoS One. 2022;17(2):e0263513.
79. Kakkos SK, Timpilis M, Patrinos P, Nikolakopoulos KM, Papageorgopoulou CP, Kouri AK, et al. Acute Effects of Graduated Elastic Compression Stockings in Patients with Symptomatic Varicose Veins: A Randomised Double Blind Placebo Controlled Trial. Eur J Vasc Endovasc Surg. 2018;55(1):118-25.
80. Knight Nee Shingler SL, Robertson L, Stewart M. Graduated compression stockings for the initial treatment of varicose veins in people without venous ulceration. Cochrane Database Syst Rev. 2021;7:CD008819.
81. Michaels JA, Brazier JE, Campbell WB, MacIntyre JB, Palfreyman SJ, Ratcliffe J. Randomized clinical trial comparing surgery with conservative treatment for uncomplicated varicose veins. Br J Surg. 2006;93(2):175-81.
82. Ratcliffe J, Brazier JE, Campbell WB, Palfreyman S, MacIntyre JB, Michaels JA. Cost-effectiveness analysis of surgery versus conservative treatment for uncomplicated varicose veins in a randomized clinical trial. Br J Surg. 2006;93(2):182-6.
83. Sell H, Vikatmaa P, Alback A, Lepantalo M, Malmivaara A, Mahmoud O, et al. Compression therapy versus surgery in the treatment of patients with varicose veins: A RCT. Eur J Vasc Endovasc Surg. 2014;47(6):670-7.
84. Lurie F, Kistner RL. Trends in patient reported outcomes of conservative and surgical treatment of primary chronic venous disease contradict current practices. Ann Surg. 2011;254(2):363-7.
85. Epstein D, Onida S, Bootun R, Ortega-Ortega M, Davies AH. Cost-Effectiveness of Current and Emerging Treatments of Varicose Veins. Value Health. 2018;21(8):911-20.
86. Epstein D, Bootun R, Diop M, Ortega-Ortega M, Lane TRA, Davies AH. Cost-effectiveness Analysis of Current Varicose Veins Treatments. J Vasc Surg Venous Lymphat Disord. 2021.
87. Teter KA, Kabnick LS, Sadek M. Endovenous laser ablation: A comprehensive review. Phlebology. 2020;35(9):656-62.

88. Kabnick LS, Sadek M. Fiber type as compared to wavelength may contribute more to improving postoperative recovery following endovenous laser ablation. J Vasc Surg Venous Lymphat Disord. 2016;4(3):286-92.
89. Dietzek AM. Endovenous radiofrequency ablation for the treatment of varicose veins. Vascular. 2007;15(5):255-61.
90. Proebstle TM, Alm BJ, Gockeritz O, Wenzel C, Noppeney T, Lebard C, et al. Five-year results from the prospective European multicentre cohort study on radiofrequency segmental thermal ablation for incompetent great saphenous veins. Br J Surg. 2015;102(3):212-8.
91. Almeida JI, Javier JJ, Mackay EG, Bautista C, Cher DJ, Proebstle TM. Thirty-sixth-month follow-up of first-in-human use of cyanoacrylate adhesive for treatment of saphenous vein incompetence. J Vasc Surg Venous Lymphat Disord. 2017;5(5):658-66.
92. Proebstle T, Alm J, Dimitri S, Rasmussen L, Whiteley M, Lawson J, et al. Three-year follow-up results of the prospective European Multicenter Cohort Study on Cyanoacrylate Embolization for treatment of refluxing great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2021;9(2):329-34.
93. Bozkurt AK, Yilmaz MF. A prospective comparison of a new cyanoacrylate glue and laser ablation for the treatment of venous insufficiency. Phlebology. 2016;31(1 Suppl):106-13.
94. Eroglu E, Yasim A. A Randomised Clinical Trial Comparing N-Butyl Cyanoacrylate, Radiofrequency Ablation and Endovenous Laser Ablation for the Treatment of Superficial Venous Incompetence: Two Year Follow up Results. Eur J Vasc Endovasc Surg. 2018;56(4):553-60.
95. Elias S, Lam YL, Wittens CH. Mechanochemical ablation: status and results. Phlebology. 2013;28 Suppl 1:10-4.
96. Mohamed AH, Leung C, Wallace T, Smith G, Carradice D, Chetter I. A Randomized Controlled Trial of Endovenous Laser Ablation Versus Mechanochemical Ablation With ClariVein in the Management of Superficial Venous Incompetence (LAMA Trial). Ann Surg. 2021;273(6):e188-e95.
97. Lam YL, Alozai T, Schreve MA, de Smet A, Vahl AC, Nagtzaam I, et al. A multicenter, randomized, dose-finding study of mechanochemical ablation using ClariVein and liquid polidocanol for great saphenous vein incompetence. J Vasc Surg Venous Lymphat Disord. 2021.
98. Witte ME, Zeebregts CJ, de Borst GJ, Reijnen M, Boersma D. Mechanochemical endovenous ablation of saphenous veins using the ClariVein: A systematic review. Phlebology. 2017;32(10):649-57.
99. Tessari L, Cavezzi A, Frullini A. Preliminary experience with a new sclerosing foam in the treatment of varicose veins. Dermatol Surg. 2001;27(1):58-60.
100. Brittenden J, Cotton SC, Elders A, Ramsay CR, Norrie J, Burr J, et al. A randomized trial comparing treatments for varicose veins. N Engl J Med. 2014;371(13):1218-27.
101. Gibson K, Kabnick L, Varithena 013 Investigator G. A multicenter, randomized, placebo-controlled study to evaluate the efficacy and safety of Varithena(R) (polidocanol endovenous microfoam 1%) for symptomatic, visible varicose veins with saphenofemoral junction incompetence. Phlebology. 2017;32(3):185-93.
102. Campos W, Jr., Torres IO, da Silva ES, Casella IB, Puech-Leao P. A prospective randomized study comparing polidocanol foam sclerotherapy with surgical treatment of

patients with primary chronic venous insufficiency and ulcer. Ann Vasc Surg. 2015;29(6):1128-35.
103. Carradice D, Mekako AI, Mazari FA, Samuel N, Hatfield J, Chetter IC. Clinical and technical outcomes from a randomized clinical trial of endovenous laser ablation compared with conventional surgery for great saphenous varicose veins. Br J Surg. 2011;98(8):1117-23.
104. Carradice D, Mekako AI, Mazari FA, Samuel N, Hatfield J, Chetter IC. Randomized clinical trial of endovenous laser ablation compared with conventional surgery for great saphenous varicose veins. Br J Surg. 2011;98(4):501-10.
105. Christenson JT, Gueddi S, Gemayel G, Bounameaux H. Prospective randomized trial comparing endovenous laser ablation and surgery for treatment of primary great saphenous varicose veins with a 2-year follow-up. J Vasc Surg. 2010;52(5):1234-41.
106. Darwood RJ, Theivacumar N, Dellagrammaticas D, Mavor AI, Gough MJ. Randomized clinical trial comparing endovenous laser ablation with surgery for the treatment of primary great saphenous varicose veins. Br J Surg. 2008;95(3):294-301.
107. de Medeiros CA, Luccas GC. Comparison of endovenous treatment with an 810 nm laser versus conventional stripping of the great saphenous vein in patients with primary varicose veins. Dermatol Surg. 2005;31(12):1685-94; discussion 94.
108. Figueiredo M, Araujo S, Barros N, Jr., Miranda F, Jr. Results of surgical treatment compared with ultrasound-guided foam sclerotherapy in patients with varicose veins: a prospective randomised study. Eur J Vasc Endovasc Surg. 2009;38(6):758-63.
109. Helmy ElKaffas K, ElKashef O, ElBaz W. Great saphenous vein radiofrequency ablation versus standard stripping in the management of primary varicose veins-a randomized clinical trial. Angiology. 2011;62(1):49-54.
110. Flessenkamper I, Hartmann M, Stenger D, Roll S. Endovenous laser ablation with and without high ligation compared with high ligation and stripping in the treatment of great saphenous varicose veins: initial results of a multicentre randomized controlled trial. Phlebology. 2013;28(1):16-23.
111. Gonzalez Canas E, Florit Lopez S, Vilagut RV, Guevara-Noriega KA, Santos Espi M, Rios J, et al. A randomized controlled noninferiority trial comparing radiofrequency with stripping and conservative hemodynamic cure for venous insufficiency technique for insufficiency of the great saphenous vein. J Vasc Surg Venous Lymphat Disord. 2021;9(1):101-12.
112. Kushwaha JK, Gupta A, Yadav P, Sonkar AA. A Comparative Study to Evaluate Early Postoperative Complications and Short-Term Quality of Life Assessment Between Stripping and Endovenous Laser Therapy in the Treatment of Chronic Venous Insufficiency Patients: A Study From North India. Indian Journal of Public Health Research & Development 2020;11(3):134-40.
113. Liao CJ, Song SH, Li T, Zhang Y, Zhang WD. Randomized clinical trial of radiofrequency-induced thermotherapy combined with transilluminated powered phlebectomy versus high ligation and stripping for the treatment of lower limb varicose veins. J Vasc Surg Venous Lymphat Disord. 2021;9(1):95-100.
114. Lurie F, Creton D, Eklof B, Kabnick LS, Kistner RL, Pichot O, et al. Prospective randomized study of endovenous radiofrequency obliteration (closure procedure) versus ligation and stripping in a selected patient population (EVOLVeS Study). J Vasc Surg. 2003;38(2):207-14.

115. Lurie F, Creton D, Eklof B, Kabnick LS, Kistner RL, Pichot O, et al. Prospective randomised study of endovenous radiofrequency obliteration (closure) versus ligation and vein stripping (EVOLVeS): two-year follow-up. Eur J Vasc Endovasc Surg. 2005;29(1):67-73.
116. Mekako AI, Hatfield J, Bryce J, Lee D, McCollum PT, Chetter I. A nonrandomised controlled trial of endovenous laser therapy and surgery in the treatment of varicose veins. Ann Vasc Surg. 2006;20(4):451-7.
117. Mendes CA, Martins AA, Fukuda JM, Parente JB, Munia MA, Fioranelli A, et al. Randomized trial of radiofrequency ablation versus conventional surgery for superficial venous insufficiency: if you don't tell, they won't know. Clinics (Sao Paulo). 2016;71(11):650-6.
118. Nandhra S, El-sheikha J, Carradice D, Wallace T, Souroullas P, Samuel N, et al. A randomized clinical trial of endovenous laser ablation versus conventional surgery for small saphenous varicose veins. J Vasc Surg. 2015;61(3):741-6.
119. Perala J, Rautio T, Biancari F, Ohtonen P, Wiik H, Heikkinen T, et al. Radiofrequency endovenous obliteration versus stripping of the long saphenous vein in the management of primary varicose veins: 3-year outcome of a randomized study. Ann Vasc Surg. 2005;19(5):669-72.
120. Pronk P, Gauw SA, Mooij MC, Gaastra MT, Lawson JA, van Goethem AR, et al. Randomised controlled trial comparing sapheno-femoral ligation and stripping of the great saphenous vein with endovenous laser ablation (980 nm) using local tumescent anaesthesia: one year results. Eur J Vasc Endovasc Surg. 2010;40(5):649-56.
121. Rasmussen LH, Bjoern L, Lawaetz M, Blemings A, Lawaetz B, Eklof B. Randomized trial comparing endovenous laser ablation of the great saphenous vein with high ligation and stripping in patients with varicose veins: short-term results. J Vasc Surg. 2007;46(2):308-15.
122. Rasmussen LH, Bjoern L, Lawaetz M, Lawaetz B, Blemings A, Eklof B. Randomised clinical trial comparing endovenous laser ablation with stripping of the great saphenous vein: clinical outcome and recurrence after 2 years. Eur J Vasc Endovasc Surg. 2010;39(5):630-5.
123. Rasmussen L, Lawaetz M, Serup J, Bjoern L, Vennits B, Blemings A, et al. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy, and surgical stripping for great saphenous varicose veins with 3-year follow-up. J Vasc Surg Venous Lymphat Disord. 2013;1(4):349-56.
124. Rass K, Frings N, Glowacki P, Hamsch C, Graber S, Vogt T, et al. Comparable effectiveness of endovenous laser ablation and high ligation with stripping of the great saphenous vein: two-year results of a randomized clinical trial (RELACS study). Arch Dermatol. 2012;148(1):49-58.
125. Rautio T, Ohinmaa A, Perala J, Ohtonen P, Heikkinen T, Wiik H, et al. Endovenous obliteration versus conventional stripping operation in the treatment of primary varicose veins: a randomized controlled trial with comparison of the costs. J Vasc Surg. 2002;35(5):958-65.
126. Roopram AD, Lind MY, Van Brussel JP, Terlouw-Punt LC, Birnie E, De Smet AA, et al. Endovenous Laser Ablation versus Conventional Surgery in the Treatment of Small Saphenous Vein Incompetence: Short-Term Results of a Multicenter Randomized Controlled Trial. J Vasc Surg Venous Lymphat Disord. 2013;1(1):106.
127. Samuel N, Carradice D, Wallace T, Mekako A, Hatfield J, Chetter I. Randomized clinical trial of endovenous laser ablation versus conventional surgery for small saphenous varicose veins. Ann Surg. 2013;257(3):419-26.

128. Sandhya PA, Mohil RS, Sricharan R. Randomised controlled study to compare radiofrequency ablation with minimally invasive ultrasound-guided non-flush ligation and stripping of great saphenous vein in the treatment of varicose veins. Ann R Coll Surg Engl. 2020;102(7):525-31.
129. Sincos IR, Baptista APW, Coelho Neto F, Labropoulos N, Alledi LB, Marins EM, et al. Prospective randomized trial comparing radiofrequency ablation and complete saphenous vein stripping in patients with mild to moderate chronic venous disease with a 3-year follow-up. Einstein (Sao Paulo). 2019;17(2):eAO4526.
130. Shadid N, Ceulen R, Nelemans P, Dirksen C, Veraart J, Schurink GW, et al. Randomized clinical trial of ultrasound-guided foam sclerotherapy versus surgery for the incompetent great saphenous vein. Br J Surg. 2012;99(8):1062-70.
131. Stotter L, Schaaf I, Bockelbrink A. Comparative outcomes of radiofrequency endoluminal ablation, invagination stripping, and cryostripping in the treatment of great saphenous vein insufficiency. Phlebology. 2006;21:60 - 4.
132. Subramonia S, Lees T. Randomized clinical trial of radiofrequency ablation or conventional high ligation and stripping for great saphenous varicose veins. Br J Surg. 2010;97(3):328-36.
133. Wright DDI, Gobin J, Bradbury A, Coleridge-Smith PD, Spoelstra HAA, Berridge DC, et al. Varisolve polidocanol microfoam compared with surgery or sclerotherapy in the management of varicose veins in the presence of trunk vein incompetence: European randomized controlled trial. Phlebology. 2006;21:180 - 90.
134. Biemans AA, Kockaert M, Akkersdijk GP, van den Bos RR, de Maeseneer MG, Cuypers P, et al. Comparing endovenous laser ablation, foam sclerotherapy, and conventional surgery for great saphenous varicose veins. J Vasc Surg. 2013;58(3):727-34 e1.
135. Rasmussen LH, Lawaetz M, Bjoern L, Vennits B, Blemings A, Eklof B. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veins. Br J Surg. 2011;98(8):1079-87.
136. van der Velden SK, Biemans AA, De Maeseneer MG, Kockaert MA, Cuypers PW, Hollestein LM, et al. Five-year results of a randomized clinical trial of conventional surgery, endovenous laser ablation and ultrasound-guided foam sclerotherapy in patients with great saphenous varicose veins. Br J Surg. 2015;102(10):1184-94.
137. Venermo M, Saarinen J, Eskelinen E, Vahaaho S, Saarinen E, Railo M, et al. Randomized clinical trial comparing surgery, endovenous laser ablation and ultrasound-guided foam sclerotherapy for the treatment of great saphenous varicose veins. Br J Surg. 2016;103(11):1438-44.
138. Basel H, Aydin C, Ay Y, Inan B, Ekim H, Goya C, et al. Endovenous laser ablation (EVLA) versus high ligation
and striping (HL/S): Two-years follow up East J Med. 2012;17:83-7.
139. Carradice D, Samuel N, Wallace T, Mazari FA, Hatfield J, Chetter I. Comparing the treatment response of great saphenous and small saphenous vein incompetence following surgery and endovenous laser ablation: a retrospective cohort study. Phlebology. 2012;27(3):128-34.
140. Lakhwani MN, Dadlani NI, Wong YC. 980-nm laser therapy versus varicose vein surgery in racially diverse Penang, Malaysia. ANZ J Surg. 2009;79(5):352-7.

141. Leopardi M, Salerno A, Dante A, Cofini V, Necozione S, Ventura M. Endovenous Laser Ablation with 1,470-nm Diode with Tumescence Anesthesia and Saphenofemoral Ligation: Propensity Score Match Comparison. Ann Vasc Surg. 2019;58:302-8.
142. Miyazaki K, Nishibe T, Sata F, Murashita T, Kudo FA, Miyazaki YJ, et al. Long-term results of treatments for varicose veins due to greater saphenous vein insufficiency. Int Angiol. 2005;24(3):282-6.
143. Ran F, Shi Y, Qiao T, Shang T, Liu Z, Liu CJ. Comparison of Foam Sclerotherapy Alone or Combined With Stripping of the Great Saphenous Vein for Treating Varicose Veins. Dermatol Surg. 2017;43(4):541-7.
144. Siribumrungwong B, Noorit P, Wilasrusmee C, Leelahavarong P, Thakkinstian A, Teerawattananon Y. Cost-utility analysis of great saphenous vein ablation with radiofrequency, foam and surgery in the emerging health-care setting of Thailand. Phlebology. 2016;31(8):573-81.
145. Siribumrungwong B, Noorit P, Wilasrusmee C, Teerawattananon Y, Thakkinstian A. Quality of life after great saphenous vein ablation in Thai patients with great saphenous vein reflux. Asian J Surg. 2017;40(4):295-300.
146. Solís J, Ribé L, Portero J, Rio J. Stripping saphenectomy, CHIVA and laser ablation for the treatment of the saphenous vein insufficiency. Ambul Surg. 2009;15(1):11-4.
147. Theivacumar NS, Darwood R, Gough MJ. Neovascularisation and recurrence 2 years after varicose vein treatment for sapheno-femoral and great saphenous vein reflux: a comparison of surgery and endovenous laser ablation. Eur J Vasc Endovasc Surg. 2009;38(2):203-7.
148. Tonev AO, Genadiev SG, Dimitrov SG, Zahariev TT, Nachev GK. A retrospective study of 100 patients with varicose veins treated with radiofrequency ablation and stripping. Phlebolymphology. 2013;20(3):150-4.
149. Toregeani JF, Rocha AST, Kimura CJ, Araújo RAG, Kawai AK, Rotta LS, et al. Radiofrequency thermal ablation versus conventional saphenectomy. Jornal Vascular Brasileiro. 2015;14:4-9.
150. Vuylsteke M, Van den Bussche D, Audenaert E, Lissens P. Endovenous laser obliteration for the treatment of primary varicose veins. Phlebology. 2006;21(2):80-7.
151. Ay Y, Gunes E, Turkkolu ST, Selcuk E, Calim M, Akal R, et al. Comparative efficacy and life quality effects of surgical stripping, radiofrequency ablation, and cyanoacrylate embolization in patients undergoing treatment for great saphenous vein insufficiency. Phlebology. 2021;36(1):54-62.
152. Kubat E, Unal CS, Geldi O, Cetin E, Keskin A. What is the optimal treatment technique for great saphenous vein diameter of >/=10 mm? Comparison of five different approaches. Acta Chir Belg. 2021;121(2):94-101.
153. Vemulapalli S, Parikh K, Coeytaux R, Hasselblad V, McBroom A, Johnston A, et al. Systematic review and meta-analysis of endovascular and surgical revascularization for patients with chronic lower extremity venous insufficiency and varicose veins. Am Heart J. 2018;196:131-43.
154. Deak ST. Treatment of superficial venous insufficiency in a large patient cohort with retrograde administration of ultrasound-guided polidocanol endovenous microfoam versus endovenous laser ablation. J Vasc Surg Venous Lymphat Disord. 2021.

155. Jimenez JC, Lawrence PF, Pavlyha M, Farley SM, Rigberg DA, DeRubertis BG, et al. Endovenous microfoam ablation of below knee superficial truncal veins is safe and effective in patients with prior saphenous treatment across a wide range of CEAP classes. J Vasc Surg Venous Lymphat Disord. 2021.
156. Kim PS, Elias S, Gasparis A, Labropoulos N. Results of polidocanol endovenous microfoam in clinical practice. J Vasc Surg Venous Lymphat Disord. 2021;9(1):122-7.
157. Gohel MS, Epstein DM, Davies AH. Cost-effectiveness of traditional and endovenous treatments for varicose veins. Br J Surg. 2010;97(12):1815-23.
158. Poder TG, Fisette JF, Bedard SK, Despatis MA. Is radiofrequency ablation of varicose veins a valuable option? A systematic review of the literature with a cost analysis. Can J Surg. 2018;61(2):128-38.
159. Garagozlo C, Kadri O, Atalla M, Polanco F, Massaband A, Coey J, et al. The anatomical relationship between the sural nerve and small saphenous vein: An ultrasound study of healthy participants. Clin Anat. 2019;32(2):277-81.
160. Mura S, De Biasio F, Zingaretti N, Scalise A, Parodi PC. Common Peroneal Nerve Injury Related to Small Saphenous Vein Surgery: Report of 2 Cases and Review of the Literature. Case Rep Neurol. 2021;13(1):24-30.
161. Cho S, Joh JH. Cyanoacrylate Closure of Small Saphenous Vein Insufficiency. Dermatol Surg. 2021;47(3):381-4.
162. Apruzzi L, Bilman V, Ardita V, Favia N, Saracino C, Chiesa R, et al. Comparison of mechanochemical ablation versus ligation and stripping for the treatment of incompetent small saphenous vein. Phlebology. 2021:2683555211045191.
163. Kubat E, Unal CS, Geldi O, Cetin E, Keskin A, Karapinar K. Comparison of different approaches to small saphenous vein reflux treatment: a retrospective study in two centers. Sao Paulo Med J. 2020;138(2):98-105.
164. Boersma D, Kornmann VN, van Eekeren RR, Tromp E, Unlu C, Reijnen MM, et al. Treatment Modalities for Small Saphenous Vein Insufficiency: Systematic Review and Meta-analysis. J Endovasc Ther. 2016;23(1):199-211.
165. Yuce I, Oguzkurt L, Eren S, Levent A, Kantarci M, Yalcin A, et al. Assessment of posterior accessory great saphenous vein of the leg using ultrasonography: a preliminary study. Surg Radiol Anat. 2016;38(1):123-6.
166. Choi BS, Byun GY, Hwang SB, Koo BH, Lee SR. Long-segment hypoplasia of great saphenous vein with posterior accessory saphenous vein as a connecting vein: a case report. J Surg Case Rep. 2017;2017(3):rjx058.
167. Schul MW, Schloerke B, Gomes GM. The refluxing anterior accessory saphenous vein demonstrates similar clinical severity when compared to the refluxing great saphenous vein. Phlebology. 2016;31(9):654-9.
168. Schul MW, Vayuvegula S, Keaton TJ. The clinical relevance of anterior accessory great saphenous vein reflux. J Vasc Surg Venous Lymphat Disord. 2020;8(6):1014-20.
169. Baccellieri D, Ardita V, Carta N, Melissano G, Chiesa R. Anterior accessory saphenous vein confluence anatomy at the sapheno-femoral junction as risk factor for varicose veins recurrence after great saphenous vein radiofrequency thermal ablation. Int Angiol. 2020;39(2):105-11.

170. Cavallini A, Marcer D, Ferrari Ruffino S. Endovenous treatment of incompetent anterior accessory saphenous veins with a 1540 nm diode laser. Int Angiol. 2015;34(3):243-9.
171. Mishra MK, Soni RK, Mohil RS, Sinha A. Comparative Study of Outcome of Duplex Ultrasound-Guided, Catheter-Directed Foam Sclerotherapy and Radio-frequency Ablation in the Management of Great Saphenous Varicose Veins. Indian J Surg. 2016;78(5):375-81.
172. Bootun R, Lane TR, Dharmarajah B, Lim CS, Najem M, Renton S, et al. Intra-procedural pain score in a randomised controlled trial comparing mechanochemical ablation to radiofrequency ablation: The Multicentre Venefit versus ClariVein(R) for varicose veins trial. Phlebology. 2016;31(1):61-5.
173. Calik ES, Arslan U, Erkut B. Ablation therapy with cyanoacrylate glue and laser for refluxing great saphenous veins - a prospective randomised study. Vasa. 2019;48(5):405-12.
174. Gibson K, Morrison N, Kolluri R, Vasquez M, Weiss R, Cher D, et al. Twenty-four month results from a randomized trial of cyanoacrylate closure versus radiofrequency ablation for the treatment of incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2018;6(5):606-13.
175. Holewijn S, van Eekeren R, Vahl A, de Vries J, Reijnen M, group Ms. Two-year results of a multicenter randomized controlled trial comparing Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation in the treatment of primary great saphenous vein incompetence (MARADONA trial). J Vasc Surg Venous Lymphat Disord. 2019;7(3):364-74.
176. Lane T, Bootun R, Dharmarajah B, Lim CS, Najem M, Renton S, et al. A multi-centre randomised controlled trial comparing radiofrequency and mechanical occlusion chemically assisted ablation of varicose veins - Final results of the Venefit versus Clarivein for varicose veins trial. Phlebology. 2017;32(2):89-98.
177. Lattimer CR, Azzam M, Kalodiki E, Shawish E, Trueman P, Geroulakos G. Cost and effectiveness of laser with phlebectomies compared with foam sclerotherapy in superficial venous insufficiency. Early results of a randomised controlled trial. Eur J Vasc Endovasc Surg. 2012;43(5):594-600.
178. Lattimer CR, Kalodiki E, Azzam M, Makris GC, Somiayajulu S, Geroulakos G. Interim results on abolishing reflux alongside a randomized clinical trial on laser ablation with phlebectomies versus foam sclerotherapy. Int Angiol. 2013;32(4):394-403.
179. Morrison N, Kolluri R, Vasquez M, Madsen M, Jones A, Gibson K. Comparison of cyanoacrylate closure and radiofrequency ablation for the treatment of incompetent great saphenous veins: 36-Month outcomes of the VeClose randomized controlled trial. Phlebology. 2019;34(6):380-90.
180. Morrison N, Gibson K, Vasquez M, Weiss R, Cher D, Madsen M, et al. 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):321-30.
181. Morrison N, Gibson K, McEnroe S, Goldman M, King T, Weiss R, et al. Randomized trial comparing cyanoacrylate embolization and radiofrequency ablation for incompetent great saphenous veins (VeClose). J Vasc Surg. 2015;61(4):985-94.
182. Rai A, Porsalman M, Khatony A, Sobhiyeh M. Comparison of foam sclerotherapy versus radiofrequency ablation in the treatment of primary varicose veins due to incompetent great saphenous vein: Randomized clinical trial. J Vasc Nurs. 2019;37(4):226-31.

183. Tawfik AM, Sorour WA, El-Laboudy ME. Laser ablation versus mechanochemical ablation in the treatment of primary varicose veins: A randomized clinical trial. J Vasc Surg Venous Lymphat Disord. 2020;8(2):211-5.
184. Bademci MS, Kocaaslan C, Aldag M, Yalvac ESD, Oztekin A, Bulut N, et al. Single-center retrospective review of early outcomes of radiofrequency ablation versus cyanoacrylate ablation of isolated great saphenous vein insufficiency. J Vasc Surg Venous Lymphat Disord. 2019;7(4):480-5.
185. Bozoğlan O. A Comparison of NBCA and RFA in Treating Varicose Veins in the Same Patient.
. EJCM 2020;8(1):45-50.
186. Gonzalez-Zeh R, Armisen R, Barahona S. Endovenous laser and echo-guided foam ablation in great saphenous vein reflux: one-year follow-up results. J Vasc Surg. 2008;48(4):940-6.
187. Koramaz I, El Kilic H, Gokalp F, Bitargil M, Bektas N, Engin E, et al. Ablation of the great saphenous vein with nontumescent n-butyl cyanoacrylate versus endovenous laser therapy. J Vasc Surg Venous Lymphat Disord. 2017;5(2):210-5.
188. McGuinness B, Elias F, Ali KP, Ahmad MS, Namburi J, Chan B, et al. A comparison of duplex ultrasound findings after cyanoacrylate embolization versus endovenous laser ablation of the great saphenous vein. J Vasc Surg Venous Lymphat Disord. 2019;7(6):824-31.
189. Ovali C, Sevin MB. Twelve-month efficacy and complications of cyanoacrylate embolization compared with radiofrequency ablation for incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2019;7(2):210-6.
190. van Eekeren RR, Boersma D, Konijn V, de Vries JP, Reijnen MM. Postoperative pain and early quality of life after radiofrequency ablation and mechanochemical endovenous ablation of incompetent great saphenous veins. J Vasc Surg. 2013;57(2):445-50.
191. Yang GK, Parapini M, Gagnon J, Chen JC. Comparison of cyanoacrylate embolization and radiofrequency ablation for the treatment of varicose veins. Phlebology. 2019;34(4):278-83.
192. Vos CG, Unlu C, 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;5(6):880-96.
193. Kolluri R, Chung J, Kim S, Nath N, Bhalla BB, Jain T, et al. Network meta-analysis to compare VenaSeal with other superficial venous therapies for chronic venous insufficiency. J Vasc Surg Venous Lymphat Disord. 2020;8(3):472-81 e3.
194. Parsi K, Roberts S, Kang M, Benson S, Baker L, Berman I, et al. Cyanoacrylate closure for peripheral veins: Consensus document of the Australasian College of Phlebology. Phlebology. 2020;35(3):153-75.
195. Vahaaho S, Halmesmaki K, Mahmoud O, Alback A, Noronen K, Venermo M. Three-year results of a randomized controlled trial comparing mechanochemical and thermal ablation in the treatment of insufficient great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2021;9(3):652-9.
196. Lawaetz M, Serup J, Lawaetz B, Bjoern L, Blemings A, Eklof B, et al. Comparison of endovenous ablation techniques, foam sclerotherapy and surgical stripping for great saphenous varicose veins. Extended 5-year follow-up of a RCT. Int Angiol. 2017 Jun;36(3):281-288.

197. Sussman MS, Ryon EL, Bahga A, Almeida S, Almeida JI. A systematic review of the treatment of residual below the knee venous reflux after endovenous thermal ablation of the great saphenous vein. J Vasc Surg Venous Lymphat Disord. 2022;10(1):233-40.
198. Gifford SM, Kalra M, Gloviczki P, Friese J, Bjarnason H, Duncan A, et al. Reflux in the Below-knee Great Saphenous Vein Can Be Safely Treated with Endovenous Ablation. J Vasc Surg Venous Lymphat Disord. 2013;1(1):112.
199. Theivacumar NS, Gough MJ. Endovenous laser ablation (EVLA) to treat recurrent varicose veins. Eur J Vasc Endovasc Surg. 2011;41(5):691-6.
200. Jimenez JC, Lawrence PF, Pavlyha M, Farley SM, Rigberg DA, DeRubertis BG, et al. Endovenous microfoam ablation of below knee superficial truncal veins is safe and effective in patients with prior saphenous treatment across a wide range of CEAP classes. J Vasc Surg Venous Lymphat Disord. 2022;10(2):390-4.
201. Mozes G, Gloviczki P, Menawat SS, Fisher DR, Carmichael SW, Kadar A. Surgical anatomy for endoscopic subfascial division of perforating veins. J Vasc Surg. 1996;24(5):800-8.
202. Mozes G, Gloviczki P, Kadar A, Carmichael SW. Surgical Anatomy of Perforating Veins. In: Gloviczki P, Bergan JJ, editors. Atlas of Endoscopic Perforator Vein Surgery. 1st ed. London: Springer-Verlag; 1998. p. 17-28.
203. Kianifard B, Holdstock J, Allen C, Smith C, Price B, Whiteley MS. Randomized clinical trial of the effect of adding subfascial endoscopic perforator surgery to standard great saphenous vein stripping. Br J Surg. 2007;94(9):1075-80.
204. Park SW, Hwang JJ, Yun IJ, Lee SA, Kim JS, Chang SH, et al. Randomized clinical trial comparing two methods for endovenous laser ablation of incompetent perforator veins in thigh and great saphenous vein without evidence of saphenofemoral reflux. Dermatol Surg. 2012;38(4):640-6.
205. Fitridge RA, Dunlop C, Raptis S, Thompson MM, Leppard P, Quigley F. A prospective randomized trial evaluating the haemodynamic role of incompetent calf perforating veins. Aust N Z J Surg. 1999;69(3):214-6.
206. Koroglu M, Eris HN, Aktas AR, Kayan M, Yesildag A, Cetin M, et al. Endovenous laser ablation and foam sclerotherapy for varicose veins: does the presence of perforating vein insufficiency affect the treatment outcome? Acta Radiol. 2011;52(3):278-84.
207. van Neer P, Kessels A, de Haan E, Estourgie R, Veraart J, Lijnen R, et al. Residual varicose veins below the knee after varicose vein surgery are not related to incompetent perforating veins. J Vasc Surg. 2006;44(5):1051-4.
208. van Rij AM, Jiang P, Solomon C, Christie RA, Hill GB. Recurrence after varicose vein surgery: a prospective long-term clinical study with duplex ultrasound scanning and air plethysmography. J Vasc Surg. 2003;38(5):935-43.
209. Stuart WP, Adam DJ, Allan PL, Ruckley CV, Bradbury AW. Saphenous surgery does not correct perforator incompetence in the presence of deep venous reflux. J Vasc Surg. 1998;28(5):834-8.
210. Harlander-Locke M, Jimenez JC, Lawrence PF, Derubertis BG, Rigberg DA, Gelabert HA. Endovenous ablation with concomitant phlebectomy is a safe and effective method of treatment for symptomatic patients with axial reflux and large incompetent tributaries. J Vasc Surg. 2013;58(1):166-72.

211. Brown CS, Obi AT, Cronenwett JL, Kabnick L, Wakefield TW, Osborne NH. Outcomes after truncal ablation with or without concomitant phlebectomy for isolated symptomatic varicose veins (C2 disease). J Vasc Surg Venous Lymphat Disord. 2021;9(2):369-76.
212. Conway RG, Almeida JI, Kabnick L, Wakefield TW, Buchwald AG, Lal BK. Clinical response to combination therapy in the treatment of varicose veins. J Vasc Surg Venous Lymphat Disord. 2020;8(2):216-23.
213. Lane TR, Kelleher D, Shepherd AC, Franklin IJ, Davies AH. Ambulatory varicosity avulsion later or synchronized (AVULS): a randomized clinical trial. Ann Surg. 2015;261(4):654-61.
214. Monahan DL. Can phlebectomy be deferred in the treatment of varicose veins? J Vasc Surg. 2005;42(6):1145-9.
215. Welch HJ. Endovenous ablation of the great saphenous vein may avert phlebectomy for branch varicose veins. J Vasc Surg. 2006;44(3):601-5.
216. Carradice D, Mekako AI, Hatfield J, Chetter IC. Randomized clinical trial of concomitant or sequential phlebectomy after endovenous laser therapy for varicose veins. Br J Surg. 2009;96(4):369-75.
217. El-Sheikha J, Nandhra S, Carradice D, Wallace T, Samuel N, Smith GE, et al. Clinical outcomes and quality of life 5 years after a randomized trial of concomitant or sequential phlebectomy following endovenous laser ablation for varicose veins. Br J Surg. 2014;101(9):1093-7.
218. Hager ES, Ozvath KJ, Dillavou ED. Evidence summary of combined saphenous ablation and treatment of varicosities versus staged phlebectomy. J Vasc Surg Venous Lymphat Disord. 2017;5(1):134-7.
219. Aherne TM, Ryan EJ, Boland MR, McKevitt K, Hassanin A, Tubassam M, et al. Concomitant vs. Staged Treatment of Varicose Tributaries as an Adjunct to Endovenous Ablation: A Systematic Review and Meta-Analysis. Eur J Vasc Endovasc Surg. 2020;60(3):430-42.

Table 1. PICO (Patients, Intervention, Comparison, Outcome) data of studies confirming the benefit of Duplex ultrasound in the evaluation of venous reflux

N.	1st Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
1.	Darke 1997[42]	100 limbs of 73 patients with varicose veins	DU	Hand-held continuous-wave Doppler (HHD)	HHD Sensitivity for GSV reflux: 95%, SSV reflux: 90% Specificity for GSV reflux: 100% SSV reflux :93% HHD was inadequate to plan treatment of the SSV	Single-center, cross-sectional prospective study
2.	Mercer, 1998[39]	89 limbs of 61 patients with primary varicose veins	DU	HHD	HHD sensitivity: 73% at the SFJ, 77% at the SPJ, 51% for TPs Surgery planned based on HHD alone would have left residual reflux sites in 24%	Single-center, cross-sectional prospective study
3.	Rautio, 2002[40]	62 limbs of 49 primary varicose veins	DU	HHD	HHD sensitivity at the SPJ: 64%, accuracy: 71% Duplex exam changed treatment plan in 10% of the limbs	Single-center, cross-sectional prospective study
4.	Rautio, 2002[41]	142 limbs of 111 patients with primary varicose veins	DU	HHD	HHD Sensitivity for GSV reflux: 56%, SSV reflux: 23% Specificity for GSV reflux: 97% SSV reflux :96% DU modified treatment plan in 9.1%.	Single-center, cross-sectional prospective study
5.	Dhillon 2020[44]	241 patients with venous reflux symptoms	DU	HHD and point-of-care portable color Doppler ultrasound (PCD)	HHD Sensitivity: AK: 68%, BK, 94% Specificity: AK 50% - BK 12% PCD Sensitivity: AK 69%, BK 74%, Specificity: AK 79% - BK 58% Both HHD and PCD were inadequate alone for evaluation and exclusion of significant venous reflux	Single-center, cross-sectional prospective study

Table 2. The Updated Clinical, Etiology, Anatomy and Pathology (CEAP) classification of chronic venous disorders

(Adopted from Lurie F, Passman M, Meisner M, Dalsing M, Masuda E, Welch H, et al. The 2020 update of the CEAP classification system and reporting standards. J Vasc Surg Venous Lymphat Disord. 2020;8(3):342-52, with permission)

1. ***Clinical Class***

C0	No visible or palpable signs of venous disease
C1	Telangiectasias or reticular veins
C2	Varicose veins
C2r	Recurrent varicose veins
C3	Edema
C4	Changes in the skin and subcutaneous tissue due to chronic venous insufficiency
C4a	Pigmentation or eczema
C4b	Lipodermatosclerosis or atrophie blanche
C4c	Corona phlebectatica
C5	Healed venous ulcer
C6	Active venous ulcer
C6r	Recurrent active venous ulcer

Each clinical class is sub-characterized by a subscript indicating the presence (symptomatic, s) or absence (asymptomatic, a) of symptoms attributable to venous disease. Symptoms can include ache, pain, tightness, skin irritation, heaviness, muscle cramps, as well as other complaints attributable to venous dysfunction

2. ***Etiology***

Ec Congenital

Ep Primary

Es Secondary (postthrombotic)

En No venous etiology identified

3. Anatomy

As Superficial veins

Ap Perforator veins

Ad Deep veins

An No venous location identified

4. ***Pathophysiology***

Pr Reflux

Po Obstruction

Pr,o Reflux and obstruction

Pn No venous pathophysiology identifiable

Table 3. PICO (Patients, Intervention, Comparison, Outcome) data of studies comparing outcomes of thermal vs non-thermal ablations of refluxing superficial truncal veins.

N	1st Author, Year	Patients	Intervention	Comparison	Outcomes	Study Design
1	Morrison, 2015[181] Morrison 2017,[180]	222 patients with varicose veins (C2-C4)	RFA of GSV (n=114)	CAC of GSV (n=108)	No difference in intra-procedural and 24 hr pain scores, more ecchymosis after RFA (P<.01) At 1 month, 100% occlusion after CAC , 87% occlusion after RFAs.	Randomized Controlled Trial (VeClose)

	Morrison 2020[12]	89 patients with 60 months follow-up	RFA (n=33)	CAC (n=47) (+9 roll-in patients)	At 1 year no difference in occlusion , recanalization, symptoms or QoL. At 5 years both treatments effective, non-inferiority of CAC vs RFA was demonstrated.	
2.	Koramaz, 2017[187]	339 patients with varicose veins (C2-C5)	EVLA (n=189)	CAC** (n=150)	At 12 months, occlusion rates were 98.6% vs 97.3%, P=.65)	Retrospective comparative study
3.	Yang, 2019[191]	335 patients with varicose veins, 476 veins treated (GSV;403, SSV:54,AAGSV:17, Perforator: 2)	RFA (338 veins)	CAC (148 veins)	Same early closure rates (100%vs 99%) More post-operative phlebitis after RFA (16% vs 5%, P<.05) 3 infections from glue clumps needed excision and drainage	Retrospective cohort study
4.	Bozkurt, 2016 [93]	310 patients with varicose veins *C2-C4)	EVLA (n=156)	CAC *(n=154)	Periprocedural pain less with CAC (P<.001) Ecchymosis at 3 days less with CAC. At 6 months and one year, no difference in QOL or closure rates.	Prospective nonrandomized comparative trial
5.	Calik, 2019[173]	412 limbs in 400 patients with varicose veins (C2-C4)	EVLA (n=204)	CAC * (n= 208)	Periprocedural pain less after CAC (P<001) Induration, ecchymosis, and paresthesia rates were higher with EVLA.(P<.001) 12 months QoL and closure rates similar (96.6% vs 94.1%)	Prospective nonrandomized, comparative
6.	Ovali, 2019[189]	244 patients with varicose veins (C2-C4)	RFA of GSV (n=128)	CAC * of GSV (n=116)	Technical success 100% in both groups. Early severe pain, ecchymosis, discomfort significantly more after RFA (P<.05) At 1 year similar occlusion rates and QoL.	Non-randomized retrospective Comparative study
7.	Vahaaho, 2021[195]	132 patients with varicose veins (C2-C4) randomized (intention to treat)	EVLA (n=34) RFA (n=33) (3-year follow-up: 31,25)	MOCA (n=65) (3 y-ear follow-up: 50)	At 3 years closure rate was significantly lower for MOCA than for EVLA or RFA (82% vs 100%, P<.005)	Randomized controlled trial
8.	Lane, [176]	170 patients with varicose veins (GSV or SSV)	RFA (n=83)	MOCA (n=87))	Intraprocedural pain (maximum and average pain scores significantly less after MOCA (P<.003). No difference between groups in return to work or normal activities. At 1 and 6 months no difference in QoL between groups	
9.	Mohamed, 2021[96]	150 patients with varicose veins(C2-C6)	EVLA (n=75)	MOCA (n=75)	Similar intra-procedural pain scores (P=.021) At 1 year, occlusion rates after EVLA were 63/69 (91%) compared to 53/69 (77%) in the MOCA group; P = 0.020.	Randomized controlled trial

					At 1 year both groups had similar, significant improvement in VCSS and AVVQ	
10	Lawaetz, 2017[7]	500 patients (580 limbs) with varicose veins (GSV)	EVLA (n-=125) RFA (n-=125), HL&S (n-=125)	UGFS, using physician-compounded foam (3% polidocanol) (n-=125),	At 5 years, all treatment modalities were efficacious and resulted in a similar improvement in VCSS and QOL. Significantly more recanalizations of the treated vein and more reoperations with UGFS, using physician-compounded foam	Randomized Controlled Trial
11.	Vahaaho, 2015[8]	196 patients with varicose veins (166 in the 5 - year follow-up), (GSV)	EVLA (n=57) HL&S (n=50)	UGFS, using physician-compounded foam (1% polidocanol, 1 or 3% sodium tetradecyl sulphate) (n-=59),	At 5 years UGFS had the lowest occlusion rate without additional intervention (41% vs 89% vs 96%, P<.001). AVSS scores were similar	Randomized controlled trial
12.	Brittenden, 2014[100] Brittenden, 2019[10]	798 patients with varicose veins randomized, (GSV or SSV), C2-C6) At 5 years 595 patients studied	EVLA (n=212) Open surgery (289)	UGFS, using physician-compounded foam (1 or 3% sodium tetradecyl sulphate) (n-=292),	Ablation rates at 6 weeks and 6 months were lower after UGFS. At 5 years, disease specific QoL was worse after UGFS. Cost-effectiveness model iteration favored EVLA.	
13.	Biemans, 2013[134]	240 patients with varicose veins (GSV) C2-C5)	EVLA (n=78) HL&S (n=68)	UGFS, using physician-compounded foam (n=77),	At 1 year EVLA was superior to UGFS in terms of GSV closure (P<001). No differences in QoL.	
14.	Lattimer, 2013 [178]	100 patients with varicose veins (GSV) CC2-C6)	EVLA (n=50)	UGFS, using physician-compounded foam (n=50)	Costs and post-procedure pain were significantly less and treatment duration, and time to recover y significantly shorter after UGFS. After UGFS ,56% required additional treatment (vs. 6% with EVLA)	Randomized Controlled Trial
15.	Rasmussen, 2011[135] Rasmussen, 2013[123]	580 limbs of 500 patients with varicose veins (GSV) (C2-4)	EVLA (n=125) RFA (n=125) HL&S (n=124)	UGFS, using physician-compounded foam (n=124)	Postintervention pain score significantly less after UGFS and RFA. At 1 year GSV closure was significantly lower after UGFS. QoL improved in all groups At 3 years more recanalization and more reoperations after UGFS. QoL improved in all groups.	Randomized Controlled Trial
16.	Gonzalez-Zeh, 2008[186]	98 patients with varicose veins (GSV), (C2-C6)	EVLA (n=45)	UGFS, using physician-compounded foam (n=50) (n=53)	Procedure associated pain worse after EVLA (P<.0001) .At 1 year, GSV closure was higher after EVLA 93% vs 77% P<.046) VCSS improved in both groups (P < .0001).	Nonrandomized prospective trial

17.	Deak, 2022[154]	1070 patients with varicose veins (C2-C6) (C2, n=469)	EVLA (n=550)	UGSF, using PEM (polidocanol endovenous microfoam)	Reflux eliminated in 93.5% (514/550) after PEM and 92.8% (482/520) after EVLA. Follow-up 3 years. No neurological or cardiac adverse events after PEM	Retrospective cohort study

*NBCA: VariClose Vein Sealing System (VVSS); Biolas, Ankara, Turkey

Table 4. PICO (Patients, Intervention, Comparison, Outcome) data of studies comparing outcomes of saphenous ablation with and without perforator vein ablation in patients with varicose veins.

N.	1st Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
1.	Kianifard, B 2007[203]	72 patients randomized	38 patients underwent standard surgery + SEPS (71% C2 disease)	32 underwent only standard surgery (75% C2 disease)	At 1-year significant reduction in number of IPVs and limbs with IPVs with addition of SEPS No significant difference in pain (VAS), mobility, cosmetic score or QoL (SF-36, AVVQ) between groups.	Randomized control trial
2.	Park S W, 2012[204]	69 Patients with varicose veins (C2/C3) with thigh IPV without SFJ reflux but with IPV reflux into GSV	Endovenous laser ablation (EVLA) of IPVs in the thigh followed by ablation of the GSV (IPVA) below the IPV (n=34)	EVLA of the GSV (GSVA) starting just proximal to the thigh IPV without ablation of the IPV itself (n=35)	Technical success was significantly lower with IPVA (76.5%) compared to the than GSVA (100%) [p = .002]. No significant difference in clinical success (continued closure of treated vein) between IPVA and GSVA (1 week - 96.1% vs 100%; 1 month - 100% vs 97.1%; 3, 6 and 12 months - 100% for both groups). No significant difference in occurrence and degree of complications between the two groups.	Randomized control trial

3.	Fitridge R A, 1999[205]	38 limbs in 35 patients with incompetent great saphenous veins and one or more IPV	GSV stripping and phlebectomy with open ligation of IPV (n=21)	GSV stripping and phlebectomy only (n=17)	No significant difference between groups in either their preoperative or their postoperative venous function (Venous volume [VV], venous filling index [VFI] and ejection fraction [EF]) At 3 months, DUS failed to identify previously seen incompetent perforators in approximately 50% of patients (8/17) who did not undergo open ligation of IPV	Randomized control trial
4.	Koroglu M, 2011[206]	60 limbs in 55 patients (C1 to C5; C2 = 21 [35%])	EVLA of refluxing saphenous vein and foam sclerotherapy (FS) of venous varicosities	EVLA of refluxing saphenous vein and FS of venous varicosities + FS of IPV	At 6 months complete occlusion of IPV noted in 75% compared to 98.6% for the saphenous veins No significant difference in improvement of VCSS between groups Improvement in VAS score greater after treatment of isolated saphenous vein reflux ($p<0.05$)	Single-center prospective study

GSV great saphenous vein; SFJ – Saphenofemoral junction; SEPS – Subfascial endoscopic perforator surgery; IPV – Incompetent perforator vein; VAS – Visual Analog Scale; QoL – Quality of Life; AVVQ – Aberdeen Varicose Vein Questionnaire.

SUPPLEMENTARY TABLES (on-line only)

Supplementary Table 1. Terminology. The most frequently used anatomical, clinical, physiological and descriptive venous terms include the following:

Term	Definition
Axial reflux	Uninterrupted retrograde venous flow from the groin to the calf. Superficial reflux is confined to the superficial venous system, deep reflux is confined to the deep venous system, and combined reflux involves any combination of the three main venous systems (superficial, deep, perforating).
Chronic venous disorders	Includes the full spectrum of morphological and functional abnormalities of the venous system
Chronic venous disease	Morphological and functional abnormalities of the venous system of long duration manifested by symptoms or signs or both indicating the need for investigation and/or care.
Chronic venous insufficiency	This term is reserved for advanced chronic venous disease (C3-C6 classes of the CEAP classification) that is applied to functional abnormalities of the venous system producing edema, skin changes, or venous ulcers.
Congenital venous reflux	Retrograde venous flow of abnormal

	duration in any venous segment, caused by the absence or abnormal development of venous valves.
Mechanochemical ablation (Mocca procedure)	A non-tumescent non-thermal technique to ablate superficial truncal veins. An oscillating rotating wire disrupts the endothelial lining of target veins allowing the simultaneously injected sclerosant to penetrate the deeper layers of the vein wall, ultimately resulting in vein sclerosis and obstruction.
Mini-phlebectomy:	Removal of a vein segment through a small skin incision or stab wound. Synonyms include phlebectomy, ambulatory phlebectomy, microphlebectomy or stab phlebectomy.
Non-truncal vein:	Un-named or nonlongitudinal saphenous or deep vein
Post-thrombotic syndrome:	Chronic venous symptoms and/or signs secondary to deep vein thrombosis and its sequelae.
Primary venous reflux	Retrograde venous flow of abnormal duration in any venous segment,

	caused by idiopathic venous valve dysfunction.
Reticular veins	Dilated bluish subdermal veins that range from 1 mm to <3 mm in diameter and are usually tortuous. This excludes normal visible veins in people with thin, transparent skin. Synonyms include blue veins, subdermal varices, and venulectasias. In the CEAP classification, reticular veins are part of the C1 clinical class.
Secondary venous reflux	Retrograde venous flow of abnormal duration in any venous segment, caused by thrombosis, trauma, or mechanical, thermal, or chemical etiologies.
Sclerotherapy:	Obliteration of a vein by chemical introduction (liquid, physician generated foam or polidocanol endovenous microfoam).
Truncal vein	named longitudinal saphenous or deep veins
Diseased tributaries	Varicose veins or telangiectasias

	associated with the vein in question
Stripping	Removal of a long vein segment, usually most of the great saphenous or the small saphenous vein by means of a device.
Teleangiectasia	Small, dilated, flat, thin-walled, blue or red veins <1 mm in diameter that are seen near the surface of the skin. Numerous telangiectasias near the foot and ankle are termed corona phlebectatica. Commonly termed spider veins, they are distinguished from reticular veins by having no profile, but telangiectasia, spider veins, and reticular veins are all classified as C1 according to the CEAP classification.
TESSARI technique	Method of producing foam for immediate use by agitating liquid sclerosant with a gas at a predefined ratio using two interconnected syringes, which are pumped back and forth rapidly about 10 times until compact foam with microscopic bubbles is produced. Named after L. TESSARI (Italy).

Varicose veins	Subcutaneous dilated vein 3 mm in diameter or larger, when measured in an upright position. May involve the saphenous veins, saphenous tributaries, or nonsaphenous superficial leg veins. Varicose veins are usually tortuous, but tubular saphenous veins with demonstrated reflux may be classified as varicose veins.
Venous ablation	Removal, occlusion or destruction of a vein by mechanical, thermal, or chemical means.
Venous compression:	Narrowing or occlusion of the venous lumen as a result of extra-luminal pressure.
Venous occlusion	Total obliteration of the venous lumen.
Venous obstruction	Partial or total blockage to venous flow.
Venous reflux	Retrograde venous flow of abnormal duration in any venous segment.
Venous valvular incompetence	Venous valve dysfunction resulting in retrograde venous flow of abnormal

	duration.

Supplementary Table 2. Evidence to decision framework table.
Duplex ultrasound scanning vs hand-held Doppler evaluation or other diagnostic methods

Domain	Evidence/panel input	Judgment
How substantial are the desirable anticipated effects of the strategy?	DU changed the intervention plan in 10-25% of cases. HHD had the sensitivity only of 51-77%.	Large
How substantial are the undesirable anticipated effects?	No known undesirable effects. DU is a non-invasive, safe and convenient diagnostic test.	Trivial
Do the desirable effects outweigh the undesirable effects?	Clearly there are benefits of DU and no undesirable effect.	Yes
Is there important uncertainty or variability about how much people value the main outcomes?	No available direct data	Probably no important uncertainty or variability
What is the overall certainty of the evidence of effects?	In addition to the available data, there is an overwhelming opinion of experts supporting DU as the evaluation of choice for patients with varicose veins.	Moderate
How large are the resource requirements associated with the intervention?	DU equipment is already available in most vein clinics and the cost is likely small relative to the overall cost of care.	Small costs
How large is the incremental cost relative to the net benefit?	The strategy of DU evaluation is already implemented in the vein clinics. The benefit of more precise diagnosis with DU could bring only savings, although there is no cost-effectiveness analysis available.	Unknown
What would be the impact on health inequities?	No available data	Unknown

Is the option acceptable to key stakeholders?	There is also a clear agreement among the most experts and practitioners about evaluating patients with DU.	Yes
Is the option feasible to implement?	As DU equipment is already available in most vein clinics, the option feasibility should not be difficult.	Yes

Supplementary Table 3. Evidence to decision framework table. Endovenous ablation vs. high ligation and stripping vs. compression stockings, in patients with symptomatic varicose veins and axial reflux in the superficial truncal veins

Domain	Evidence/panel input	Judgment
How substantial are the desirable anticipated effects of the strategy?	Decrease in peri-operative pain and earlier return to normal activity and reduced risk of varicosities at 5 years are more likely with endovenous venous intervention. High ligation and stripping was associated with higher anatomic closure rates at 30 days and 5 years when compared with radiofrequency ablation and ultrasound-guided foam sclerotherapy, while no significant difference was seen when compared with endovenous laser ablation at 5 years.	Moderate
How substantial are the undesirable anticipated effects?	Increased risk of pigmentation and some procedural pain are expected. Need for analgesia is higher with ligation and stripping.	Small
Do the desirable effects outweigh the undesirable effects?	For most patients, the desirable effects outweigh the undesirable effects.	Yes
Is there important uncertainty or variability about how much people value the main outcomes?	Studies on patient preference demonstrate significant heterogeneity in patient preferences with one study reporting that a majority of patients are not concerned about missing work, another reporting that cost was the most important component and variable responses regarding ranking of discomfort and long term risk of	Possibly important uncertainty or variability

	recurrence . Given that superficial venous disease is a chronic disease and there is lack of consensus regarding patient preference, the committee prioritized quality of life at 5 years and recurrence/need for reintervention over short term results.	
What is the overall certainty of the evidence of effects?	Moderate certainty for venous intervention vs. compression stockings. Low certainty for head-to-head comparisons.	Moderate
How large are the resource requirements associated with the intervention?	The type of insurance often drives costs and out of pocket expenses. Out of pocket procedural costs vary widely.	Unknown
How large is the incremental cost relative to the net benefit?	One study from the UK showed that endovenous therapies were most cost effective, followed by UGFS, HL&S, then conservative therapy.	Unknown
What would be the impact on health inequities?	For patients who do not have access, or for whom the cost of endovenous therapy is prohibitive, HL&S is an acceptable strategy.	Unknown
Is the option acceptable to key stakeholders?	All studies showed either strategy is acceptable when compared to no therapy. Individuals who place high priority on long-term outcomes would likely not choose UGFS.	Probably Yes
Is the option feasible to implement?	Yes, it is a widely adopted technology. High ligation and stripping can be used if technology or expertise for endovenous ablation is not available, or if venous anatomy precludes endovenous treatment.	Probably Yes

Supplementary Table 4. Evidence to decision framework table. Thermal ablation versus non-thermal ablation of saphenous veins

Domain	Evidence/panel input	Judgment
How substantial are the desirable anticipated effects of the strategy?	There is no clear difference in terms of outcomes between thermal and non-thermal vein ablation as the data is	Unknown

	indeterminate and the non-thermal group is heterogeneous.	
How substantial are the undesirable anticipated effects?	Unclear difference in outcomes. Thermal interventions may be associated with lower generic quality of life scores and an increased risk of adverse events when compared with CAC or n-butyl cyanoacrylate, but this evidence is uncertain	Small
Do the desirable effects outweigh the undesirable effects?		Probably no
Is there important uncertainty or variability about how much people value the main outcomes?	There is uncertainty about the value patients place on procedural pain versus closure rates or long term QOL. These leave the available expertise of the treating physician and the preference of the patient as important components of the decision.	Possibly important uncertainty or variability
What is the overall certainty of the evidence of effects?		Very low when comparing the two strategies. Moderate for either strategy
How large are the resource requirements associated with the intervention?	Unknown	Unknown
How large is the incremental cost relative to the net benefit?	Some data suggest that CAC may not be as cost-effective as the other ablation techniques. Cost factors do remain an important factor in some settings and are an important part of the decision making process.	Unknown
What would be the impact on health inequities?	No data available. Allowing physicians and patients to determine which may be the better route should help minimize inequity.	Unknown
Is the option acceptable to key stakeholders?	No data available.	Probably Yes
Is the option feasible to implement?	Prior RCTs do suggest that choosing between thermal or non-thermal options is often feasible.	Probably Yes

Supplementary Table 5. Evidence to decision framework table.
Treatment of incompetent perforators in patients with C2 disease vs. no treatment

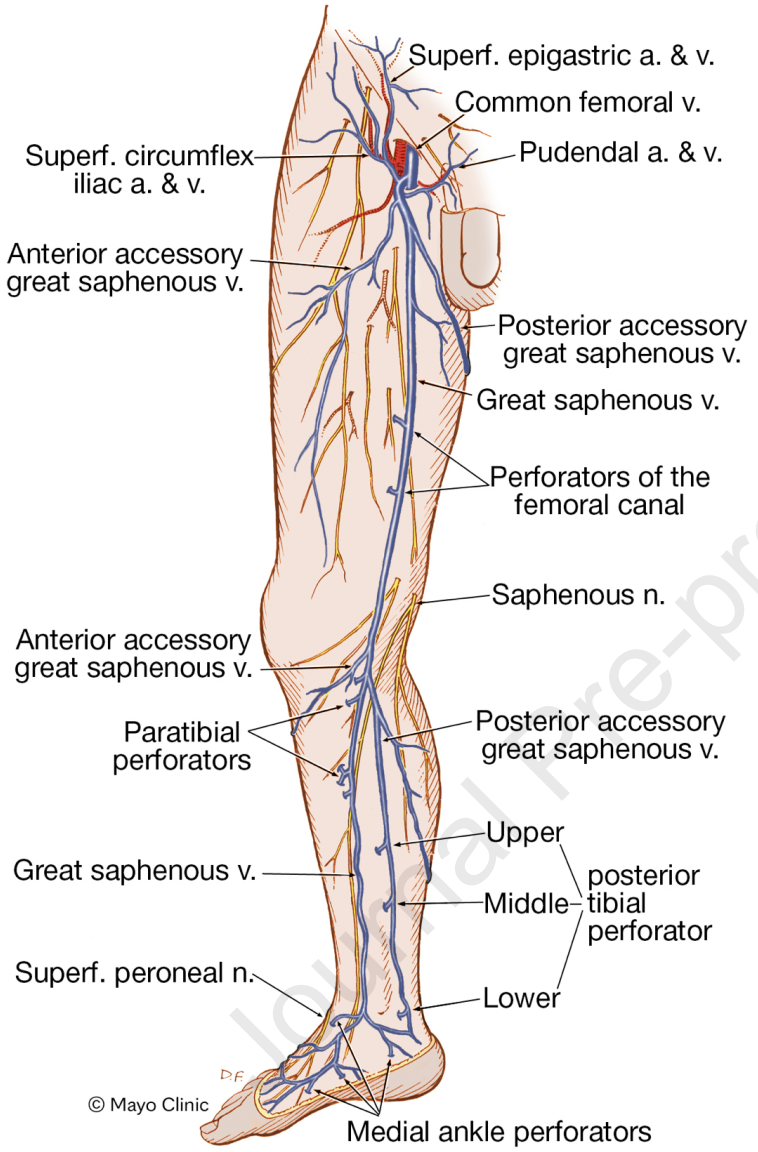
Domain	Evidence/panel input	Judgment
How substantial are the desirable anticipated effects of the strategy?	Not substantial. Intervention for incompetent perforator veins does not improve hemodynamic status, clinical presentation or quality of life compared to treatment of superficial reflux alone. Treatment however may have a role in patients with persistent symptoms post superficial venous surgery with persistent superficial reflux or initial presence of deep venous reflux.	Trivial
How substantial are the undesirable anticipated effects?	Not Substantial. Undesirable effects such as venous thrombotic event, skin/soft tissue injury and nerve injury are possible.	Trivial
Do the desirable effects outweigh the undesirable effects?	They do not, given the lack of significant evidence to proceed with intervention for incompetent perforator veins in C2 disease and the potential for undesirable effects.	Probably no
Is there important uncertainty or variability about how much people value the main outcomes?	Unknown. Intervention for incompetent perforator veins treatment in C2 may result in over treatment or undertreatment.	Unknown
What is the overall certainty of the evidence of effects?	Data are derived from many prospective cohort studies and limited data from randomized clinical trials.	Low
How large are the resource requirements associated with the intervention?	It may lead to added cost to index procedure	Moderate costs
How large is the incremental cost relative to the net benefit?	Unknown	Unknown
What would be the impact on health inequities?	Unknown	Unknown
Is the option acceptable to key stakeholders?	Unknown	Unknown
Is the option feasible to implement?	While it may be feasible, routine treatment of incompetent	Probably Yes

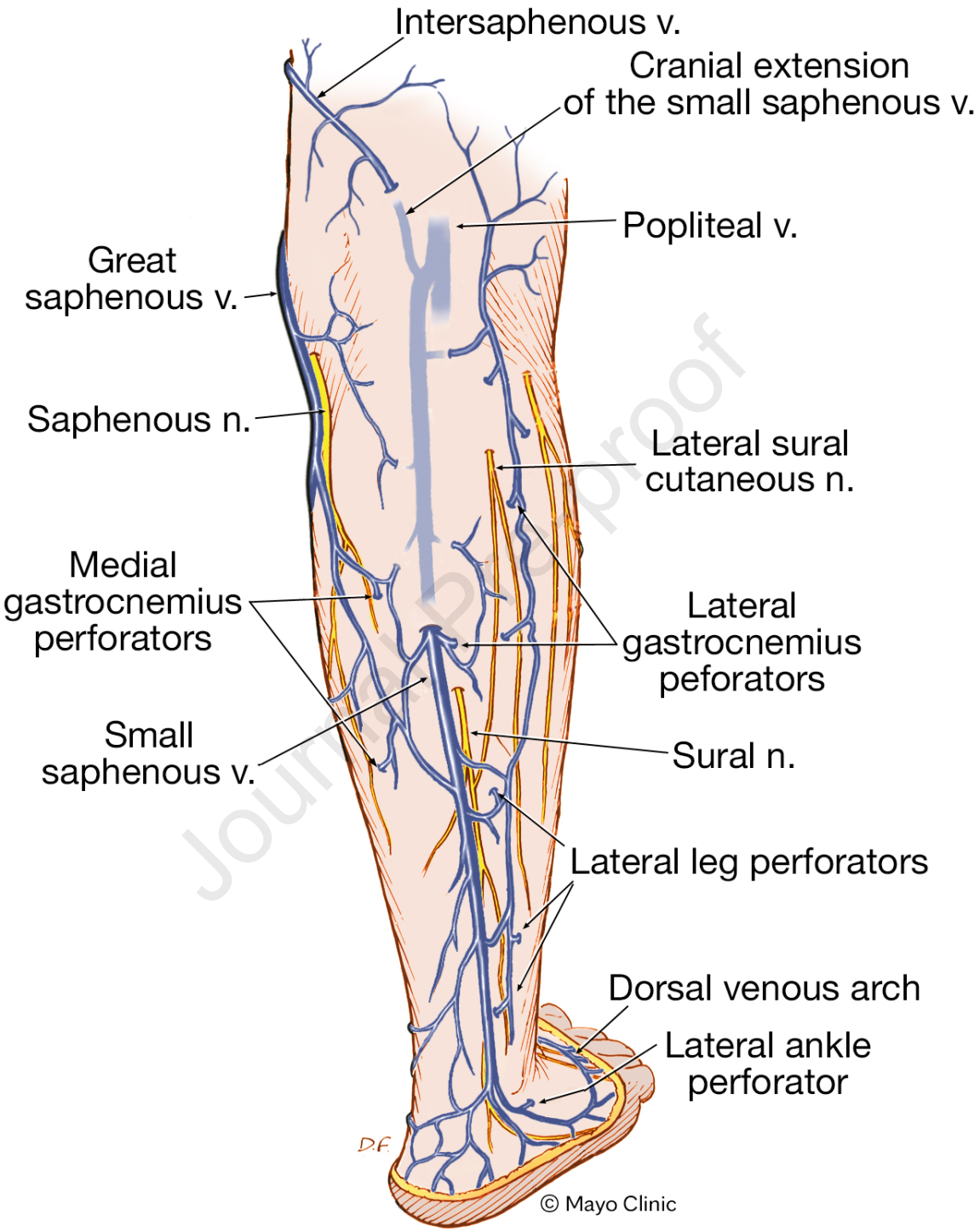
	perforators in patients with C2 disease does not have a documented benefit	

Supplementary Table 6. Evidence to decision framework table.
Concomitant phlebectomy with Saphenous Vein Ablation, vs staged phlebectomy after Saphenous Vein Ablation

Domain	Evidence/panel input	Judgment
How substantial are the desirable anticipated effects of the strategy?	There are important upsides to treating all lower extremity varicose veins in one setting.	Moderate
How substantial are the undesirable anticipated effects?	Likely small increase in post-operative pain. 50%-70% of patients would not need subsequent phlebectomy due to symptom relief after Saphenous vein ablation	Moderate
Do the desirable effects outweigh the undesirable effects?	For some patients, the desirable effects would outweigh the undesirable effects. When combined therapy was compared to ablation only, multivariate analysis revealed significant reduction of the VCSS scores on the CT vs the UT groups (P=.002)	Probably yes
Is there important uncertainty or variability about how much people value the main outcomes?	Short term results confirmed that concomitant phlebectomy prolonged the ablation procedure but reduced the need for secondary procedures and significantly improved the quality of life. Five-year results of the same RCT showed excellent and similar clinical results and quality of life scores in both groups, but concomitant treatment was associated with optimal improvement in both QoL and the severity of clinical disease. While both strategies are acceptable, concomitant procedures (combined treatment -CT), are more often chosen by the patient.	Probably not important uncertainty or variability
What is the overall certainty of the evidence of effects?		Low

How large are the resource requirements associated with the intervention?	One study showed CT procedure time was significantly longer than UT alone (65 min vs 45 min, P=0.002). From the panel's practice, patient satisfaction with CT seems to outweigh the added time.	Small costs
How large is the incremental cost relative to the net benefit?	One study suggested non-significance between CT vs UT in return to work (10 vs 3 days respectively) and return to normal activities (8 vs 2 days respectively) this is likely a Type 2 error as only 50 patients were randomized. From the practice of the panel, they we see that most patients are not concerned with the additional recovery time.	Unknown
What would be the impact on health inequities?	Unknown	Unknown
Is the option acceptable to key stakeholders?	All studies showed either strategy is acceptable, depending upon patient preference. From the practice of the panel, they see more patients choosing CT vs UT.	Probably Yes
Is the option feasible to implement?	All studies showed it is feasible to implement. From the practice of the panel, they observe that it is easy to implement	Probably Yes





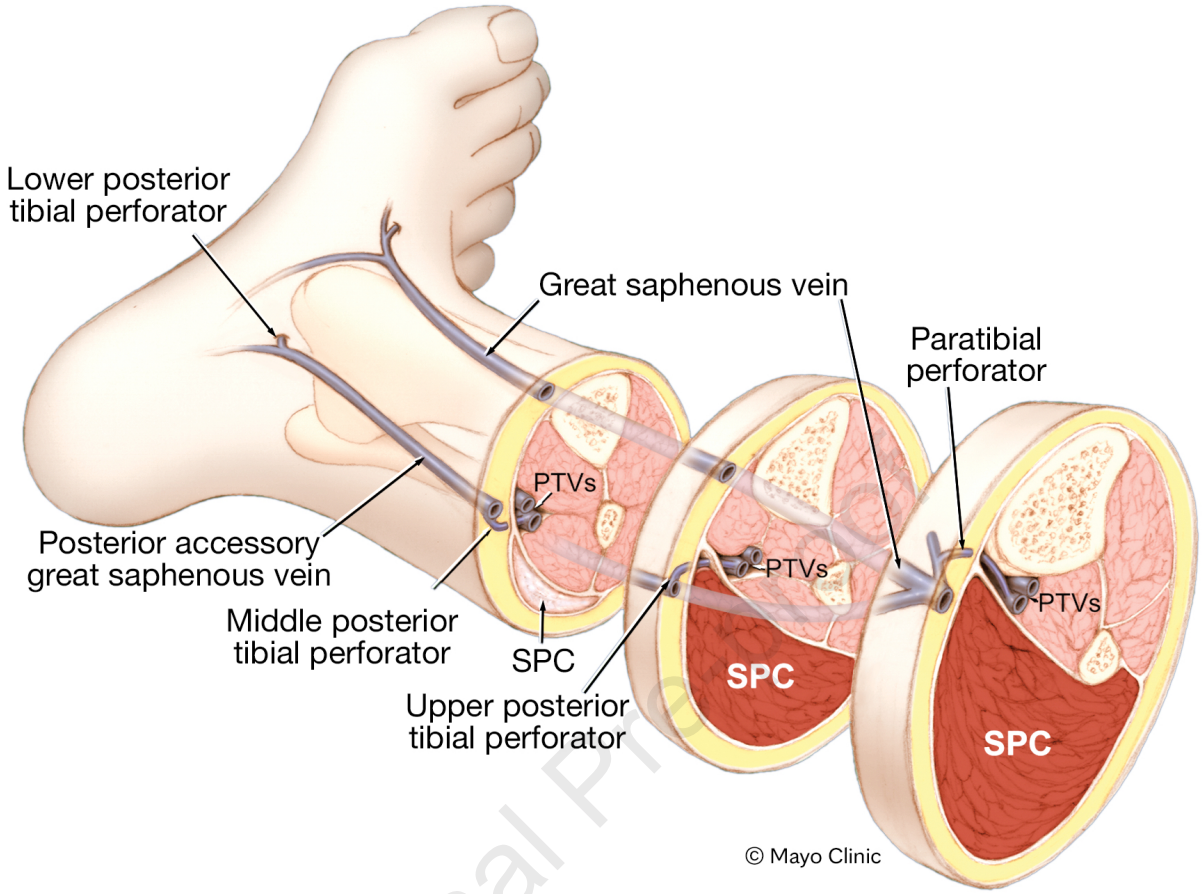


Figure Legends

Varicose Vein Clinical Practice Guidelines. Gloviczki et al.

Fig. 1. Anatomy of the great saphenous vein and its tributaries. Used with permission of Mayo Foundation for Education and Research, all rights reserved.

Fig.2. Anatomy of the small saphenous vein and its tributaries. Used with permission of Mayo Foundation for Education and Research, all rights reserved.

Fig.3. Perforating veins of the leg. (SPC= superficial posterior compartment, PTV= posterior tibial vein). Used with permission of Mayo Foundation for Education and Research, all rights reserved.

Table Legends.

Table 1. PICO (Patients, Intervention, Comparison, Outcome) data of studies confirming the benefit of Duplex ultrasound in the evaluation of venous reflux

Table 2. The Updated Clinical, Etiology, Anatomy and Pathology (CEAP) classification of chronic venous disorders. Adopted from Lurie F, Passman M, Meisner M, Dalsing M, Masuda E, Welch H, et al. The 2020 update of the CEAP classification system and reporting standards. J Vasc Surg Venous Lymphat Disord. 2020;8(3):342-52, with permission.

Table 3. PICO (Patients, Intervention, Comparison, Outcome) data of studies comparing outcomes of thermal vs non-thermal ablations of refluxing superficial truncal veins.

Table 4. PICO (Patients, Intervention, Comparison, Outcome) data of studies comparing outcomes of saphenous ablation with and without perforator vein ablation in patients with varicose veins.

Supplementary Table 1. Terminology. The most frequently used anatomical, clinical, physiological and descriptive venous terms include the following:

Supplementary Table 2. Evidence to decision framework table.

Duplex ultrasound scanning vs hand-held Doppler evaluation or other diagnostic methods

Supplementary Table 3. Evidence to decision framework table.
Endovenous ablation vs. high ligation and stripping vs. compression stockings, in patients with symptomatic varicose veins and axial reflux in the superficial truncal veins

Supplementary Table 4. Evidence to decision framework table.
Thermal ablation versus non-thermal ablation of saphenous veins

Supplementary Table 5. Evidence to decision framework table.
Treatment of incompetent perforators in patients with C2 disease vs. no treatment

Supplementary Table 6. Evidence to decision framework table.
Concomitant phlebectomy with Saphenous Vein Ablation, vs staged phlebectomy after Saphenous Vein Ablation