The 2023 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 II.

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Author conflict of interest: J.F. is a paid speaker for Janssen Pharmaceuticals. M.L.G. has been paid a consulting fee by VitasupportMD and is on their advisory board. R.K. is a paid consultant for Abbott Laboratories, Auxetics, Avail Medsystems, Boston Scientific, Inari, Medtronic, Penumbra, Prairie Education and Research Co-operative, Philips, SurModics, and Syntactx. M.H. Murad was funded by the Society for Vascular Surgery to conduct systematic reviews and provide methodology expertise. A.T.O. is a primary investigator for preclinical research grants funded by Medtronic and SurModics. K.J.O. is an Intersocietal Accreditation Commission board member, a speaker/U.S. course host for Medtronic, and a speaker for Boston Scientific. S.M.W is a paid speaker for Janssen Pharmaceuticals and on advisory board of Tactile Inc. P.G., P.F.L., M.H. M., J.A., K.B., R.L.B., M.D., E.F., A.H., A.J., S.V., and H.J.W. have no conflicts of interest.

Independent peer review and oversight was provided by the members of the SVS Document Oversight Committee (Marc L. Schermerhorn, Chair, Britt Tonnessen, Vice Chair, Kellie Brown, Mohammad H. Eslami, Raul J. Guzman, Peter Henke, Vikram Kashyap, Ahmed Kayssi, Chris Kwolek, Erica Mitchell, Patrick Muck, William P. Robinson, Evan Ryer, Palma Shaw, Christopher Smolock, Chandu Vemuri, Greg Westin, and Karen Woo).

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ABSTRACT

The Society for Vascular Surgery (SVS), the American Venous Forum (AVF), and the American Vein and Lymphatic Society (AVLS) recently published Part I of the 2022 clinical practice guidelines on varicose veins. Recommendations were based on the latest scientific evidence researched following an independent systematic review and meta-analysis of five critical issues affecting the management of patients with lower extremity varicose veins, using the PICO (patients, interventions, comparators, and outcome) system to answer critical questions. Part I discussed the role of Duplex ultrasound scanning (DUS) in the evaluation of varicose veins and treatment of superficial truncal reflux. Part II focuses on evidence supporting the prevention and management of varicose vein patients with compression, on treatment with drugs and nutritional supplements, on evaluation and treatment of varicose tributaries, on superficial venous aneurysms, and on the management of complications of varicose veins and their treatment. All Guidelines were based on systematic reviews, and they were graded according to the level of evidence and the strength of recommendations, using the GRADE method. All ungraded Consensus Statements were supported by an extensive literature review and the unanimous agreement of an expert, multidisciplinary panel. Ungraded Good Practice Statements are recommendations that are supported only by indirect evidence. The topic, however, is usually non-controversial and agreed upon by most stakeholders. The Implementation Remarks contain technical information that supports the implementation of specific recommendations. This comprehensive document includes a list of all recommendations (Part I-II), ungraded consensus statements, implementation remarks, and best practice statements to aid practitioners with appropriate, up-to-date management of patients with lower extremity varicose veins.

Keywords: Ablation; Compression; Cyanoacrylate; Mechanochemical; Endovascular; Endovenous; Foam; Guidelines; Thrombosis; Thrombophlebitis; Venoactive drugs; Laser; Radiofrequency; Sclerotherapy; Saphenous vein; Varicose veins; Venous insufficiency

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1. EVALUATION OF PATIENTS WITH VARICOSE VEINS

1.1. Classification and grading of clinical severity of chronic venous disorders

	GOOD PRACTICE STATEMENTS
1.1.1.	We recommend the use of the 2020 updated CEAP classification system for chronic venous disorders. The clinical or basic CEAP classification can be used for clinical practice, and the full CEAP classification system should be used for clinical research.
1.1.2.	We recommend the use of the revised Venous Clinical Severity Score (VCSS) for patients with chronic venous disorders for grading of clinical severity and for assessment of post treatment outcome.

1.2-1.5. Duplex ultrasound scanning (DUS)

	GUIDELINE	Grade of Recommendation	Quality of Evidence
1.2.1.	For patients with chronic venous disease of the lower extremities, we recommend DUS as the diagnostic test of choice to evaluate for venous reflux.	**1 (strong)**	**B (moderate)**
	IMPLEMENTATION REMARKS		
1.3.1.	Reflux is defined as a minimum value >500 ms of reversed flow in the superficial truncal veins [great saphenous vein (GSV), small saphenous vein (SSV), anterior accessory great saphenous vein (AAGSV), posterior accessory great saphenous vein (PAGSV)] and in the tibial, deep femoral, and perforating veins. A minimum value of >1 second of reversed flow is diagnostic of reflux in the common femoral, femoral, and popliteal veins. There is no minimum diameter required to have pathologic reflux.		
1.3.2.	Axial reflux of the GSV is defined as uninterrupted retrograde venous flow from the groin to the upper calf. Axial reflux in the SSV is defined as being from the knee to the ankle. Axial reflux in the AAGSV and PAGSV is retrograde flow between two measurements, at least five cms apart. Retrograde flow can occur in the superficial or deep veins, with or without perforating veins. Junctional reflux is limited to the saphenofemoral or saphenopopliteal junction (SPJ). Segmental reflux occurs in only a portion of a superficial or deep truncal vein.		
1.3.3.	A definition of "pathologic" perforating veins in patients with varicose veins (CEAP [Clinical Class, Etiology, Anatomy, Pathology] clinical class C2 includes those with an outward flow duration of >500 ms and a diameter of >3.5 mm on duplex ultrasound.		
	GOOD PRACTICE STATEMENTS		
1.4.1.	We recommend that evaluation of reflux with DUS be performed in an Intersocietal Accreditation Commission or American College of Radiology accredited vascular laboratory by a credentialed ultrasonographer, with the patient standing whenever possible. A sitting or reverse Trendelenburg position can be used if the patient cannot stand.		

1.4.2.	We recommend that for evaluation of reflux with DUS, the sonographer use either a Valsalva maneuver or augmentation to assess the common femoral vein and SFJ 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 the 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.
1.4.3.	We recommend that a complete DUS examination for venous reflux in the lower extremities include transverse gray scale images without and with transducer compression of the common femoral, proximal, mid, and distal femoral and popliteal veins, SFJ, and at least two segments along the GSV and SSV.
1.4.4.	We recommend that a complete DUS examination for venous reflux in the lower extremities include measurement of the spectral Doppler waveform using calipers. Reflux at baseline and in response to a Valsalva maneuver or distal augmentation in the common femoral vein and at the SFJ and in response to distal augmentation in the mid-femoral and popliteal vein should be documented. Reflux in the GSV at the proximal thigh and knee, in the AAGSV or PAGSV at the SFJ and at the proximal thigh and in the SSV at SPJ and at the proximal calf should be documented.
1.4.5.	We recommend that a complete DUS examination for venous reflux in the lower extremities include diameter measurements in patients with the leg in the dependent position, from the anterior to the posterior wall, in the GSV 1 cm distal to the SFJ (SFJ), at the proximal thigh and at the knee, in the AAGSV and PAGSV in the proximal thigh, and in the small saphenous vein at the SPJ (SPJ) and the proximal calf. Images of both normal and abnormal findings should be documented in the records of the patient.
CONSENSUS STATEMENTS	
1.5.1.	In asymptomatic patients with telangiectasias or reticular veins (CEAP Class C1) DUS evaluation of the lower extremity veins should not be routinely performed, since testing could result in unnecessary saphenous vein ablation procedures.
1.5.2.	In symptomatic CEAP Class C1 patients with bleeding or with severe symptoms of pain or burning due to moderate to severe telangiectasias or reticular veins, DUS evaluation may be performed to exclude associated venous incompetence; however, saphenous ablation for C1 disease without bleeding is rarely required.
1.5.3.	In symptomatic patients with varicose veins (CEAP Class C2) the deep venous system should be routinely evaluated for infrainguinal obstruction or valvular incompetence
1.5.4.	In symptomatic patients with varicose veins (CEAP Class C2) evaluation for iliofemoral venous obstruction with DUS or with other imaging studies should be performed if suprapubic or abdominal wall varicosities are present and in patients with symptoms of proximal obstruction, including thigh and leg fullness, heaviness, swelling and venous claudication. CEAP Classes 3-6 warrant DUS or other imaging studies to evaluate for iliofemoral obstruction.
1.5.5.	In patients with medial thigh or vulvar varicosities evaluation of pelvic venous pathology with DUS or other imaging studies is not indicated if they have no symptoms of pelvic venous disease.

2. COMPRESSION THERAPY

2.1 Compression therapy vs. intervention

GUIDELINES		Grade of recommendation	Quality of Evidence
2.1.1.	For patients with symptomatic varicose veins and axial reflux in the superficial truncal veins, we suggest compression therapy for	**2**	**C**

	primary treatment if the patient's ambulatory status and/or underlying medical conditions warrant a conservative approach, or if the patient prefers conservative treatment for either a trial period or definitive management.	**(weak)**	**(low to very low)**
2.1.2.	For patients with symptomatic varicose veins and axial reflux in the GSV or SSV who are candidates for intervention, we recommend superficial venous intervention over long-term compression stockings.	**1 (strong)**	**B (moderate)**
2.1.3.	For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, who are candidates for intervention, we suggest superficial venous intervention over long-term compression stockings.	**2 (weak)**	**C (low to very low)**
2.1.4.	In patients with symptomatic varicose veins who are candidates for endovenous therapy and wish to proceed with treatment, we suggest against a 3-month trial of compression therapy prior intervention.	**2 (weak)**	**B (moderate)**
2.2 Compression therapy after intervention			
2.2.1.	In patients undergoing thermal ablation for saphenous incompetence, with or without concomitant phlebectomy, we suggest post-procedure compression therapy for a minimum of 1 week for pain reduction.	**2 (weak)**	**B (moderate)**
3. PHARMACOLOGICAL TREATMENT			
GUIDELINES		**Grade of recommendation**	**Quality of Evidence**
3.1.	In symptomatic patients with varicose veins who are not candidates for intervention, or who are waiting for intervention or have symptoms after intervention, we suggest Micronized Purified Flavonoid Fraction (MPFF) or Ruscus extracts for treatment of vein related pain, leg heaviness and/or sensation of swelling. *	**2 (weak)**	**B (moderate)**
3.2.	In symptomatic patients with varicose veins who are not candidates for intervention, or who are waiting for intervention or have symptoms after intervention, we suggest Hydroxyethylrutosides, Calcium Dobesilate, Horse chestnut extract, Red vine leaf extract, or Sulodexide for treatment of vein-related pain, leg heaviness, night cramps and/or sensation of swelling.*	**2 (weak)**	**C (low to very low)**
*These products are not approved drugs by the U.S. Food and Drug Administration (FDA). FDA does not approve medical food or nutritional supplements (https://www.fda.gov/).			
4. INTERVENTIONS FOR SUPERFICIAL TRUNCAL REFLUX			
4.1. Endovenous ablation vs high ligation and stripping (HL&S)			
GUIDELINES		**Grade of recommendation**	**Quality of Evidence**
4.1.1.	For patients with symptomatic varicose veins and axial reflux in the GSV, who are candidates for intervention, we recommend treatment	**1 (strong)**	**B (moderate)**

	with endovenous ablation over high ligation and stripping (HL&S) of the GSV.		
4.1.2.	For patients with symptomatic varicose veins and axial reflux in the SSV, who are candidates for intervention, we recommend treatment with endovenous ablation over ligation and stripping of the SSV.	**1 (strong)**	**C (low to very low)**
4.1.3.	For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, who are candidates for intervention, we suggest treatment with endovenous ablation, with additional phlebectomy, if needed, over ligation and stripping of the accessory vein.	**2 (weak)**	**C (low to very low)**
4.1.4.	For patients with symptomatic varicose veins and axial reflux in the GSV or SSV, we recommend treatment with ligation and stripping of the saphenous vein if technology or expertise in endovenous ablation is not available or if the venous anatomy precludes endovenous treatment.	**1 (strong)**	**B (moderate)**
4.1.5.	For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, we suggest treatment with ligation and stripping of the accessory 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.	**2 (weak)**	**C (low to very low)**
4.1.6.	For patients with symptomatic varicose veins and axial reflux in the GSV, we suggest treatment with endovenous laser ablation (EVLA), radiofrequency ablation (RFA), or HL&S over physician-compounded ultrasound-guided foam sclerotherapy because of long-term improvement of quality of life and reduced recurrence.	**2 (weak)**	**B (moderate)**
4.1.7.	For patients with symptomatic varicose veins and axial reflux in the SSV we suggest treatment with EVLA, RFA, or ligation and stripping from the knee to the upper or mid-calf over physician-compounded ultrasound-guided foam sclerotherapy, because of long-term improvement of quality of life and reduced recurrence.	**2 (weak)**	**C (low to very low)**
4.1.8.	For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, we suggest treatment of the refluxing superficial trunk with EVLA, RFA or HL&S, with additional phlebectomy, if needed, over physician-compounded ultrasound-guided foam sclerotherapy because of long-term improvement of quality of life and reduced recurrence.	**2 (weak)**	**C (low to very low)**

4.2. Thermal vs non-thermal ablation of superficial truncal veins

	GUIDELINES	**Grade of recommendation**	**Quality of Evidence**
4.2.1.	For patients with symptomatic axial reflux of the GSV, we recommend either 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.	**1 (strong)**	**B (moderate)**
4.2.2.	For patients with symptomatic axial reflux of the SSV, we recommend either 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.	**1 (strong)**	**C (low to very low)**

4.2.3.	For patients with symptomatic axial reflux of the AAGSV or PAGSV, 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.	**2 (weak)**	**C (low to very low)**

5. FACTORS AFFECTING CHOICE OF SUPERFICIAL TRUNCAL ABLATION AND OUTCOME

GUIDELINES		**Grade of recommendation**	**Quality of Evidence**
5.1.1.	In symptomatic patients with C2 disease we suggest against using truncal vein diameter to determine which patients need venous ablation.	**2 (weak)**	**B (moderate)**
5.1.2	In patients with C2 disease with superficial incompetence and deep vein obstruction we suggest treatment of superficial incompetence first.	**2 (weak)**	**C (low to very low)**
CONSENSUS STATEMENTS			
5.2.1.	In asymptomatic patients with C2 disease, prophylactic intervention does not prevent progression of venous disease. Weight control, compression stockings and avoiding prolonged standing may be beneficial.		
5.2.2.	Interventions to treat varicose veins can be performed in an office-based setting, surgery center, or hospital operating room, at the discretion of the physician, who is specialized in vein care. Better patient experience and lower cost was reported for procedures performed in an office-based setting.		
5.2.3.	In patients with symptomatic C2 disease, isolated SFJ incompetence does not justify ablation of an otherwise competent GSV. Since the GSV may be used in the future for bypass in coronary or leg arteries, it should be preserved whenever possible.		
5.2.4.	In patients with symptomatic C2 disease, ablation of the incompetent GSV may be indicated, even if the axial reflux is not complete and the SFJ is competent. Shared decision making with the patient is warranted.		
5.2.5.	In patients with reflux in the below-knee GSV, ablation to the lowest point of reflux resulted in better early outcome. Non-thermal techniques are better for ablation of refluxing distal calf saphenous veins, to avoid thermal nerve injury.		
5.2.6.	In patients with an epifascial or superficial saphenous vein, thermal ablation may result in skin burn, while non-thermal techniques may cause hyperpigmentation or induration. Mini-phlebectomy or limited stripping is usually performed if the saphenous vein is close to the skin (<0.5 cm).		
5.2.7.	For patients with large (>10 mm), non-aneurysmal saphenous veins, thermal ablation with EVLA or RFA should be performed rather than using non-thermal ablation techniques.		
5.2.8.	The incidence of superficial thrombophlebitis has been reported to be similar for thermal and non-thermal ablations.		

6. INTERVENTIONS TO PRESERVE THE GSV

GUIDELINE		**Grade of recommendation**	**Quality of Evidence**
6.1.1.	For patients with the early stages of symptomatic varicose veins we suggest preserving the GSV using the ASVAL (ambulatory selective variceal ablation under local anesthesia) technique, if performed by a physician who is familiar with the technique.	**2 (weak)**	**B (moderate)**
6.1.2.	For patients with symptomatic varicose veins, we suggest preserving the GSV using the CHIVA (Ambulatory Conservative Hemodynamic	**2 (weak)**	**B (moderate)**

	Correction of Venous Insufficiency) technique, if performed by a physician who is familiar with the technique		

7. TREATMENT OF VENOUS TRIBUTARIES

7.1. Telangiectasias and reticular veins

GUIDELINES		Grade of recommendation	Quality of Evidence
7.1.1.	For patients with symptomatic telangiectasias and reticular veins we recommend sclerotherapy with liquid or foam.	**1 (strong)**	**B (moderate)**
7.1.2	For patients with symptomatic telangiectasias or reticular veins, we suggest transcutaneous laser treatment if the patient has sclerosant allergy, needle phobia, sclerotherapy failure or small veins (<1mm) with telangiectatic matting.	**2 (weak)**	**B (moderate)**

7.2. Varicose tributaries

GUIDELINES		Grade of recommendation	Quality of Evidence
7.2.1.	For treatment of symptomatic varicose tributaries, we recommend mini-phlebectomy or ultrasound guided sclerotherapy using physician-compounded foam (PCF) or polidocanol endovenous microfoam (PEM).	**1 (strong)**	**B (moderate)**
7.2.2.	For treatment of symptomatic varicose tributaries, we suggest transilluminated powered phlebectomy as an alternative treatment for patients with clusters of varicosities by a physician who is trained in the procedure.	**2 (weak)**	**C (low to very low)**
CONSENSUS STATEMENTS			
7.2.3.	For patients with symptomatic varicose tributaries, treatment of the tributaries should be performed even if the superficial trunks are competent.		
7.2.4.	There is no clinical evidence that foam sclerotherapy using room air is less safe and effective than using CO2 gas mixture.		
7.2.5.	There is currently no clinical study of sclerotherapy with physician-compounded foam (PCF), prepared using the Tessari-method, that shows that it is less safe or effective than polidocanol endovenous microfoam (PEM).		

8. TREATMENT OF VARICOSE TRIBUTARIES CONCOMITANT OR STAGED WITH SUPERFICIAL TRUNCAL ABLATION

GUIDELINES		Grade of recommendation	Quality of Evidence
8.1.1.	For patients with symptomatic reflux in the GSV or SSV 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.	**1 (strong)**	**C (low to very low)**
8.1.2.	For patients with symptomatic reflux in the AAGSV or PAGSV, we suggest simultaneous ablation of the refluxing venous trunk and phlebectomy or ultrasound-guided foam sclerotherapy of the varicosities with physician-compounded foam or commercial polidocanol endovenous microfoam.	**2 (weak)**	**C (low to very low)**

8.1.3	For patients with symptomatic reflux in the GSV or SSV, we suggest ablation of the refluxing venous trunk and staged phlebectomy or ultrasound-guided foam sclerotherapy of the varicosities only if anatomic or medical reasons are present. We suggest shared decision-making with the patient regarding the timing of the procedures.	**2 (weak)**	**C (low to very low)**
8.1.4.	For patients with symptomatic reflux in the AAGSV or PAGSV, we suggest ablation of the refluxing venous trunk and staged phlebectomy or ultrasound-guided foam sclerotherapy of the varicosities only if anatomic or medical reasons present. We suggest shared decision-making with the patient regarding the timing of the procedures	**2 (weak)**	**C (low to very low)**
GOOD CLINICAL PRACTICE STATEMENT			
8.2.	For patients with symptomatic reflux in the major superficial venous trunks and associated varicosities undergoing initial ablation alone, we recommend follow-up for ≥3 months to assess the need for staged phlebectomy or ultrasound- guided sclerotherapy for persistent or recurrent symptoms. Longer follow-up is recommended for those with recurrence or more advanced CEAP class.		

9. MANAGEMENT OF RECURRENT VARICOSITIES

CONSENSUS STATEMENTS	
9.1.1.	For patients with symptomatic recurrent varicosities, clinical evaluation and DUS should be performed before treatment to determine the potential source of recurrence.
9.1.2	For patients with symptomatic recurrent varicosities due to persistent or recurrent reflux of the GSV or AAGSV, treatment either with either open surgical or endovascular techniques may be performed, with good outcomes expected.
9.1.3.	For patients with symptomatic recurrent varicosities due to persistent or recurrent reflux at the groin, either EVLA or RFA can be used if there is a straight GSV stump and a long enough segment for thermal ablation. Sclerotherapy or phlebectomy should be performed for recurrence due to neovascularization.
9.1.4.	For patients with symptomatic recurrent varicosities due to persistent or recurrent reflux of the SSV, ultrasound-guided foam sclerotherapy should be performed.
9.1.5.	For patients with residual or recurrent varicosities due to incompetent perforator veins, treatment with both open and endovascular techniques may be used depending on physician's experience, patient choice and availability of technology.

10. ABLATION OF INCOMPETENT PERFORATING VEINS

GUIDELINES		**Grade of recommendation**	**Quality of Evidence**
10.1.1.	For patients with varicose veins (CEAP class C2) who have significant, symptomatic axial reflux of the GSV or SSV, we recommend against treatment of incompetent perforating veins concomitant with initial ablation of the saphenous veins.	**1 (strong)**	**C (low to very low)**
10.1.2.	For patients with varicose veins (CEAP class C2) who have significant, symptomatic axial reflux of the AAGSV or PAGSV, we suggest against treatment of incompetent perforating veins concomitant with initial ablation of the superficial truncal veins.	**2 (weak)**	**C (low to very low)**
CONSENSUS STATEMENT			

10.2.	For patients with symptomatic residual or recurrent varicose veins due to incompetent perforator veins, either open or endovascular techniques can be used to treat the perforator veins..

11. MANAGEMENT OF ABLATION RELATED THROMBUS EXTENSION (ARTE) AND DEEP VEIN THROMBOSIS (DVT) AFTER ENDOVENOUS ABLATIONS

11.1. Post-procedure duplex ultrasound

GUIDELINE		Grade of recommendation	Quality of Evidence
11.1.1.	In an average-risk patient who is asymptomatic following thermal ablation of the saphenous vein, we recommend against routine early post-procedural DUS to detect ablation-related thrombus extension (ARTE, formally known as EndoVenous Heat Induced Thrombosis (EHIT or deep vein thrombosis (DVT).	**1 (strong)**	**B (moderate)**
CONSENSUS STATEMENT			
11.1.2.	In an average-risk patient who is asymptomatic following non-thermal ablation of the saphenous vein, routine early post-procedural DUS may be performed to detect ablation-related thrombus extension (ARTE) or DVT		
11.1.3.	In a high-risk patient who is asymptomatic following thermal or non-thermal saphenous ablation, early DUS to exclude ablation-related thrombus extension (ARTE) or DVT should be performed.		

GUIDELINE		Grade of recommendation	Quality of Evidence
11.1.4.	In patients who are symptomatic following either thermal or non-thermal ablation, we recommend early DUS to exclude ablation-related thrombus extension (ARTE) or DVT.	**1 (strong)**	**A (high)**

11.2. Pharmacological thromboprophylaxis

GUIDELINE		Grade of recommendation	Quality of Evidence
11.2.1.	For high-risk patients undergoing endovenous ablation we suggest pharmacological thromboprophylaxis.	**2 (weak)**	**C (low to very low)**
CONSENSUS STATEMENT			

11.2.2.	For patients undergoing endovenous ablation routine risk stratification should be performed to assess the need for peri-procedural thromboprophylaxis.

11.3. Treatment of varicose vein procedure related DVT and ARTE

GUIDELINE*		Grade of recommendation	Quality of Evidence
11.3.1.	For patients with acute isolated distal DVT after varicose vein procedure, without symptoms or risk factors for extension we suggest serial imaging of the deep veins for 2 weeks.	**2 (weak)**	**B (moderate)**
11.3.2.	For patients with isolated distal DVT after varicose vein procedure, and symptoms or risk factors for extension we suggest anticoagulation.	**2 (weak)**	**C (low to very low)**
11.3.3.	For patients with acute proximal DVT after varicose vein procedure, we recommend anticoagulation with a direct oral anticoagulant (over a vitamin K antagonist).	**1 (strong)**	**B (moderate)**
11.3.4.	For patients with symptomatic ARTE after endovenous ablation, we recommend anticoagulation with a direct oral anticoagulant (over a vitamin K antagonist)	**1 (strong)**	**C (low to very low)**

***** We endorsed the recommendations of Stevens SM, Woller SC, Kreuziger LB, Bounameaux H, Doerschug K, Geersing GJ, et al. Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. Chest. 2021;160(6):e545-e608. The evidence base for these guidelines was adopted without review.

CONSENSUS STATEMENTS	
11.4.1.	For patients with asymptomatic ARTE III and IV after endovenous ablation, anticoagulation with a direct oral anticoagulant (over a vitamin K antagonist) should be performed.
11.4.2.	For patients who receive anticoagulation for ARTE following endovenous ablation, treatment should be continued until the thrombus retracts.

12. MANAGEMENT OF SUPERFICIAL VEIN THROMBOSIS (SVT)

Guideline 12. addresses the management of SVT in patients who have not recently undergone superficial venous interventions. The management of ARTE and other thrombotic complications of superficial venous interventions are addressed in Guideline 11.

GUIDELINES	Grade of recommendation	Quality of Evidence

12.1.1.	For patients with SVT of the main saphenous trunks and tributaries above the knee > 3cm from the SFJ and ≤5 cm in length, whether or not associated with varicose veins, we recommend fondaparinux 2.5mg subcutaneously daily for 45 days. Alternatively, rivaroxaban 10mg daily for 45 days may be appropriate for patients unwilling or unable to perform subcutaneous injections.	**1 (strong)**	**A (high)**
CONSENSUS STATEMENT			
12.1.2.	For patients with SVT of the main saphenous trunks ≤ 3 cm from the SFJ the SFJ, treatment with full anticoagulation for a minimum of 6 weeks should be continued.		
GUIDELINES		**Grade of recommendation**	**Quality of Evidence**
12.1.3.	For patients with SVT of the main saphenous trunks we recommend against using prophylactic or therapeutic dose LWMH and NSAIDs. While both have been found to reduce SVT pain and extension, they have failed to prevent VTE. If NSAIDs are used for treatment of short segment distal SVT, surveillance with DUS for VTE extension is recommended due to the high prevalence of concomitant DVT.	**1 (strong)**	**A (high)**
12.1.4.	For selected patients with isolated thrombosis of varicose tributaries or limited involvement of the GSV, we suggest phlebectomy as a safe alternative.	**2 (weak)**	**B (moderate)**
CONSENSUS STATEMENT			
12.1.5.	In patients with saphenous thrombophlebitis, ablation should be performed once the inflammation has resolved if there is evidence of pathologic reflux on DUS.		

13. MANAGEMENT OF BLEEDING VARICOSE VEINS

CONSENSUS STATEMENTS	
13.1.	For patients with bleeding due to varicose veins, prompt referral to a venous specialist should be done.
13.2.	For patients presenting with acute bleeding from varicose veins, direct compression and sclerotherapy should be attempted before suture ligation to control bleeding.

13.3.	For patients who presented with bleeding from varicose veins, after the bleeding has been controlled, evaluation for superficial venous incompetence and appropriate intervention on the responsible veins should be done to control venous hypertension and reduce the risk of recurrent hemorrhage.
13.4.	Patients with varicose veins or venous ulcerations should be counseled on the possibility of venous bleeding and their families, caregivers, or friends educated regarding simple compression techniques to control severe bleeding.

14. MANAGEMENT OF SUPERFICIAL VEIN ANEURYSMS

CONSENSUS STATEMENTS	
14.1.	For patients with a superficial truncal vein aneurysm, located within 3 cm of the SFJ or SPJ, open surgical excision, with high proximal and distal ligations should be performed. If symptomatic saphenous reflux is present, endovenous or open surgical ablation (phlebectomy or limited stripping) of the distal saphenous vein should be performed.
14.2.	For patients with an asymptomatic superficial truncal vein aneurysm, located >3 cm distal to the SFJ, endovenous ablation alone should be performed. Thrombo-prophylaxis in these patients reduces the risk of VTE.
14.3.	Patients with symptomatic, thrombosed, or large (> 3cm) aneurysms in the superficial veins should be treated with surgical excision.

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INTRODUCTION

Varicose veins of the lower extremities are among the most frequent medical conditions affecting millions of people worldwide.[1-3] Chronic venous disease (CVD) may cause minimal symptoms , but varicose veins may often be the source of discomfort, pain, swelling, thrombosis, bleeding and ulcerations, causing disability and a negative impact on physical, psychological, and social functioning components of quality of life.[4] Patients with chronic venous insufficiency (CVI) may progress to phlebolymphedema, skin changes with chronic inflammation, and venous leg ulcerations.[5, 6]

The Society for Vascular Surgery (SVS), the American Venous Forum (AVF), and the American Vein and Lymphatic Society (AVLS) have collaborated to update the 2011 SVS/AVF guidelines on CVD[7]and recently published Part I of the 2022 clinical practice guidelines for the management of varicose veins of the lower extremities.[8] All recommendations in Part I were based on a new, independent systematic review and meta-analysis[9] that provided the latest scientific evidence to support updated or completely new guidelines on evaluation with Duplex scanning and on the management of superficial truncal reflux in patients with varicose veins. The writing committee recognized, however, that several additional important clinical issues need to be addressed, but many have varying levels of scientific evidence.[10-41] When a systematic review was not available, the writing committee based ungraded statements on a comprehensive review of the literature, combined with unanimous consensus of the expert panel.

Part II of the guidelines focuses on the rationale and scientific evidence for prevention and management of varicose veins with compression, medications, and nutritional supplements, as well as on evaluation and treatment of varicose tributaries, factors affecting treatment

outcomes, the management of superficial vein thrombosis, thrombotic complications of varicose vein treatments, thrombus extension following ablation, management of bleeding varicose veins and the treatment of superficial vein aneurysms. This comprehensive guide provides a list of all recommendations (Part I-II), as well as consensus and best practice statements to aid practitioners with up-to-date, appropriate management of patients with symptomatic lower extremity varicose veins (CEAP Class C2 disease). Updates of previous society guidelines[5, 7, 42, 43] will address the management of venous ulcers, associated with varicose veins (C5-C6 disease), evaluation and treatment of deep vein obstructions and chronic pelvic venous disorders.

METHODS

A multi-society and multispecialty writing group that included 20 members authored both Part I and Part II of these varicose vein guidelines. The methods of writing Part I of the guidelines was described previously.[8] For Part II, the writing committee conducted a survey and held several meetings to compose a list of important clinical topics, not addressed in Part I, which are intended to guide comprehensive, up-to-date prevention and management of varicose veins and associated complications. A final list of 80 questions were divided into five sections, with each assigned to a writing group. The members of the groups performed an extensive search, up to January 31st, 2023, of the English language literature on their relevant topic, using the Ovid MEDLINE, Ovid Embase, PubMed, Scopus, Web of Science, Cochrane Library and Ovid Cochrane Database of Systematic Reviews databases. Systematic reviews, meta-analyses, randomized controlled trials (RCTs), and prospective and retrospective observational studies that included more than 10 patients with varicose veins were used. Drafts of the writing groups were discussed on Zoom meetings, and all recommendations and statements were unanimously approved by the writing committee. All clinical practice guidelines in Part II were based on

evidence established with one or several systematic reviews, with or without meta-analysis, using the GRADE method,[44-46] as described in detail in Part I of the guidelines.[8] We used the standard nomenclature of "we recommend" and "we suggest" to describe strong and weak recommendations, respectively.

To make this guideline comprehensive and practical for clinicians, we developed 3 other types of ungraded statements, in addition to formal graded recommendations. *Good Practice Statements* are recommendations that are supported by indirect evidence that cannot be easily synthesized, yet the topic is usually non-controversial and agreed upon by most stakeholders.[47] *Implementation Remarks* contain technical information that supports the implementation of specific recommendations. [48] *Ungraded Consensus Statements* referred to evaluation or treatment as a unanimous consensus of the expert panel, based on their own comprehensive review of the literature, even though some of the topics had minimal or low-quality evidence.

RECOMMENDATIONS AND STATEMENTS

1. EVALUATION OF PATIENTS WITH VARICOSE VEINS

1.1. Classification and grading of clinical severity of chronic venous disorders

1.1.1. We recommend the use of the 2020 updated CEAP (Clinical stage, Etiology, Anatomy, Pathology) classification system for chronic venous disorders. The clinical or basic CEAP classification can be used for clinical practice, and the full CEAP classification system should be used for clinical research.

GOOD PRACTICE STATEMENT

Rationale and Evidence. The CEAP classification of was designed at a consensus meeting of international experts in 1994,[49] it was updated in 2004,[50] and most recently in 2020.[51] The

223 classification is based on clinical signs, etiology, anatomy and pathology (reflux and obstruction)
224 of chronic venous disorders. The basic or clinical CEAP classification reports the single highest
225 C class, and the advanced CEAP reports all C classes present in the limb. Patients with reticular
226 veins (subdermal veins between 1 and <3 mm in diameter) and telangiectasias (subdermal
227 "spider veins", < 1 mm in size) belong to Class C1. Varicose veins are dilated subcutaneous
228 tributaries ≥3 mm in diameter and patients with varicose veins belong to CEAP Class C2.
229 Chronic venous disease (CVD) is defined as CEAP Class C2-C6, chronic venous insufficiency
230 (CVI) includes limbs with CEAP Class 3-6. [50, 52-54] The term CVI is reserved for advanced CVD
231 with functional abnormalities of the venous system producing edema, skin changes or venous leg
232 ulcers. [52] Each clinical class has a subscript indicating the presence or absence of symptoms (s or
233 a). Symptoms of varicose veins may include pain, burning, cramping, feeling of limb heaviness
234 or swelling, restless leg or itching. The most important of these have been identified as HASTI
235 [TM] symptoms and include heaviness in the legs, achiness, swelling, throbbing, and itching.[55, 56]
236 CEAP is a descriptive instrument designed to categorize the affected limb and not a quantitative
237 severity scale or scoring system nor an outcome measure that reflects changes over time. For a
238 table of the updated CEAP classification please see Part I. of the Guidelines.[8]
239

240 **1.1.2. We recommend the use of the revised Venous Clinical Severity Score (VCSS) for**
241 **patients with chronic venous disorders for grading of clinical severity and for assessment of**
242 **post treatment outcome.**

243 **GOOD PRACTICE STATEMENT**

244 *Rationale and Evidence.* The revised Venous Clinical Severity Score (VCSS) is a physician-
245 derived evaluative instrument that is useful to describe the severity of chronic venous disorders.

VCSS is responsive to changes over time and is suitable to document response to treatment. VCSS, together with the CEAP classification, has been widely adopted in North American[5, 57] and international [58-63] venous guidelines. The instrument comprises nine categories, each graded on a scale of 0-3. The categories include pain, varicose veins, edema, pigmentation, inflammation, induration, presence and size of ulcers and use of compression therapy (Table 1.). VCSS has been validated and there is correlation between VCSS, CEAP, the modified Chronic Venous Insufficiency Questionnaire (CIVIQ) patient-reported outcome instrument and venous duplex findings.[64] The strongest correlation occurred in pain (r=0.55, P<.0001). A good correlation was also found in the ability of VCSS and the Villalta-Prandoni scale to detect mild to moderate post-thrombotic chronic venous disease (gamma statistic = 0.71–0.98; $P < 0.05$).[65]

Table 1. Revised Venous Clinical Severity Score (VCSS)

Pain or other discomfort (i.e., aching, heaviness, fatigue, soreness, burning) Presumes venous origin	**None:** 0	**Mild:** 1 Occasional pain or other discomfort (i.e., not restricting regular daily activity)	**Moderate:** 2 Daily pain or other discomfort (i.e., interfering with but not preventing regular daily activities)	**Severe:** 3 Daily pain or discomfort (i.e., limits most regular daily activities)
Varicose veins "Varicose" veins must be ≥3 mm in diameter to qualify	**None:** 0	**Mild:** 1 Few: scattered (i.e., isolated branch varicosities or clusters) Also includes corona phlebectatica (ankle flare)	**Moderate:** 2 Confined to calf or thigh	**Severe:** 3 Involves calf and thigh
Venous edema Presumes venous origin	**None:** 0	**Mild:** 1 Limited to foot and ankle area	**Moderate:** 2 Extends above ankle but below knee	**Severe:** 3 Extends to knee and above
Skin pigmentation Presumes venous origin Does not include focal pigmentation over varicose veins or pigmentation due to other chronic diseases (i.e., vasculitis purpura)	**None:** 0 None or focal	**Mild:** 1 Limited to perimalleolar area	**Moderate:** 2 Diffuse over lower third of calf	**Severe:** 3 Wider distribution above lower third of calf
Inflammation More than just recent pigmentation (i.e., erythema, cellulitis, venous eczema, dermatitis)	**None:** 0	**Mild:** 1 Limited to perimalleolar area	**Moderate:** 2 Diffuse over lower third of calf	**Severe:** 3 Wider distribution above lower third of calf
Induration Presumes venous origin of secondary skin and subcutaneous changes (i.e., chronic edema with fibrosis, hypodermitis) Includes white atrophy and lipodermatosclerosis	**None:** 0	**Mild:** 1 Limited to perimalleolar area	**Moderate:** 2 Diffuse over lower third of calf	**Severe:** 3 Wider distribution above lower third of calf
Active ulcer number	0	1	2	≥3
Active ulcer duration (longest active)	N/A	<3 months	>3 months but <1 year	Not healed for >1 year
Active ulcer size (largest active)	N/A	Diameter <2 cm	Diameter 2–6 cm	Diameter >6 cm
Use of compression therapy	0 Not used	1 Intermittent use of stockings	2 Wears stockings most days	3 Full compliance: stockings

1.2 – 1.5. Evaluation with Duplex Ultrasound Scanning (DUS)

1.2.1. For patients with chronic venous disease of the lower extremities, we recommend DUS as the diagnostic test of choice to evaluate for venous reflux.

GUIDELINE. Grade of recommendation: 1 (strong), Quality of Evidence: B (Moderate)

For Rationale and Evidence, please see Part I of the varicose vein guidelines.[8]

IMPLEMENTATION REMARKS

1.3.1. Reflux is defined as a minimum value >500 ms of reversed flow in the superficial truncal veins [great saphenous vein (GSV), small saphenous vein (SSV), anterior accessory great saphenous vein (AAGSV), posterior accessory great saphenous vein (PAGSV)] and in the tibial, deep femoral, and perforating veins. A minimum value of >1 second of reversed flow is diagnostic of reflux in the common femoral, femoral, and popliteal veins. There is no minimum diameter required to have pathologic reflux.

1.3.2. Axial reflux of the GSV is defined as uninterrupted retrograde venous flow from the groin to the upper calf. Axial reflux in the SSV is defined as being from the knee to the ankle. Axial reflux in the AAGSV and PAGSV is retrograde flow between two measurements, at least five cm apart. Retrograde flow can occur in the superficial or deep veins, with or without perforating veins. Junctional reflux is limited to the saphenofemoral or saphenopopliteal junction (SPJ). Segmental reflux occurs in only a portion of a superficial or deep truncal vein.

1.3.3. A definition of "pathologic" perforating veins in patients with varicose veins (CEAP [Clinical Class, Etiology, Anatomy, Pathology]) clinical class C2 includes those with an outward flow duration of >500 ms and a diameter of >3.5 mm on duplex ultrasound.

For Rationale and Evidence supporting the Implementation Remarks 1.3.1-3, please see Part I of the varicose vein guidelines.[8]

GOOD PRACTICE STATEMENTS

1.4.1. We recommend that evaluation of reflux with DUS be performed in an Intersocietal Accreditation Commission or American College of Radiology accredited vascular laboratory by a credentialed ultrasonographer, with the patient standing whenever

possible. A sitting or reverse Trendelenburg position can be used if the patient cannot stand.

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

1.4.3. We recommend that a complete DUS examination for venous reflux in the lower extremities includes transverse grayscale images without and with transducer compression of the common femoral vein, proximal, mid, and distal femoral veins, popliteal veins, the SFJ, and at least two segments along the GSV and SSV.

1.4.4. We recommend that a complete DUS examination for venous reflux in the lower extremities includes measurement of the spectral Doppler waveform using calipers. Reflux at baseline and in response to Valsalva or distal augmentation in the common femoral vein and at the SFJ should be documented. Reflux in response to distal augmentation in the mid-femoral and popliteal veins, GSV at the proximal thigh and knee, in the AAGSV and SSV at the SPJ or proximal calf should also be documented.

1.4.5. We recommend that a complete DUS examination for venous reflux in the lower extremities includes diameter measurements with the patient's leg in the dependent position, from the anterior to posterior wall, , in the GSV 1 cm distal to the SFJ, at the proximal thigh and knee, in the AAGSV, and in the SSV at the SPJ or proximal calf.

Images of both normal and abnormal findings should be documented in the patient's records.

For Rationale and Evidence supporting Good Practice Statements 1.4.1-1.4.5, please see Part I. of the varicose vein guidelines.[8]

CONSENSUS STATEMENTS

1.5.1. In asymptomatic patients with telangiectasias or reticular veins (CEAP Class C1) DUS evaluation of the lower extremity veins should not be routinely performed since testing could result in unnecessary saphenous vein ablation procedures.

Rationale. Asymptomatic CEAP Class C1 venous disorder is usually a cosmetic problem; asymptomatic telangiectasias or reticular veins should not be treated for the purpose of preventing progression to more advanced venous disease. Saphenous vein ablation is not indicated in these patients for medical reasons. The GSV may need to be used in the future as a conduit for bypass in coronary or leg arteries, and therefore it should be preserved whenever possible. Thus, DUS evaluation of the venous system should not be performed.

Evidence. There is no scientific evidence that complications of venous disorders can be prevented by treatment of asymptomatic telangiectasias or reticular veins. Since the GSV can be used as a conduit for bypass in coronary or leg arteries, it should be preserved whenever possible. The Society for Vascular Surgery published the "Choosing Wisely" initiative which suggests that routine venous ultrasound testing in asymptomatic C1 patients should not be performed and that it could result in unnecessary saphenous vein ablation procedures.[66] Ruckley et al.[67] found a significant but weak association between advanced grade 2/3 telangiectasias, located at the medial thigh and GSV incompetence.

1.5.2. In symptomatic CEAP Class C1 patients with bleeding or with severe symptoms of pain or burning due to moderate to severe telangiectasias or reticular veins, DUS evaluation may be performed to exclude associated venous incompetence; however, saphenous ablation for C1 disease without bleeding is rarely required.

Rationale. DUS exam is only indicated in patients with a complicated C1 disorder. The most severe complication is bleeding, but in rare cases, pain and burning due to telangiectasias or reticular veins are also indications for DUS to evaluate and treat associated superficial venous incompetence. Patients with mild symptoms and certainly those with cosmetic telangiectasias with intermittent itching or other mild symptoms do not need Duplex evaluation that could ultimately lead to unnecessary ablation of superficial truncal veins.

Evidence. Studies of Ruckly et al.[67] suggest that there are some patients with symptomatic advanced C1 disorder, with telangiectasia and reticular veins located medially along the GSV, who are candidates for saphenous ablation. Evaluation with DUS is recommended by several groups prior to sclerotherapy in patients with symptomatic telangiectasias and reticular veins. [59, 68, 69] Engelhorn et al. examined 269 limbs of women with telangiectasias (CEAP C1 class).[70] GSV reflux was detected in 44%, but it was segmental in 73% and only 4% had SFJ reflux. The authors propose further research on management of the GSV in these patients. Interestingly, in this study 78% of the limbs with C1 disease were symptomatic. Studies of Somjen et al.[68] has been quoted as evidence for performing DUS in patients with telangiectasias. We agree with Somjen et al,[68] that incompetent reticular veins, present in 80 to 90% of these cases, should also be treated together with sclerotherapy of the telangiectasias. However, these larger (1-3 mm)

reticular veins are always located above the superficial fascia, so they can be well seen with magnification, or easily detected during the ultrasound guided liquid or foam sclerotherapy.

1.5.3. In symptomatic patients with varicose veins (CEAP Class C2) the deep venous system should be routinely evaluated for infrainguinal obstruction or valvular incompetence.

Rationale. Deep venous pathology, including reflux and obstruction, may affect outcome and complications following interventions for superficial venous incompetence. Evaluation of the deep system in C2 patients with symptomatic CVD, therefore, is recommended.[8, 71]

Evidence. Among 4881 patients who underwent endovenous ablation for superficial truncal vein in the Vascular Quality Initiative (VQI) database, 2254 patients (46.2%) had combined deep and superficial reflux. After a median follow-up of 336 days symptoms improved in both groups and improvement in VCSS score was greater in patients with deep vein reflux. These patients, however, had substantially higher rates of complications (10.4% vs 3.0%; $P < .001$), including paresthesias (2.5% vs 0.7%; $P < .001$), skin pigmentation (1.2% vs 0.4%; $P = .023$), superficial phlebitis (2.0% vs 0.9%; $P = .018$), wound infection (0.8% vs 0.2%; $P = .040$), and proximal thrombus extension (3.1% vs 1.1%; $P < .001$). After controlling for confounding factors, the estimate of effect size for any complication had an odd ratio (OR) of 5.72 ($P < .001$).[72] Gianesini and colleagues [73] retrospectively analyzed long-term results of the CHIVA procedure in 381 patients and found an increased risk of GSV reflux recurrence among those patients who initially had refluxing common femoral veins.[73] Others found that ablation of superficial reflux may restore segmental competence of the deep veins[74] and that clinical outcome is excellent after superficial ablation, despite the presence of deep venous reflux.[63, 75] In one study, those with

379 persistent symptoms after superficial vein ablation had femoral or popliteal vein reflux velocities
380 greater than 10 cm/sec.[63]

381 Data on infrainguinal deep vein obstruction and interventions on superficial veins are
382 sparse since many vascular specialists avoid superficial truncal ablation in patients with
383 extensive post-thrombotic deep vein obstruction. There is low level of evidence that saphenous
384 ablation can be performed in patients with femoro-popliteal venous occlusion.[76] It is important
385 to remember that in severely symptomatic patients with infrainguinal obstruction the GSV may
386 be used for deep vein recontruction.[77] Occasionally, reconstruction of the femoral vein may be
387 performed after superficial truncal ablation in patients who have congenital absence or severe
388 hypoplasia of the deep veins.[78]

389 In a systematic review of superficial venous reflux in patients with deep venous
390 obstruction, Benfor and Peden suggested that superficial ablation can be performed in patients
391 with deep vein occlusions, but noted that the evidence to support this recommendation was
392 weak.[25] Most patients in this review had suprainguinal/iliofemoral obstruction and most had
393 advanced CVD. In a series of 29 patients with a history of previous deep vein thrombosis (DVT)
394 Puggioni et al. did not find an increased incidence of thrombotic complications after RFA. [79]

395

396 **Table. 2. Outcome of superficial truncal ablation in patients with deep vein reflux**

First author, year	Patients /limbs	Intervention	Comparison	Outcomes	Study design
Sales, 1996 [80]	17 patients (C2-C6)	HL&S phlebectomy, perforator vein ligation	None	94% (16/17) resolution of DVR* at a mean of 62 days (range:4 – 278)	Retrospective review
Puggioni 2003[81]	33/38 (C1-C6)	HL&S or RFA, perforator ligation, sclerotherapy	None	24% (9/38) had complete resolution, 32% (19/59 segments) had segmental resolution of DVR	Retrospective review

Knipp,2008 [75]	364/460 (C1-C6)	EVLA +/- phlebectomy +/- perforator ligation (311 limbs with DVR)	EVLA +/- phlebectomy +/- perforator ligation (132 limbs without DVR)	Improvement (VCSS) was independent of DVR. DVR had no effect on EHIT, thrombophlebitis, paresthesias, saphenous occlusion rates or bruising	Retrospective review
Kim, 2017[82]	100/139	RFA +/- stab avulsions +/- perforator ligation (43 limbs with DVR)	RFA +/- stab avulsions +/- perforator ligation (96 limbs without DVR)	DVR improved (all) or resolved (30.2%) with superficial venous ablation. DVR did not impact symptom/QoL improvement after superficial venous ablation	Retrospective review
Nishibe, 2020 [83]	154/223 (C2 disease)	RFA, 74 limbs (33.2%) with DVR	RFA 80 limbs without DVR	DVR was reduced to 29 limbs (13%, P<001) by RFA. Deep vein diameters were also reduced.	Retrospective review
Brown, 2021[72]	4881 patients (C2-C6)	RFA or EVLA 2254 patients (46.2%) with DVR	RFA or EVLA 2627 patients (53.8%) without DVR	No difference in symptom improvement between groups. Greater improvement in VCSS score in patients with DVR. These patients also had increased rate of complications, particularly in proximal thrombus extension (3.1% vs 1.1%, P< .001)	Retrospective review of the VQI registry

*DVR= deep vein reflux

1.5.4. In symptomatic patients with varicose veins (CEAP Class C2) evaluation for iliofemoral venous obstruction with DUS or with other imaging studies should be performed if suprapubic or abdominal wall varicosities are present and in patients with symptoms of proximal obstruction, including thigh and leg fullness, heaviness, swelling and venous claudication. CEAP Classes 3-6 warrant DUS or other imaging studies to evaluate for iliofemoral obstruction.

Rationale. Varicose veins can be associated with primary or secondary iliofemoral venous obstruction. While many C2 patients with simple varicose veins need no evaluation for proximal venous obstruction, those who have more advanced symptoms or signs (C3-C6) due to iliofemoral disease need further investigation and appropriate treatment.

Evidence. In a recent systematic review of 944 limbs with previous DVT or current deep vein obstruction, most patients had iliofemoral venous disease and advanced CEAP class (C4-C6).[25]

These patients had better results when vein ablation was combined with treatment of iliac vein obstruction. It should be noted, however, that only a few C2 patients were included in the review leaving this issue unexplored and unresolved. In the case of iliofemoral venous obstruction, interventions on the superficial venous system should not impair venous return from the limb. For this reason, in patients with symptoms of proximal outflow obstruction, like venous claudication, thigh swelling and pain, or in those with suprapubic or abdominal wall varicosities, or with continuous flow and lack of respiratory variations in the common femoral vein on DUS, investigation of the iliac veins is warranted. During ablation of the incompetent superficial veins, collaterals to the suprapubic and abdominal wall veins should be preserved.

1.5.5. In patients with medial thigh or vulvar varicosities evaluation of pelvic venous pathology with DUS or other imaging studies is not indicated if they have no symptoms of pelvic venous disease.

Rationale. There is an association between pelvic venous insufficiency and medial thigh and vulvar varicosities, and lower extremity varicosities are often more severe in patients with associated pelvic varicose veins.[84] While ovarian vein embolization in patients with pelvic venous disorders may be helpful for lower extremity varicosities, embolization in varicose vein patients without chronic pelvic pain has not been studied. In contrast, direct treatment of pelvic origin lower extremity, vulvar or perineal varicose veins without ovarian vein embolization can be effective and durable.[85]

Evidence. Non-saphenous, pelvic origin varicose veins occur in women in the medial and posterior thigh, vulva and inguinal area.[86] They are the result of reflux from the internal iliac vein through the inguinal, obturator, perineal and gluteal escape points.[42] Vulvar varicosities are

estimated to occur in 22-34% of women with varicose veins of the pelvis and in 18-22% of pregnant women.[19]

In one study of 72 symptomatic patients with pelvic source varicose veins, however, only 7% had chronic pelvic pain.[87] In a systematic review of 13 studies on ovarian vein embolization in 866 women, technical success was 99.8%; significant improvement of pelvic pain was reported in nine studies.[88] In another study, lower extremity varicosities recurred only in 13% at 5 years after embolization. Hartung et al reported 51% improvement in lower extremity varicosity following ovarian vein embolization in 119 women, who had both pelvic symptoms and lower extremity varicose veins.[89] In another study of 43 patients, Castenmiller et al showed improvement after ovarian vein embolization in the lower extremity varicose veins in 14%, but success rate was 88% for treatment of vulvar varicose veins.[90]

Gavrilov reported good clinical results with direct treatment of vulvar varicosities with foam sclerotherapy and phlebectomy.[85] In 32 patients with asymptomatic pelvic varicose veins, phlebectomy alone for vulvar varices resulted in no recurrence at 3 to 8 years after the procedure. Sclerotherapy was effective at 1 year in 10 of 12 patients. [85] Current consensus of experts supports the strategy of direct treatment of pelvic origin varicose veins in patients with asymptomatic pelvic reflux using liquid or foam sclerotherapy, phlebectomy, or pelvic escape points ligation, without the need for pelvic vein embolization.[59, 85, 86]

2. COMPRESSION THERAPY

2.1. Compression therapy vs. intervention

2.1.1. 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 or underlying medical conditions warrant a conservative approach or, if the patient prefers conservative treatment, for either a trial period or definitive management.

GUIDELINE. Grade of recommendation: 2 (weak), Quality of evidence: C (low to very low)

Rationale. In patients with varicose veins, compression therapy has been used for decades to decrease pain and swelling. Graduated elastic compression stockings oppose tissue expansion when muscles contract. It can narrow the superficial vein diameter and therefore decrease the venous reflux and venous hypertension, key elements in the pathophysiology of CVD.

Evidence. The clinical benefit of compression stockings for the initial treatment of varicose veins has been studied in a recent Cochrane review of 13 trials, encompassing over 1,000 patients[91]. Compression stockings were compared to no stockings or placebo stockings.[91] Four RCTs showed improvement in symptoms, but they were subject to bias. Three of the four studies reported side effects of discomfort, appearance, and application difficulty. The benefits of stockings were offset by highly variable reports of compliance, presumably due to the most common side effects of itching and irritation. Graduated compression stockings are classified according to the pressure applied at the level of the ankle. Class 1 low pressure stockings exert an ankle pressure <20 mmHg, Class 2 moderate compression is between 20- and 30-mm Hg and Class 3 stocking are high compression stockings with ankle pressures above 30 mmHg. [92] When comparing against different levels of compression and lengths of stockings, there was no clear difference in this Cochrane review. [91] Patient preference for one stocking over another was largely driven by comfort. None of the studies assessed quality of life. Overall, there was insufficient high quality of evidence to determine whether compression stockings are effective as

the primary treatment for symptomatic varicose veins and if one stocking is better than the other.[91] Real world data suggests that compliance with compression stockings can be as low as 37%[93]. For additional evidence, see Part I of the Guidelines.[8]

Table. 3. Evidence to support compression stockings for patients with varicose veins

First author, year	**Patient**	**Intervention/exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Knight Nee Shingler , 2021[91]	Adults with varicose veins (CEAP2)	Compression therapy	No compression therapy	Insufficient high-certainty evidence to determine if compression stockings are effective as the sole treatment of varicose veins, or if any type of stocking is superior to any other type.	Cochrane review, English language RCTs	Age, sex, stocking type, outcomes

2.1.2. For patients with symptomatic varicose veins and axial reflux in the GSV or SSV who are candidates for intervention, we recommend superficial venous intervention over long-term compression stockings.

GUIDELINE. Grade of recommendation: 1 (strong), Quality of evidence: B (moderate)

2.1.3. For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, who are candidates for intervention, we suggest superficial venous intervention over long-term compression stockings.

GUIDELINE. Grade of recommendation: 2 (weak), Quality of evidence: C (low to very low)

For Rationale and Evidence for Guidelines 2.1.2. – 2.1.3, see Part I of the varicose vein guidelines.[8]

2.1.4. In patients with symptomatic varicose veins who are candidates for endovenous therapy and wish to proceed with treatment, we suggest against a 3-month trial of compression therapy prior intervention.

GUIDELINE. Grade of recommendation: 2 (weak), Quality of evidence: B (moderate)

Rationale. There is no rationale for a 3-month trial of compression therapy prior to intervention for patients with CEAP C2 class symptomatic varicose veins, who are candidates for endovenous therapy and wish to proceed. Evidence for efficacy of compression therapy in these patients is less than for efficacy of endovenous ablation.

Evidence. Insurance companies and the Centers for Medicare and Medicaid Services (CMS) frequently require a 3-month trial of compression stockings prior to intervention for patients with C2 disease, despite a lack of evidence for efficacy.[93] In a UK-based cost analysis,[94] accounting for clinical recurrences and need for further treatment, analysis included cost of procedure and subsequent procedures and quality adjusted life years (QALY). Across all measures, compression therapy was found to be inferior to minimally invasive endovenous therapies [including ultrasound guided foam sclerotherapy (UGFS) and endovenous thermal ablation (ETA)].[94] Although the cost effectiveness was calculated for the UK, sensitivity analysis suggests that the conclusions are robust to substantial changes in relative cost, and pertinent to other global healthcare markets.

As an example, the REACTIV Trial, in which a subgroup of patients with severe varicosities were randomized to surgical therapy (HL&S, phlebectomy) compared to compression therapy.[95] Consistently, surgical therapy produced better results with regards to anatomic disease extent, patient satisfaction, QoL and cost effectiveness.[95]

Table. 4. Benefits of compression therapy for varicose veins before intervention

First author, year	**Patient**	**Intervention/ exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Marsden, 2015[94]	Adults with varicose veins (CEAP2)	Compression therapy 3 months before thermal or non-thermal ablation, or surgical stripping	No compression therapy in the months preceding thermal or non-thermal ablation, or surgical stripping.	Interventional treatment is cost-effective, thermal ablation is the most cost-effective.	Economic analysis and meta-analysis of English language RCTs,	Age, sex, concomitant phlebectomy or sclerotherapy
Michael, 2006[95]	Adults with varicose veins (CEAP2)	Surgical treatment (HL&S) and phlebectomy	Compression therapy	Standard surgical treatment is more effective and more cost-effective than compression alone.	English language RCT, observational trial	Age, sex, concomitant phlebectomy or sclerotherapy

2.2. Compression therapy after intervention

2.2.1. In patients undergoing thermal ablation for saphenous incompetence, with or without concomitant phlebectomy, we suggest post-procedure compression therapy for a minimum of 1 week for pain reduction.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: B (Moderate)

Rationale. Compression therapy has been used to reduce postoperative bleeding, bruising, edema, and pain after thermal ablation of superficial venous trunks.[96] The type of compression therapy prescribed following treatment of varicose veins is widely variable and driven by institutional, physician and insurer level preferences. Most commonly, postprocedural compression therapy is delivered with gradient elastic compression stockings or elastic bandages. The presence of a pressure gradient, with the strongest compression at the level of the ankle and lightest at the top provides the most favorable hemodynamic profile for reducing limb edema. Stockings are constructed in various lengths, such as knee high or thigh high, with variable levels of compression. Compression levels range from I-III, with I representing the lowest level of compression, and III the highest. Similarly, elastic stockings vary in compressive properties based on upon the length and type of bandage used.

Evidence. The use of compression therapy after ablation of superficial truncal veins is controversial[97]. In a meta-analysis including 6 RCTs with patients Class C2 or higher, those treated with compression had less pain within the first 10 days postoperatively, and earlier return to daily activities.[13] No differences were noted in bruising score, VCSS, QoL, complications, and vein occlusion rate. A subgroup analysis of a meta-analysis, encompassing 1,147 patients, suggested that the greatest benefits in pain reduction were in patients undergoing EVLA, with no benefit seen after RFA.[26] This is consistent with other studies demonstrating greater pain with EVLA compared to RFA.[98, 99] An RCT by Bootun et al[100] demonstrated clear benefit of compression leading to significantly better pain scores for the first 5 days after endothermal

559 ablation of saphenous veins. Compression was effective in reducing early pain also in patients
560 who underwent concurrent phlebectomies.

561 The duration of therapy has been studied in the context of short term (24-48 hours), mid
562 (1-2 weeks) and long term (3-6 weeks) therapy. A meta-analysis of 775 patients undergoing
563 endothermal ablation found a difference in postoperative pain at 1 week but not at later time
564 points in patients undergoing 1-2 weeks of compression compared to those with 24-48 hours.[101]
565 Long term therapy has been shown to have equivalent outcomes to mid-term therapy.[102]
566 Therefore, application of compression for 1 week after any endothermal treatment, especially
567 those with concurrent phlebectomy may be useful for pain reduction. . In the recently published
568 multicenter society guidelines, a compression dressing of >20mmHg (corresponding to class II
569 compression stocking pressure) with eccentric pads over the ablation point is recommended for
570 patients undergoing vein ablation for greatest reduction in post operative pain [103].

571

572
573 **Table. 5. Benefit of compression therapy after endovenous ablation for varicose veins**
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575

First author, year	**Patient**	**Intervention/ exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Huang, 2013[102]	Adults with varicose veins (C2)	Surgery with compression therapy post procedure	Surgery without compression therapy post procedure	No additional benefit of the long-duration (3-6 weeks) over short-duration (3-10 days) compression after surgery	Systematic review and meta-analysis of RCTs	Age, sex, concomitant phlebectomy or sclerotherapy
Ayo, 2017[97]	Adults with varicose veins (C2)	Thermal ablation EVLT or RFA) with compression	Thermal ablation (EVLT or RFA) without compression	No significant differences between groups in VCSS, reduction in pain (VAS);	RCT	Age, sex, concomitant phlebectomy or sclerotherapy

		therapy 7 days post procedure.	therapy 7 days post procedure	bruising score; improvement in quality of life (CIVIQ); GSV closure		
Chou, 2019[101]	Adults with varicose veins (C2)	Thermal ablation (EVLT or RFA) with compression therapy post procedure	Thermal ablation (EVLT or RFA) without compression therapy post procedure	Compression therapy following thermal ablations for 1–2 weeks is better than for 24–48 hours in terms of postoperative pain at 1 week and recovery	Systematic review and meta-analysis of RCTs	Age, sex, concomitant phlebectomy or sclerotherapy
Bootun, 2021[100]	Adults with varicose veins (C2)	Thermal ablation (EVLT or RFA) with compression therapy post procedure	Thermal ablation (EVLT or RFA) without compression therapy post procedure	Median pain score in the compression group (7 days) was significantly lower on days 2-5, compared to the no compression group. No difference in clinical score, time to return to normal activities, and ecchymosis.	RCT (COMETA Trial)	Age, sex, concomitant phlebectomy or sclerotherapy
Ma, 2022[13]	Adults with varicose veins (C2) undergoing	Thermal ablation (EVLT or RFA) with compression therapy post procedure	Thermal ablation (EVLT or RFA) without compression therapy post procedure	Post-operative compression reduced the mean pain score in the first 10 days and the time to return to normal activities. No difference for other outcomes.	Systematic review and meta-analysis of RCTs	Age, sex, concomitant phlebectomy or sclerotherapy
Hu, 2022[26]	Adults with varicose veins (C2)	Thermal ablation (EVLT or RFA) with compression therapy post procedure	Thermal ablation (EVLT or RFA) without compression therapy post procedure	Lower post-operative pain scores with compression. No difference for QoL, vein occlusion rate or time to return to work.	A systematic review and meta-analysis of RCTs	Age, sex, concomitant phlebectomy or sclerotherapy

3. DRUGS AND NUTRITIONAL SUPPLEMENTS

3.1. In symptomatic patients with varicose veins, who are not candidates for intervention, who are waiting for intervention or have symptoms after intervention, we suggest Micronized Purified Flavonoid Fraction (MPFF) or Ruscus extracts for treatment of vein related pain, leg heaviness and/or sensation of swelling. *

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: B (Moderate)

3.2. In symptomatic patients with varicose veins, who are not candidates for intervention, who are waiting for intervention or have symptoms after intervention, we suggest Hydroxyethylrutosides or Calcium Dobesilate or Horse chestnut extract or Red vine leaf extract or Sulodexide for treatment of vein-related pain, leg heaviness, night cramps, and/or sensation of swelling.*

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (Low to very low)

****These products are not approved drugs by the U.S. Food and Drug Administration (FDA). FDA does not approve medical food or nutritional supplements (https://www.fda.gov/).*Rationale.* Venoactive drugs (VADs), also called phlebotropics or phlebotonics, have shown varying benefits in patients with chronic venous disorders. VADs have been largely prescribed in Europe and other parts of the world, [104] but recently they have gained interest in the United States, where they are available now, mainly as nutritional supplements.[105, 106] The most frequently used VADs include micronized purified flavonoid fraction (MPFF), diosmin, Ruscus extracts, Hydroxyethylrutosides, Calcium dobesilate, Horse chestnut

602 extract/escin, and Red vine leaf extract. Sulodexide doesn't belong to the VAD family, but it has
603 been used for CVD (Table 6.)

604 **Table. 6. Summary of the pharmacologic properties of venoactive drugs used for chronic**
605 **venous disorders ***
606
607

Venoactive Drugs	Pharmacologic properties							
	Venous tone	Vein wall and valve	Capillary leakage	Lymphatic drainage	Hemorheological disorders	Antioxidant properties	Inflammatory reaction	Endothelial function
Micronized Purified Flavonoid Fraction (MPFF)	+	+	+	+	+	+	+	+
Ruscus extracts	+	+	+	+	+		+	
Hydroxyethyl rutosides	+		+	+	+	+	+	
Calcium dobesilate	+		+	+	+	+		
Horse chestnut extract/escin	+		+			+		+
Red vine leaf extract			+			+		
Sulodexide							+	+

608
609
610 *Adapted from Nicolaides A, Kakkos S, Baekgaard N, Comerota A, de Maeseneer M, Eklof B,
611 et al. Management of chronic venous disorders of the lower limbs. Guidelines According to
612 Scientific Evidence. Part I. Int Angiol. 2018;37(3):181-254. [60]
613

614

615 *Evidence.* The efficacy and safety of VADs was extensively studied in patients with CVD in
616 double-blind, placebo-controlled, randomized trials and meta-analyses. There have been two
617 Cochrane reviews, the most recent in 2020, that included a systematic review and meta-analysis
618 of 7690 patients, enrolled in 56 studies.[107, 108] The VAD used included rutosides, hidrosmine and
619 diosmin, calcium dobesilate, Centella asiatica, aminaftone, French maritime pine bark extract,

and grape seed extract. Diosmin is only one component of MPFF and MPFF studies were analyzed together with non-micronized diosmin trials. Most studies included patients with varicose veins (C2), but also with more advanced CVI, like venous edema (C3), skin changes (C4-5), venous ulcers (C6). Pooled data analysis of VADs was given, although the document also includes breakdown of the different effect of individual products as well. The number of patients included in many studies was low and the follow-up was short. The review found moderate-certainty evidence that phlebotonics in patients with CVI probably reduced edema in the lower legs, compared with placebo (RR 0.70, 95% CI 0.63 to 0.78; 13 studies; 1245 participants); and probably reduced ankle circumference (MD -4.27 mm, 95% CI -5.61 to -2.93 mm; 15 studies; 2010 participants). Moderate-certainty evidence showed that phlebotonics probably make little or no difference in QoL compared with placebo (SMD -0.06, 95% CI -0.22 to 0.10; five studies; 1639 participants); and low-certainty of evidence suggested that they may have little or no effect on ulcer healing (RR 0.94, 95% CI 0.79 to 1.13; six studies; 461 participants). There was low-certainty of evidence that phlebotonics may reduce pain, measured as a continuous variable, compared to placebo (SMD -0.35, 95% CI -0.54 to -0.17; 12 studies; 2232 participants). Thirty-seven studies reported on adverse events, the most frequent were gastrointestinal symptoms. Findings for specific groups of VADs were limited due to small study numbers in some studies and the heterogeneous results. The authors downgraded certainty in the evidence from 'high' to 'moderate' because of risk of bias concerns, and further to 'low' because of imprecision. It is clear from this review and multiple other meta-analyses,[14-16, 104] however, that some of these drugs or supplements are better than the others.

The clinical benefits of two compounds, Micronized Purified Flavonoid Fraction (MPFF) and Ruscus extracts have been studied more extensively in double blind, placebo controlled

643 RCTs and meta-analyses and they are discussed in more detail here. For evidence of clinical
644 efficacy of other VADs, including hydroxyethylrutosides, calcium dobesilate, horse chestnut
645 extract, red vine leaf extract and sulodexide for treatment of CVD, see Appendix I. Most studies
646 with these products have short (3 to 6 months) follow-up, therefore long-term efficacy and
647 possible side-effects of long-term treatment have not been formally assessed.
648
649 ***Clinical benefit of MPFF***
650 *Rationale.* MPFF is composed of 90% diosmin and 10% hesperidin fraction (hesperidin,
651 diosmetin, linarin and isorhoifolin). Its beneficial effects in patients with symptomatic varicose
652 veins are related to the effect on venous tone, microcirculation, trophic disorders, edema,
653 inflammation, leukocyte adhesion and activation.[104] Pharmaceutic formulations that increase
654 intestinal absorption as micronized form, including the Micronized Purified Flavonoid Fraction
655 (MPFF) represent an innovation and improvement of the therapeutic efficacy.
656 *Evidence.* MPFF has shown several effects beneficial for patients with varicose veins and CVD.
657 Among them are an increase of the venous tone,[109] potentiation of the venous response to
658 norepinephrine, [110]antioxidant and anti-inflammatory properties.[111,112] Leukocytes adhesion
659 molecules inhibition was confirmed in patients with CEAP Class C2-C4, in parallel to the
660 improvement of leg heaviness scores.[113] The transient venous reflux (TVR) was reduced in
661 patients with telangiectasias and reticular veins treated with MPFF.[114]
662 A meta-analysis by Kakkos and Nicolaides[14] analyzed seven RCTs in 1692 patients with
663 CVD. Based on high quality evidence, the study concluded that MPFF was highly effective in
664 improving leg symptoms, edema and quality of life in patients with CVD. The RELIEF study
665 enrolled 4527 patients with CEAP Class C0-C4. Approximately 40% of patients belonged to

CEAP Class C2. Participants were treated for a period of 6 months and had significant evolving improvement of symptoms, QoL measured by the CIVIQ instrument and edema assessed by leg circumference. More recently, an RCT compared two galenic formulations of MPFF, tablets and sachets, and included 1139 patients with C2s stage representing 44.95-49.46%.[115]. The authors concluded that both formulations resulted in similar improvement of symptoms and QoL.

A meta-analysis of 10 trials included 1010 patients treated with MPFF, hydroxyethylrutosides, ruscus extracts and diosmin. MPFF significantly reduced ankle edema, ($P<0.0001$), while the efficacy of the other two VADS was comparable.[116] Another meta-analysis[15] compared the efficacy of sulodexide, MPFF, hydroxyethyl-rutosides, calcium-dobesilate, ruscus extracts, horse chestnut extracts and pentoxifylline. The primary outcome was ulcer healing, but the drug effects on the leg volume, ankle circumference, symptoms, as well as QoL (CIVIQ-20 score) were also assessed. MPFF had superior effectiveness in leg volume reduction, pain, and improved QoL. Although not within the scope of this guideline, it is worth mentioning that in a meta-analysis of 5 RCTs, MPFF improved ulcer healing. [11715] The main MPFF component, diosmin, is effective alone, although its efficacy is significantly less than that of MPFF.[116, 118]

Five unblinded open-label clinical trials were included in a systematic review investigating the effects of VADs on recovery after surgery, endovenous ablation, or sclerotherapy[20]. All used micronized purified flavonoid fraction (MPFF); in one study, sulodexide was also given. Three studies reported significantly less post-procedural pain, one observed no significant effect. Two studies reported significant reduction in post-procedural bleeding. Three studies reported greater symptomatic improvement with MPFF treatment. Based on these results, MPFF may help reduce post-procedural pain, hemorrhage, and CVD-specific

689 symptoms. These benefits appear to be greater when treatment is started 2 weeks prior to the
690 procedure. When VAD treatment was started only after varicose veins surgery, [119] no benefit
691 was noted.

692 In a non-randomized, controlled multicenter prospective study (DEFANCE trial),[120] 245
693 C2 patients underwent HL&S combined with stab avulsion. Patients in one group (n=200)
694 received 1000 mg of MPFF daily, the control group (n= 45) had no drug treatment. Compression
695 (class 2) was prescribed for 4 weeks after surgery for all patients. Hematoma ($p<0.05$) and pain
696 (VAS) ($p<0.05$) were significantly lower in the MPFF group. Same results were observed for leg
697 heaviness and fatigue.

698
699 **Table. 7. Clinical benefit of Micronized Purified Flavonoid Fraction (MPFF)**
700

First author, year	**Patient**	**Intervention/ exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Kakkos SK, 2018[14]	Adults with CVD including CEAP C2	MPFF	Placebo	Subjective symptoms, edema assessed by ankle circumference, and/or leg or foot volume. Other objective outcomes: leg redness, skin changes, and clinical improvement assessed by the physician. QoL assessed by CIVIQ-20 MPFF was highly effective in improving leg symptoms, edema and QoL	Systematic review and meta-analysis of 7 double-blind, randomized, placebo-controlled trials	Age, sex, different stages of CVD in patients with varicose veins

Allaert FA, 2012[116]	Adults with lower extremity venous edema	MPFF, hydroxyethylrutosides, ruscus extracts and diosmin	Placebo or other VAD	Reduction of ankle edema. The meta-analysis supports assigning Grade A evidence to MPFF in the management of symptoms and edema.	Systematic review and meta-analysis of 10 double-blind, randomized, placebo or other VAD-controlled trials	Age, sex, different stages of CVD in patients with varicose veins
Pompilio G, 2021[15]	Adults with Chronic Venous Disease	MPFF, sulodexide, hydroxyethyl rutosides, calcium-dobesilate, ruscus extracts, horse chestnut extracts and pentoxifylline	Placebo in 45 RCTs	Ulcer healing, leg volume, ankle circumference, symptoms such as pain assessed by VAS, feeling of swelling, heaviness, as well as QoL (CIVIQ-20 score). MPFF was the most effective treatment in reducing lower leg volume, CIVIQ-20 score and pain VAS scale.	Systematic review and meta-analysis of 45 RCTs and separated analysis of 17 observational studies with sulodexide	Age, sex, different stages of CVD in patients with varicose veins

Table 8. MPFF therapy as adjuvant treatment with intervention

First author, year	**Patient**	**Intervention/ exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Mansilha A, 2019[20]	Adults with varicose veins	VAD (MPFF and sulodexide)	Control with no VAD treatment	Post-procedural pain, CVD symptoms and hemorrhage. MPFF reduced post-procedural pain, hemorrhage and CVD specific symptoms.	Systematic review of 5 studies	Age, sex, different stages of CVD in patients with varicose veins
Pokrovsky, AV, 2007[121]	Adults with CEAP C2 undergoing	MPFF	Control	Hematoma, pain (VAS), leg	Controlled multicenter prospective trial	Age, sex, different stages of CVD in

	stripping of the GSV combined with stab avulsion			heaviness and fatigue MPFF in the pre- and postoperative period after phlebectomy attenuated pain, decreased postoperative hematomas and accelerated their absorption.		patients with varicose veins

Clinical benefit of Ruscus extracts

Rationale. Ruscus extracts increase capillary resistance and reduce capillary filtration.[122]

Evidence. A systematic review and meta-analysis [123] included 20 RCT vs placebo, five vs comparative VAD (hydroxyrutosides [HR] and MPFF), and 6 observational studies, with a total of 10,246 patients. Varicose veins were listed in the inclusion criteria of some of the trials (e.g. Capelli[124]), most of them focusing on CVI with CEAP class from C2 to C5. Data quality was heterogeneous, but the study concluded that Ruscus extracts significantly improved symptoms compared to placebo. The best effects were observed on leg heaviness (p=0.001), pain (p=0.02), cramps (p=0.025), and paresthesia (p=0.031). Venous capacity, assessed by plethysmography, decreased by 0.7 ml/100 ml compared vs placebo (p=0.014). Comparison with HR and MPFF showed similar effects on the symptoms. A more recent systematic review and meta-analysis [16] included 10 high quality double blind, placebo-controlled RCTs with a total number of 719 patients (CEAP C2 to C5). Compared to placebo, the risk ratio (RR) for pain was 0.35 ($p<0.00001$), for heaviness 0.26 ($p<0.00001$), for sensation of swelling 0.53 ($p<0.0001$), for paresthesia 0.27 ($p<0.0001$), and for global symptoms 0.54 ($p<0.00001$). Ankle circumference and leg volume were significant reduced, and the study concluded that Ruscus extracts were

723 effective in reducing symptoms and edema in patients with CVD.[16] In a meta-analysis[116]
724 Ruscus extracts significantly reduced ankle circumference versus placebo (p<0001), more so
725 than diosmin. Another systematic review and meta-analysis[15] found that Ruscus extracts were
726 the most effective in decreasing foot volume and ankle circumference.

727
728 **Table 9. Clinical benefit of Ruscus extracts**
729

First author, year	**Patient**	**Intervention/exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Boyle, 2003[123]	Adults with CVI including CEAP C2	Ruscus extracts	Placebo in 20 RCTs, comparator VAD (MPFF, hydroxyethyl rutosides, dihydroergolamine) in 5 RCTs	4-point symptoms scores (all studies), venous capacity (6 studies) and venous refilling time (5 studies). Calf and ankle circumference (11 and 6 studies). Strong and objective demonstration of the clinical efficacy Ruscus in treating patients with CVI	Systematic review and meta-analysis of 25 RCTs (20 vs placebo and 5 vs other VAD) and 6 single-arm studies	Age, sex, different stages of CVD in patients with varicose veins
Kakkos, 2017[16]	Adults with venous symptoms and edema	Ruscus extracts	Placebo	Symptoms and leg edema "Ruscus extract highly effective in reducing symptoms and edema in patients with CVD"	Systematic review and meta-analysis of 10 double-blind, randomized, placebo-controlled trials	Age, sex, different stages of CVD in patients with varicose veins
Allaert, 2012[116]	Adults with lower extremity venous edema	Ruscus extracts, MPFF, hydroxyethyl-	Placebo or other VAD	Reduction of ankle edema. Ruscus extract second best after MPFF in	Systematic review and meta-analysis of 10 double-blind, randomized, placebo	Age, sex, different stages of CVD in patients with varicose veins

		rutosides, and diosmin		reducing ankle edema.	or other VAD-controlled trials	
Pompilio, 2021[15]	Adults with Chronic Venous Disease	Ruscus extracts, MPFF, sulodexide, hydroxyethyl rutosides, calcium-dobesilate, , horse chestnut extracts and pentoxifylline	Placebo in 45 RCTs	Ulcer healing, leg volume, ankle circumference, symptoms such as pain assessed by VAS, feeling of swelling, heaviness, as well as QoL (CIVIQ-20 score) Ruscus was the most effective in ankle circumference reduction.	Systematic review and meta-analysis of 45 RCTs and separated analysis of 17 observational studies with sulodexide	Age, sex, different stages of CVD in patients with varicose veins

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735 **4. INTERVENTIONS FOR SUPERFICIAL TRUNCAL REFLUX**

736 4.1. Endovenous ablation vs high ligation and stripping (HL&S)

737 **4.1.1. For patients with symptomatic varicose veins and axial reflux in the GSV, who are**

738 **candidates for intervention, we recommend treatment with endovenous ablation over**

739 **HL&S of the GSV.**

740 **GUIDELINE: Grade of recommendation: 1 (strong), Quality of Evidence: B (moderate)**

741

742 **4.1.2. For patients with symptomatic varicose veins and axial reflux in the SSV, who are**

743 **candidates for intervention, we recommend treatment with endovenous ablation over**

744 **ligation and stripping of the SSV.**

745 **GUIDELINE: Grade of recommendation: 1 (strong), Quality of Evidence: C (low to very**

746 **low)**

4.1.3. For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, who are candidates for intervention, we suggest treatment with endovenous ablation, with additional phlebectomy, if needed, over ligation and stripping of the accessory vein.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

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

GUIDELINE: Grade of recommendation: 1 (strong), Quality of Evidence: B (moderate)

4.1.5. For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, we suggest treatment with ligation and stripping of the accessory 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.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

4.1.6. For patients with symptomatic varicose veins and axial reflux in the GSV, we suggest treatment with endovenous laser ablation (EVLA), radiofrequency ablation (RFA), or

HL&S over physician-compounded ultrasound-guided foam sclerotherapy because of long-term improvement of quality of life and reduced recurrence.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: B (moderate)

4.1.7. For patients with symptomatic varicose veins and axial reflux in the SSV, we suggest treatment with laser ablation, radiofrequency ablation, or ligation and stripping from the knee to the upper or mid-calf over physician-compounded ultrasound-guided foam sclerotherapy because of long-term improvement of quality of life and reduced recurrence.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

4.1.8. For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, we suggest treatment of the refluxing superficial trunk with endovenous laser ablation, radiofrequency ablation, or high ligation and stripping, with additional phlebectomy, if needed, over physician-compounded ultrasound-guided foam sclerotherapy because of long-term improvement of quality of life and reduced recurrence.**GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)**

For Rationale and Evidence supporting Guidelines 4.1.1. – 4.1.8, please see Part I of the varicose vein guidelines.[8]

4.2. Thermal vs. non-thermal ablation of superficial truncal veins

4.2.1. For patients with symptomatic axial reflux of the GSV, we recommend either 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.

GUIDELINE: Grade of recommendation: 1 (strong), Quality of Evidence: C (low to very low)

4.2.2. For patients with symptomatic axial reflux of the SSV, we recommend either 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.

GUIDELINE: Grade of recommendation: 1 (strong), Quality of Evidence: B (moderate)

4.2.3. For patients with symptomatic axial reflux of the AAGSV or PAGSV, 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.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

For Rationale and Evidence supporting Guidelines 4.2.1. – 4.2.3, please see Part I. of the varicose vein guidelines.[8]

5. FACTORS AFFECTING CHOICE OF SUPERFICIAL TRUNCAL ABLATION AND OUTCOMES

5.1.1. In symptomatic patients with C2 disease we suggest against using truncal vein diameter to determine which patients need venous ablation.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: B (moderate)

Rationale. A commonly accepted diameter threshold for ablation of the GSV or the SSV has been 5 mm. However, data show that ablation of veins <5mm in diameter also improves symptoms.[125, 126]

Evidence. Several studies demonstrated a weak correlation between saphenous vein diameter and increased CEAP clinical class or VCSS; a correlation between quality of life (QoL) and saphenous vein diameter has not been found. [125, 127] Most studies segregated veins diameters into greater or less than 5 mm. Tan et al performed a systematic review of 11 studies and 2,732 limbs. Four studies correlated truncal vein diameter with QoL, while seven reported only on clinical severity measures. Four studies found a weak correlation between vein diameter and VCSS, while one demonstrated correlation with VCSS components. [127] The diameters were a poor predictor of HRQoL, with no relationship to patients' perceived impact on CVD. The review concluded that vein diameters should not be used as a single determinant of who needs venous intervention. [127] Perrins et al examined the clinical and anatomic outcomes of RFA of symptomatic small-diameter GSVs. [125, 126] RFA of symptomatic small diameter GSV (<5mm) provided comparable clinical outcomes (vein closure and improved VCSS at 3 months) and the study suggested that patients with GSV size <5mm benefit from RFA. [125] Bendix et al reviewed the VQI VV Registry and divided patients into those with GSV <5mm (Group 1) vs. those with GSV ≥5mm (Group 2). Both groups had improvement in the VCSS and HASTI scores. [126] Group 2 had more complications, more adverse VTE events, required more anticoagulation, developed more recanalization and

836 missed more days of work than Group 1. They authors concluded that patients with a smaller vein
837 size should not be denied intervention based on size alone. [126]

838

839 **5.1.2. In patients with C2 disease with superficial incompetence and deep vein obstruction**
840 **we suggest treatment of superficial incompetence first.**

841 **GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very**
842 **low)**

843 For Rationale and Evidence supporting Guidelines 5.1.1. and 5.1.2. please see Consensus
844 Statements 1.5.3 and 1.5.4. above, in this document (Part II)

845 **Table. 10. Outcome of superficial truncal ablation in patients with deep vein obstruction**

Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Benfor and Peden [25]	2428/2476	Concomitant treatment of DVO and SVR in 483 limbs (51.2%)	Treatment of DVO alone in 168 limbs (17.8%) Treatment of SVR alone in 293 limbs (31%)	Ablation of SVR is safe for patients with DVO. Patients with advanced CEAP class (≥4) had better results when ablation of superficial truncal veins was combined with treatment of iliac vein obstruction. Patients with early CEAP class (<4) had a staged approach with initial ablation of SVR and stenting for DVO if no improvement was noted.	Systematic review

846

847 **5.2.1. In asymptomatic patients with C2 disease, prophylactic intervention does not**
848 **prevent progression of venous disease. Weight control, compression stockings and**
849 **avoiding prolonged standing may be beneficial.**

850 **CONSENSUS STATEMENT**

851 *Rationale.* Studies have noted progression with worsening CEAP class over time.[128-130] This
852 raises the question about the role of prophylactic intervention in asymptomatic patients with
853 varicose veins, to prevent progression to symptomatic disease.

Evidence. As discussed before, the CEAP classification is not a severity scale but a classification scheme for patients with chronic venous disorders describing the clinical, etiologic, anatomic and pathophysiologic features. Conceptually, however, it has often been pondered whether patients with varicose veins (C2) can undergo treatment to prevent progression to CVI later in life. In the Bonn Vein Study [131] 1978 participants were followed up for a mean of 6.6-years. The prevalence of varicose veins rose from 22.7% to 25.1%. Participants with C2 disease increased to higher C-classes in 19.8% for non-saphenous varicose veins and in 31.8% for saphenous varicose veins. The main risk factor for progression was obesity. The Edinburgh Vein Study had a 13-year follow-up; a progression rate of 57.8% (4.3% per year) was reported, of those with C2 disease at baseline, 31.9% progressed to CVI **[129]**. Risk factors for progression included a family history of varicose veins, previous DVT and obesity. Kostas et al. followed 73 mostly asymptomatic contralateral limbs for 5 years in patients who underwent treatment of symptomatic varicose veins of one lower extremity. CVD progression was significantly less in patients who were not obese and did not gain weight during the study. [128] Patients who did not use compression stockings preoperatively and during the follow-up or had stopped using them also had significantly higher incidence of progression compared with those who used compression. [128]

A Cochrane study in 2013 looked at non-pharmacological interventions to prevent CVI in standing workers.[132] This systemic review concluded that due to the limited number of trials and study participants, there was insufficient evidence to draw any conclusions as to whether non-pharmacologic strategies including compression were effective at preventing the development of CVI in standing workers. Another systematic review of compression for uncomplicated C2 disease found no consensus on the class of compression needed for the effective management of varicose veins and no evidence that wearing compression slows the progression or recurrence of

varicose veins. [133] Although evidence presented in these guidelines show that interventions on varicose veins are associated with improved quality of life and decreased morbidity, no study examined the role of surgical or endovascular therapies on C2 patients to prevent longitudinal progression to CVI. The role of treatment in preventing such progression remains undefined.

Table. 11. Disease progression in patients with varicose veins (C2 disease).

Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Palfreyman , 2009[133]	C2 disease 25 studies	Compression therapy	no therapy	Benefit of compression hosiery for varicose veins was equivocal	Systematic review
Kostas, 2010 [128]	73 limbs	Treated symptomatic varicose veins	Untreated asymptomatic/min symptomatic contralateral limb	A clinical deterioration of > 2 CEAP classes was seen in 23 limbs (32%), only 2 (3%) progressed to C4 disease, none to C6 disease.	Prospective observational cohort
Rabe 2010 [134]	1978 patients	6.6 yr. F/U	Pts w pre-existing CVD vs pts with no CVD	Prevalence of varicose veins 22.7% to 25.1% CVI 14.5 to 16%. Incidence of new varicose veins 13.7% and new CVI 13.0%	Population-based cohort study
Robertson , 2013[135]	1 study (n=19) (1620 studies excluded)	Compression stockings in standing workers	no compression	No progression to CVI	Systematic review
Wrona, 2015[131]	3072 patients (6.6 yr follow-up)	none	none	C2 disease patients increased to higher C-classes in 19.8% for nonsaphenous varicose vein and in 31.8% for saphenous varicose vein. The main risk factor for progression was obesity.	Prospective observational
Lee, 2015[129]	880 patients (13.4 yr follow-up)	none	none	progression rate of 57.8% (4.3% per year). Of those with	Prospective observational

				C2 disease only at baseline, 31.9% progressed to CVI	

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885 **5.2.2. Interventions to treat varicose veins can be performed in an office-based setting,**
886 **surgery center, or hospital operating room, at the discretion of the physician who is**
887 **specialized in vein care.** Better patient experience and lower costs were reported for
888 procedures performed in an office-based setting.

889 **CONSENSUS STATEMENT**

890 *Rationale.* In the United States most venous disease practitioners perform venous procedures,
891 including thermal or non-thermal endovenous ablation, mini-phlebectomy and sclerotherapy in an
892 office-based setting. A comparison to the historical method of providing such interventions in the
893 hospital operating room or in surgical centers helps guide **the physician who is specialized in**
894 **vein care** .

895 *Evidence:* Endovenous procedures are safe and effective with high patient satisfaction when
896 performed in an office-based setting. Studies have shown high technical success for venous
897 interventions in the office-based setting, which is on par with the operating room setting.[136-138]
898 Venous procedures in the office-based setting have a low overall complication rate, comparable to
899 most published series that evaluated similar interventions in the operating room.[136, 138, 139] Jain et
900 al. found that 99% of patients surveyed indicated they would come back to the office for additional
901 procedures.[139] Perkowski et al. treated 165 patients in an outpatient office setting with endovenous
902 laser ablation of either the GSV, SSV or accessory saphenous veins. No DVT or nerve injury were
903 reported and 97% of patients were mostly or very satisfied with their treatment results. [140] In a
904 retrospective study of 429 office based stand-alone RFA procedures, performed under local

tumescent anesthesia in 394 patients with varicose veins, Somasundaram et al. reported > 75% had resolution of symptoms within 1 year, with 3 endothermal heat induced thrombosis (EHITs) and no major complications. Only 23% needed additional treatments. [136] Cost was significantly lower when compared to RFA procedures performed in a day surgery setting. [136] Combining thermal ablation and other venous treatments such as phlebectomy and sclerotherapy during the same procedure is also safe and effective. Jarjous et al. treated 72 extremities in 63 consecutive patients with RFA of the truncal and perforator veins, combined with US guided foam sclerotherapy procedures of tributary and accessory veins.[141] They reported 100% closure of the treated GSV and SSV and 91.7% closure of tributary veins, 13.9% needed additional treatment and there were no major or minor complications. [141] Lin et al. reported on 3073 office-based venous procedures: 285 saphenous vein ablations, 185 mini-phlebectomies, and 261 venous ablations with concomitant mini-phlebectomy. [137] Overall technical success was 99.2%, with a complication rate of 1%. [137] There are a few studies that looked at patient satisfaction in an office setting compared to an operating room setting. Varetto et al treated 112 patients with GSV insufficiency. Roughly half underwent EVLA in day-surgery and half in an outpatient office-based setting. There was no statistical difference in the postoperative success or complications between the two groups. [138] QoL measures did not significantly differ between groups, except for the over 65 year-old group which demonstrated better QoL in office-based setting compared to the day surgery group. [138] Another prospective study sent questionnaires to patients who underwent endovenous ablation with concomitant phlebectomy in the office-based setting and found a high (98.1%) satisfaction level, with 94.7% of the patients stating they would undergo the same procedure again in the same setting, if needed. [142] In summary, varicose vein procedures in the office-based setting have a low complication rate, high patient satisfaction and they are cost effective.

928

929 **Table. 12. Outcome of interventions performed in outpatient office-based settings**

1st Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Jain 2013 [139]	785 patients and 1019 venous procedures: 512 EVLT w phlebectomies, 390 phlebectomies, 110 RFA w phlebectomies	EVLT or RFA +- phlebectomies	none	99% patient satisfaction, 2.2% complication rate	Retrospective review
Perkowski 2004 [140]	165 pts 203 limbs	EVLA	none	97% clinical success rate, 97% patient satisfaction, 84% at 1 yr. had minimal to no symptoms	Retrospective review
Somasundaram 2019 [136]	429 procedures in 394 pts	RFA alone in office-based outpatient setting	none	No major complications, 3 EHIT, reduced cost compared to day surgery, 23% needed further treatment following standalone RFA	Retrospective review
Jarjous 2015 [141]	73 limbs, 63 pts	Office based RFA & UGFS, evaluated at 1 and 6wk	Office based RFA & Foam vs success/complications of staged	100% closure rate of GSV and SSV. 91.7% closure rate of tributaries, No major or minor complications	Controlled non-randomized observational
Lin 2017 [137]	3073 venous proc, 285 saphenous ablation, 185 phlebectomies, 265 ablations & phlebectomies	Treatment in Office based suite	none	99.2% technical success, complication rate 1%	Retrospective review
Varetto 2018 [138]	112 pts	EVLA	Day surgery vs Outpatient office-based setting	No difference between groups in technical success, complications, patient's functional and aesthetic satisfaction. * In pts >65 years of age better QoL in outpatient setting	Prospective cohort study

Hannon 2022 [142]	195 pts with 83% (162) responses	Endovenous ablation w/ phlebectomies in out-pt office	none	98.1% pts satisfied, 99.4% treatment met their expectations, 94.7% would undergo treatment again in outpatient setting	Prospective cohort study

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931 **5.2.3.In patients with symptomatic C2 disease, isolated SFJ (SFJ) incompetence does not**
932 **justify ablation of an otherwise competent GSV. Since the** GSV may be used in the
933 future **for bypass in coronary or leg arteries, it should be preserved whenever**
934 **possible.**

935 **CONSENSUS STATEMENT**

936 *Rationale.* The impact of junctional reflux on clinical manifestations and treatment outcomes is
937 not clear. Reflux patterns and the presence or absence of SFJ reflux have been evaluated in
938 multiple studies and a significant percentage of symptomatic patients have been shown to have
939 lower extremity reflux without SFJ insufficiency. [143] [144, 145] Nevertheless, the presence of
940 junctional reflux often determines insurance coverage for ablation. Assessing the role that
941 junctional reflux plays in patients with symptomatic varicose veins is important to ensure
942 appropriate care.

943 *Evidence.* Studies have indicated that the theory of descending saphenous valvular incompetence
944 starting at the SFJ may be inaccurate and therefore there is no rationale for treatment of SFJ
945 incompetence in the setting of a normal GSV.[143-145] Abu-Own et al. used DUS to assess 190 limbs
946 with primary varicose veins. Sixty-three limbs (33%) had no SFJ incompetence. [143] Labropoulos
947 and colleagues looked at 255 limbs in 217 patients with superficial venous insufficiency and
948 normal deep veins and perforator veins with DUS. Isolated below knee reflux was associated with
949 more symptoms and signs than isolated above knee reflux. [146] Another study by Labropoulos et al.
950 looked at the prevalence of reflux in age-matched asymptomatic young patients and found that

reflux can occur in any vein segment and the most common site was the below knee GSV. [144] Fassiadis et al. studied 611 limbs with primary varicose veins. Of 454 limbs that showed GSV reflux on DUS, 240 limbs exhibited reflux of both the GSV and SFJ and 214 limbs (35%) showed isolated GSV reflux with a competent SFJ. The authors suggested that reflux starts distally and progresses proximally. [145] In light of these studies, treatment of isolated SFJ reflux appears unnecessary.

5.2.4. In patients with symptomatic C2 disease, ablation of the incompetent GSV may be indicated even if the axial reflux is not complete and the SFJ is competent. Shared decision making with the patient is warranted.

CONSENSUS STATEMENT

Rationale and Evidence. Reflux patterns have been evaluated in multiple studies, and as discussed above, a significant percentage of symptomatic patients have been shown to have lower extremity axial reflux without SFJ insufficiency. Engelhorn et al. found SFJ incompetence in only 12% of 590 limbs of 326 women with varicose and spider veins (CEAP Class C1-C2). [147] Aurshina et al in their single center retrospective review of 265 patients including 41 without junctional reflux noted that the location of reflux did not affect patient presentation or outcomes at two years after vein ablation. [148] Others reported more advanced clinical disease in patients with reflux involving the SFJ. [149] The common observation in these studies is that early ablation of the GSV results in good outcome in symptomatic patients, who have competent SFJ but incompetent distal GSV.

Table. 13. Outcome of interventions in patients, somewith competent saphenofemoral junction (SFJ)

1st Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Abu-Own 1994 [143]	167 pts with VV	Ultrasound	Patterns of Reflux on US	190 limbs with GSV reflux, 63 had no SFJ reflux	Retrospective review
Engelhorn 2012 [147]	326 pts 590 limbs	US in pts w VV but w/out edema, skin changes or ulcers	Patterns of reflux	Reflux in 80%, Junctional reflux only in 12%	Prospective observational study
Chastanet 2013 [149]	1882 limbs 1449 Pts	Ultrasound	Patterns of reflux	In 1772 limbs w/ VV 36.1% the GSV and SFJ was competent. In 987 limbs w VV and GSV reflux SFJ was competent in 29.4%	Prospective observational study
Yilmaz 2021 [150]	503 pts 787 limbs with GSV insufficiency	DUS, exam CEAP, VCSS	Patterns of reflux	14.8% of limbs GSV reflux w/out SFJ & malleolar reflux and 10.4% with GSV (including malleolar) but no SFJ reflux	Retrospective review

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977 **5.2.5. In patients with reflux in the below-knee GSV, ablation to the lowest point of reflux**
978 **resulted in better early outcome. Non-thermal techniques are preferred for ablation**
979 **of refluxing distal calf saphenous veins to avoid thermal nerve injury.**

980 **CONSENSUS STATEMENT**

981 *Rationale.* Studies have shown that thermal ablation of the below knee (BK) GSV is feasible and
982 safe. [151] In addition, non-thermal techniques are available if there are concerns about saphenous
983 nerve injury. Elimination of BK GSV reflux has been shown to improve symptoms and reduce
984 the need for additional procedures, compared with ablation of the above knee (AK) GSV only.
985 [152-154]

986 *Evidence.* Several studies showed better results of AK GSV ablation when there was no residual
987 BK GSV reflux. [152 153] In a systematic review, Sussman et al.[33] found that AK-BK EVLA was

associated with significantly lower odds of BK-GSV reflux recurrence compared with AK-EVLA only (P < .0001). Theivacumar et al[152] randomized 68 limbs of 65 patients with varicosities and both AK and BK GSV reflux to either EVLA AK, EVLA to BK mid-calf, or AK EVLA with concomitant BK foam sclerotherapy. There was improvement in the Aberdeen Varicose Vein Severity Score (AVVSS) at 6 weeks in all groups, although it was greater in the latter two groups; patient satisfaction at twelve weeks was not different between the groups. Compared with AK-EVLA, concomitant BK ablation (laser or sclerotherapy) resulted in fewer varicosities and superior symptom relief at 6 weeks. [152] In another study the same authors treated 69 limbs with AK EVLA, 40 with C2 disease.[153] At 6 weeks, residual varicosities, if present, were treated with foam sclerotherapy. Reflux in the BK GSV was evaluated, and the limbs were allocated into three groups: Group A: no reflux; Group B: flash reflux <1s; Group C: significant reflux >1s. Delayed foam sclerotherapy was required in 12% in Group A, 14% in Group B, and 89% in Group C. The improvement in AVVSS at 6 weeks was 86.2% in Group A, 82.1% in Group B, and 59.1% in Group C (P<.001 vs A and B). While EVLA of the AK GSV improved all patients, those with persistent reflux in the BK GSV had the least improvement. In a different study of 50 patients with complete GSV reflux, 16 patients had EVLA in the AK and BK GSV in separate sessions, 34 patients had EVLA in the AK and BK GSV in the same session. [154] Patients with complete GSV reflux complained of ankle pain and swelling. At 11 months, all patients had resolution of their ankle pain, with 44 patients having resolution of swelling. There were four instances of paresthesias. [154] Carradice et al randomized surgical stripping versus EVLA for treatment of varicose veins. Twelve of 23 recurrences of varicosities were due to an incompetent BK GSV. GSV ablation in this study could be safely performed in

the distal leg.[155] Gifford et al. treated 79 limbs with BK-GSV EVLT or RFA for reflux at this site, 43 had Class 1-3 disease. Only three patients (4%) suffered transient paresthesia.

Table. 14. The benefit of treatment of the incompetent below-knee great saphenous vein (GSV).

1st Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Theivacumar 2008 [152]	65/68	EVLA	EVLA-AK v. ELVA-BK v. ELVA AK + BK foam sclero	AVVSS improvement in all groups, least in EVLA-AK. Concomitant BK ablation (laser or sclero) had fewer varicosities and symptoms at 6 weeks	RCT
Theivacumar 2009 [153]	64/69	EVLA	Pts with reflux >1s in BK GSV v no reflux or <1s reflux	Pts with continued reflux in BK GSV had less symptom relief and greater need for sclerotherapy to treat residual varicose veins	Retrospective review
Timperman 2007 [154]	50/50	EVLA	EVLA-AK v. EVLA-BK	EVLA-AK patients had incomplete relief of ankle pain and swelling	Retrospective review
Carradice 2011 [155]	280/280	EVLA or conventional surgery	EVLA v. HL&S	ELVA had lower rates of clinical recurrence (4.0% vs. 20.4%)	Randomized clinical trial

5.2.6. In patients with an epifascial or superficial saphenous vein, thermal ablation may result in skin burn, while non-thermal techniques may cause hyperpigmentation or induration. Mini-phlebectomy or limited stripping is usually performed if the saphenous vein is close to the skin (<0.5 cm).

CONSENSUS STATEMENT

Rationale. Thermal techniques pose the potential for skin burn if the area of ablation is close to the skin. Use of tumescence anesthesia helps overcome this problem in most cases. Non-thermal

non-tumescent techniques may also be used, although it is not known whether one technique is superior to others for veins close to the skin.

Evidence. There is no scientific evidence that supports one type of ablation technique over another, based-on depth of vein below the skin. The risk of skin burns appears to be high in limbs with the vein located <0.5 cm from the skin in spite of injecting tumescent anesthesia subdermally. Pigmentation has also been observed in these patients. In a systematic review and network analysis that included 51 studies on EVLA, RFA, n-butyl cyanoacrylate NBCA ablation or foam sclerotherapy, Gasior et al did not report on skin burn as a complication. [156] In the 16 studies that Alozai and colleagues included in their systematic review/meta-analysis of treatment modalities of the AAGSV, there was a 0.7% incidence of paresthesias [29] with no instances of skin burn. The ablation modalities included RFA, EVLA, NBCA and sclerotherapy. [29] The MARADONA trial, a multicenter randomized study that compared MOCA to RFA, did not find a significant difference in the incidence of skin burn or saphenous neuralgia between the two techniques at 30 days. [157]

5.2.7. For patients with large (>10 mm), non-aneurysmal saphenous veins, thermal ablation with EVLA or RFA should be performed rather than over non-thermal techniques.

CONSENSUS STATEMENT

Rationale. While there are many techniques to perform venous ablation and they provide favorable outcomes in the setting of large diameter (>10 mm) veins, thermal ablations have superiority over other treatments.

Evidence. Hamann et al examined the safety and effectiveness of endovenous thermal ablation (EVTA) in 11 limbs with a large GSV, but < 2cm in size close to the junction. [158] No DVT or EHIT was noted, and truncal obliteration was 80% at one year. Atasoy reviewed 44 consecutive

patients with large GSVs, with a mean diameter of 16.95 mm (range 15-26mm)] and found 100% occlusion rate at 1 year after treatment. All patients had clinical improvement and improved QoL scores.[159] Calcagno et al found no difference in occlusion rates of 246 limbs with saphenous vein diameter ≤ 12 mm diameter (mean 8 +/- 2mm) and of 96 with vein >12 mm (mean 17 +/- 4mm) when treated with RFA.[160] Fernandez et al. treated 183 patients with a GSV diameter < 12 mm and 74 with a GSV diameter ≥ 12 mm. There was significant improvement in pain and QoL in both groups, with no difference in occlusion rates or adverse effects at 1, 6, and 12 months. [161] Borsuk and Fokin did a prospective study of 261 EVLA procedures of the GSV with 1470 nm radial tip laser. Mean diameter of GSV at the SFJ was 24 +/- 6 mm (range 21-43mm). [162] 88% of veins were occluded on day 1; of the 31 non-occluded veins, 21/31 were occluded by day 7. Ochoa Chaar et al reviewed 732 laser ablations, 88 were performed on veins measuring > 10 mm in diameter.[163] Complication and closure rates were similar for larger and smaller veins, unsuccessful closure was more likely in the SSV and AASV than in the GSV. [163] In a small case series, Florescu et al performed 20 ablations of veins > 10mm and 4 ablations on veins ≥ 20mm in diameter; successful ablation was achieved in 100%. [164] In a retrospective study, 129 patients with a GSV ≥14 mm underwent either stripping or RFA. [165] A composite endpoint of pain, subcutaneous hemorrhage, paresthesia; and technical outcome at 1 year was evaluated. There were favorable outcomes in 30.8% of the stripping group vs. 95.3% in the RFA group. [165] Postoperative pain was associated with increased BMI and large vein diameter. For large diameter veins, RFA was superior to stripping. These data support that thermal ablation techniques are safe and effective in treating large diameter saphenous veins. There have been no large case series using non-thermal techniques in large veins.

Table. 15. Outcome of interventions with >10mm superficial truncal veins

1st Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Hamann 2019 [158]	13/15	EVLA (4/15 with EVLA+HL	Pts with GSV >20mm or SSV >15 mm close to deep junction	No severe adverse events (no EHIT or DVT). Significant improvement of VCSS at 1 yr (6 pre to 2 post procedure)	Single center prospective observational cohort study
Atasoy 2015 [159]	44/49	EVLA for Mean GSV diameter 16.95 mm (15-26 mm)	none	Technical success 97.9% at one month and 100% at 6 months	Retrospective review
Calcagno 2009 [160]	338 limbs	ClosureFAST RFA	Saphenous vein diameter >12mm v. <12 mm	Vein diameter >12mm had no effect on closure rate.	Retrospective review
Fernandez 2017 [161]	257/257	RFA	GSV diameter >12mm v. <12mm	No difference in occlusion rates, pain and QoL improvements or adverse events	Single center prospective study
Borsuk 2020 [162]	231/261	EVLA for GSV diameter >20mm	none	88% occluded on day 1, 96% by day 7. Recanalization of 0.8%	Prospective non-comparative study
Ochoa Chaar 2011[163]	732/732	EVLA GSV, SSV, AASV	Saphenous vein diameter >10mm v. <10mm	Complication rates not significantly different for veins >10mm in diameter vs. smaller veins	Retrospective review
Florescu 2014 [164]	24 limbs	EVLA	Saphenous vein diameter >10 mm, 4 with diameter >20mm	Successful ablation in 100%	Retrospective review
Shaidakov 2016 [165]	129/129 Saphenous vein diameter >14mm	RFA	HL&S	Favorable outcome (technical, pain, hemorrhage, paresthesia) was 30.8% after HL&S and 95.3% after RFA	Multicenter retrospective cohort study

5.2.8. The incidence of superficial thrombophebitis has been reported to be similar for thermal and non-thermal ablations.

CONSENSUS STATEMENT

Rationale. Different rates of post-procedure thrombophlebitis were reported for different ablation techniques, but most RCTs and meta-analyses found no significant difference in the rates of thrombophlebitis as a minor complication after endovenous ablations. [166]

Evidence. In one of the largest single center retrospective trials of 808 patients, Aurshina et al.[167] compared acute thrombotic complications after EVLA with RFA. The incidence of acute superficial thrombosis in varicose veins in the ipsilateral leg was 4.6%, and overall thrombotic complications occurred in 10.5%, more frequent after EVLA than after RFA (11.4% vs. 7.7%, P=.007). Thrombotic complications in this study, however, also included EHIT that occurred in 5.9%. When EHIT class 1 was excluded, the true EHIT rate was 1.16%. There was no difference in thrombophlebitis following EVLA and RFA in a systematic review of 12 studies that included 1577 patients (RR:1.03, 95% CI:0.56 to 1.92). [56]

When comparing non-thermal and thermal techniques, a systematic review and meta-analysis by Hassanin et al[21] found no significant difference in phlebitis rates between groups (pooled RR, 0.70; 95% CI, 0.32-1.54). Non-thermal ablations in this study included mechanochemical ablation and cyanoacrylate vein ablations. A meta-analysis from Chen et al[22] found similar results, with no difference in phlebitis rates between cyanoacrylate ablations vs. RFA (OR 5 1.22, 95% CI:0.70–2.13, p=.479). Single center studies published on higher rate of mild phlebitis after cyanoacrylate ablation, likely also due to a periphlebitic allergic reaction to cyanoacrylate,[168] while other scoping and systematic reviews and meta-analyses showed lower phlebitis rates after cyanoacrylate treatment of truncal veins vs thermal ablations.[23, 169, 170] There was a large heterogeneity in these trials and patients represented encompassed the entire spectrum of chronic venous disease (CEAP Class 2-6).

There was no difference in phlebitis rates, when mechanochemical ablation was compared to EVLA in the LAMA trial occurring in 7% (5/69) after EVLA compared with 13% (9/69) after MOCA (P = .262).[171] In a retrospective trial with 979 limbs, Obi et al[172] found, not surprisingly, more asymptomatic phlebitis in patients who underwent RFA plus transilluminated

powered phlebectomy as compared to RFA alone. Combined therapy of endovenous thermal ablation with polidocanol endovenous microfoam (PEM) sclerotherapy also had higher incidence of phlebitis than thermal ablation combined with placebo sclerotherapy (18/79 vs 0/30).[173]

6. INTERVENTIONS TO PRESERVE THE GSV

6.1.1. For patients with early stages of symptomatic varicose veins we suggest preserving the GSV using the ASVAL (ambulatory selective variceal ablation under local anesthesia) technique, if performed by a physician who is familiar with the technique.

GUIDELINE. Grade of recommendation 2 (weak), Quality of Evidence B (moderate)

Rationale. The ambulatory selective variceal ablation under local anesthesia (ASVAL) is a GSV sparing method that involves detailed DUS mapping of all varicose tributaries connecting to the GSV and ambulatory phlebectomy. [174, 175] The operation is based on the ascending theory which is that the venous disease process develops in tributaries and distal truncal veins and "ascends" to the junction and the deep venous system. [176] A systematic review of the ASVAL procedure in 2021 included two RCTs, one case-control and three cohort studies, and five case series. Varicose vein recurrence at 1 year ranged from 0.55 to 13.5%, and GSV incompetence resolved in 50% to 85% at 1 year after the intervention. [31] Another study reported absence of GSV reflux at 1-year in 98% of limbs with competent SFJ at presentation and in 42% of those with an incompetent SFJ at presentation.[177] Although the level of evidence was low in the systematic review, ambulatory phlebectomy of varicose tributaries creating a venous reservoir may have a positive effect on truncal reflux and ASVAL may be an effective minimally invasive treatment of CVD. Best results were seen in those patients who had a competent terminal valve at the SFJ**.** [177]The level of evidence for ASVAL was upgraded to B (moderate) because of the recently

published SAPTAP RCT.[178] In this multicenter, non-inferiority RCT single ambulatory phlebectomy (SAP) was performed in 227 patients and RFA with phlebectomy was done in 237 patients, all with truncal reflux and varicose veins. At 1 year, VEINES-QOL/Sym scores were non-inferior after SAP compared to TAP and SAP was a cost-effective alternative to TAP. Twenty six percent of the SAP patients underwent additional truncal ablation.[178]

Table. 16. Benefits of the ASVAL procedure

Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Richards, 2020[31]	Patients with varicose veins and truncal reflux	ASVAL	none	Recurrent varicose veins at 1-year: 0.5-13.5%, GSV reflux resolution at 1 year: 50% to 85%	Systematic review
Scheerders, 2023[178]	Patients with varicose veins and truncal reflux (C2-C6)	ASVAL (SAP: single ambulatory phlebectomy) N=227 pts	TAP: Thermal truncal ablation and concomitant phlebectomy N=237 pts	At 1 year, SAP pts had non-inferior HQL compared to TAP pts. SAP was cost-effective to TAP. 25.6% of SAP pts underwent additional truncal ablation.	Non-inferiority RCT (SAPTAP Trial)

6.1.2. For patients with symptomatic varicose veins, we suggest preserving the GSV using the CHIVA (Ambulatory Conservative Hemodynamic Correction of Venous Insufficiency) technique, if performed by a physician who is familiar with the technique.

GUIDELINE. Grade of recommendation 2 (weak), Quality of Evidence C (low)

Rationale. The Ambulatory Conservative Hemodynamic Correction of Venous Insufficiency Method (CHIVA) was designed to approach venous hemodynamic insufficiency while preserving the GSV, lower transmural pressure in the superficial venous system and avoid removal of varicose tributaries. [179] The goal of CHIVA is to correct the abnormal hemodynamic pathways that are identified with detailed preoperative mapping using DUS. Three types of "shunts" are identified during DUS. Truncal veins are ligated selectively, at the "escape points",

where the reflux starts, and the "reentry points', the perforators, where blood enters from the superficial into the deep system, are preserved. Phlebectomies are not performed and reduction of the venous pressure reduces the size of varicose veins a few months after the operation. [179]

Evidence. Two systematic reviews by Bellmutt-Montoya et al [27, 28] studied the CHIVA procedure, comparing them to HL&S and to endovenous procedures. The last review in 2021[28] included six RCTs and 1160 patients, three RCTs compared CHIVA to HL&S, one to compression treatment of venous ulcers, one to HL&S and RFA and another to HL&S and EVLA. Five studies reported recurrence of varicose veins at 18 months to 10 years. The review concluded that CHIVA may make little or no difference to the recurrence of varicose veins compared to stripping (RR 0.74, 95% CI 0.46 to 1.20), and it may make little or no difference in preventing recurrence compared to RFA (RR 2.02, 95% CI 0.74 to 5.53) or to EVLA (RR 0.20, 95% CI 0.01 to 4.06). Side effects were similar, but CHIVA may reduce slightly nerve injury compared to HL&S and may cause more bruising than RFA. Evidence supporting all results in this Cochrane review were of low certainty, based on a small number of trials with high risk of bias, with imprecise results due to the small number of events.

A retrospective study by Maeso et al, reported better clinical results after CHIVA than after HL&S at 3 years. [180] In a subsequent prospective study by the same group, 58 patients underwent the CHIVA procedure, with ligation of the GSV tributary, that connected to a re-entry perforator. The ligation eliminated SFJ reflux in all but 5 patients (8%). Saphenous reflux, however, returned in 88% of the limbs by 6 months and 46 patients required a second operation to ligate and divide the proximal GSV. Elimination of the reflux in the GSV after the interruption of the insufficient collaterals was temporary[181].

A recent RCT by Gonzalez Canas et al,[182] analyzed results of RFA, HL& S and CHIVA in 214 limbs. Clinical recurrence rates at 24 months were 4.3%, 7.2% and 14.7% for HL&S, RFA and CHIVA, respectively. Ultrasound recurrences were 7.1% for HL&S, 13% for RFA and 46.7% for CHIVA. With an 80% power to assess noninferiority, the study found RFA to be non-inferior to CHIVA in terms of clinical recurrence. Considering the steep learning curve of the drained and nondrained strategies, the different types of venous-venous shunts , the need for staged procedures[183 176, 184, 185] and that all patients require an individualized strategy, it is clear that CHIVA should only be performed by well qualified surgeons who are dedicated experts in venous hemodynamics and DUS.[186]

Table. 17. Benefits of the CHIVA procedure

Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Bellmunt-Montoya 2015,[27]	4 RCTs 796 patients	CHIVA	HL&S Compression (C6)	There may be little or no difference in the recurrence of varicosities	Systematic review
Bellmunt-Montoya 2021,[28]	6 RTCs 1160 patients	CHIVA	HL&S, Compression (C6), RFA, EVLA	There may be little or no difference in the recurrence of varicosities	Systematic review
Maeso 2001,[180]	175 patients	CHIVA (90) patients)	HL&S +- phebectomy (85)	Less complication in CHIVA group	Retrospective case review
Canas 2020,[182]	225 limbs	RFA,	HL&S, CHIVA	RFA was noninferior in terms of clinical recurrence to CHIVA	RCT, single center,
Alozai, 2021,[29]	16 studies on treatment of AAGSV	CHIVA	Thermal ablation, cyanoacrylate, sclerotherapy,	Lower closure rates with sclerotherapy and CHIVA	Systematic review

7. TREATMENT OF VENOUS TRIBUTARIES

7.1. Telangiectasias (spider veins) and reticular veins

7.1.1. **For patients with symptomatic telangiectasias and reticular veins we recommend sclerotherapy with liquid or foam.**

GUIDELINE. Grade of recommendation 1 (strong), Quality of Evidence B (moderate)

Rationale. Sclerotherapy has been used for decades for treatment of telangiectasias or spider veins (subdermal veins <1 mm in size) and reticular veins (veins <3 mm in size), with good results. Foam sclerotherapy has been preferred recently for larger reticular veins.

Evidence. In a recent Cochrane systematic review and meta-analysis 3632 patients from 35 RCTs were studied.[187] Treatments of telangiectasias and reticular veins included sclerosing agents, laser and compression. There was moderate-certainty evidence that sclerotherapy was better than placebo (standard mean difference, SMD, 3.08, 95% CI 2.68 to 3.48), but it resulted in more hyperpigmentation, matting and pain. Polidocanol had results similar to other sclerosing agents, but it was less painful. Sodium tetradecyl sulphate (STS) sclerotherapy resulted in resolution or improvement of telangiectasias similar to other agents but there was more hyperpigmentation, matting and probably more pain. Foam likely caused more matting than liquid sclerosing agents. In the United States, 0.5% intravenous polidocanol is approved by the FDA to treat uncomplicated spider veins (varicose veins ≤1 mm in diameter) and 1% polidocanol for uncomplicated reticular veins (varicose veins 1 to 3 mm in diameter. The maximum recommended volume per treatment session is 10 mL. 1% and 33% intravenous sodium tetradecyl sulfate is also approved for treatment of small uncomplicated varicose veins, for a maximum single treatment of 10 mL. Polidocanol injectable foam was approved by the FDA in 2013 for treatment of incompetent GSV, accessory saphenous veins, and visible varicosities of

the GSV system above and below the knee. Each ml of the injectable foam contains 1.3 mg of polidocanol.

7.1.2 **For patients with symptomatic telangiectasias or reticular veins we suggest transcutaneous laser treatment if the patient has sclerosant allergy, needle phobia, sclerotherapy failure or small veins (<1mm) with teleangiectatic matting.**

GUIDELINE. Grade of recommendation 2 (weak), Quality of Evidence B (moderate)

Rationale and Evidence. Surface lasers used to treat telangiectasias have wavelength between 532 nm and 1064 nm.[188] The Nd:YAG 1064 nm laser has shown results close to sclerotherapy but more pain was reported after laser treatment. [189] Parlar et al. recommended laser for those who have needle phobia, allergy to sclerosants and for small veins with telangiectatic matting, while sclerotherapy is more effective for larger, feeder veins.[189] The 2021 Cochrane review found no clear difference in resolution or improvement of telangiectasias or matting when laser was compared to sclerotherapy. There was maybe less hyperpigmentation (RR 0.57, 95% CI 0.40 to 0.80;) in the laser group. There was more resolution or improvement of telangiectasias in the combined laser and polidocanol group compared to polidocanol alone (low-certainty evidence). Laser treatment may result in less hyperpigmentation (moderate-certainty evidence). Further well-designed studies are required to provide evidence for other available treatments and important outcomes (such as recurrence, time to resolution and delayed adverse events); and to improve our confidence in the identified comparisons.

<u>7.2. Varicose tributaries</u>

7.2.1. For treatment of symptomatic varicose tributaries, we recommend mini-phlebectomy or ultrasound guided sclerotherapy using physician-compounded foam (PCF) or polidocanol endovenous microfoam (PEM).

GUIDELINE. Grade of recommendation 1 (strong), Quality of Evidence B (moderate)

For Rationale and Evidence supporting Guideline 7.2.1., please see Part I. of the varicose vein guidelines.[8]

7.2.2. For treatment of symptomatic varicose tributaries, we suggest transilluminated powered phlebectomy as an alternative treatment for patients with large clusters of varicosities by a physician who is trained in the procedure.

GUIDELINE. Grade of recommendation 2 (weak), Quality of Evidence C (low to very low)

Rationale. In patients with large, clustered patterns of varicose veins, transilluminated powered phlebectomy remains an acceptable alternative treatment option which requires fewer incisions and shorter treatment times.

Evidence. Several studies have described the safety and efficacy of ambulatory phlebectomy.[172, 190, 191] Transilluminated powered phlebectomy is a minimally invasive alternative treatment for varicose veins, it is performed under general or local tumescent anesthesia, combined with irrigated illumination and endoscopic-powered venous resection.[192] Two RCTs concluded that powered phlebectomy procedures are quicker and require fewer incisions than traditional phlebectomy, but a steep learning curve is expected.[193, 194] Chetter et al [194] found, however that compared to ambulatory phlebectomy, ecchymosis (39% v. 25%, $p < .001$) and pain were more frequent with powered phlebectomy and reduced the early postoperative QoL. A meta-analysis of Luebke and Brunkwall concluded that powered phlebectomy decreased the number of incisions,

improved mean cosmetic score and shortened the duration of the procedure in patients with extensive varicosities. There was less calf hematoma after hook phlebectomy and a worse mean pain score after powered phlebectomy.[11]

7.2.3. For patients with symptomatic varicose tributaries, treatment of the tributaries should be performed even if the superficial trunks are competent.

CONSENSUS STATEMENT

Rationale. In general, treatment for primary or recurrent varicose veins irrespective of axial competence has been shown to be effective and indicated for patients with symptomatic C2 disease.

Evidence. Surgical intervention for symptomatic varicose veins has been widely accepted as being an effective, appropriate therapy with good outcomes for pain reduction and improvement in QoL. A Cochrane review in 2004 compared treatments of varicose veins with surgery versus sclerotherapy and concluded that there was insufficient evidence to preferentially recommend the use of sclerotherapy or surgery.[195] A systematic review in 2009 by Leopardi and colleagues concluded that sclerotherapy and phlebectomy may be appropriate in patients with minor superficial varicose veins not related to reflux of the saphenous system or as a post- or adjunctive treatment of varicose tributaries, but data were limited.[196] A recent Cochrane review in 2021 addressed the efficacy of sclerotherapy alone for treatment of varicose veins. [197] The study included 28 RCTs involving 4278 participants. None of the RCTs compared sclerotherapy, however, to no intervention or to pharmacological therapy. There was very low to low-certainty evidence that foam sclerotherapy alone improved cosmetic appearance, residual varicose veins

and symptoms compared to placebo and possible improved QoL and VCSS. The study concluded that there is a need for high-quality trials using standardized sclerosant doses, with well-defined outcome measures and measurement time points to increase the certainty of the evidence. There has been a number of studies that showed benefit of treatment of recurrent varicosities after saphenous ablation using either mini-phlebectomy or sclerotherapy, with good results.[198, 199] Currently, ultrasound guided foam sclerotherapy is most commonly used for treatment of recurrent varicose veins,[199] and re-exploration of the groin or phlebectomy in that region is avoided. In the absence of superficial refluxing axial veins or for patients with prior axial reflux ablation, conservative measures, such as compression or VADs can also be considered for varicose tributaries (see Guidelines 2. and 3.)

7.2.4. There is no clinical evidence that foam sclerotherapy using room air is less safe and effective than using CO2 gas mixture.

CONSENSUS STATEMENT

Rationale. Many studies show the benefit of foam sclerotherapy for treatment of superficial venous disease, with minimal side effects. While in theory felt to be safer, there is limited data that directly compares the use of CO2 or CO2/O2 based foam to room air when treating with foam sclerosants.

Evidence. Ultrasound-guided foam sclerotherapy (UGFS) has been shown to be safe and effective for the treatment of superficial venous disease, and it is currently recommended for treatment of reticular and varicose veins, in addition of superficial truncal veins. In a comprehensive review of the literature Cartee et al[200] discussed factors affecting foam stability and found that the half-life of room air foam was reported to be three times longer than that of CO_2 alone and 1.5 times longer than O2/CO2.[201, 202]

Morrison et al[203] showed that bubbles were detected in the right heart in all patients after room air foam sclerotherapy and high-intensity transient signals were seen in the middle cerebral artery in 4 of 21 patients. Morrison et al[204] looked at side effects using air and CO2 foam for endovenous chemical ablation and found visual disturbances were experienced by 3.1% (4/128) and 8.2% (4/49) patients in the CO_2 and room air groups respectively (P = .15). Respiratory difficulties or circumoral paresthesia each occurred in 0.8% (n = 1) of the CO_2 patients. Incidence of chest tightness (3.1% vs 18%), dry cough (1.6% vs 16%), or dizziness (3.1% vs 12%) were significantly lower in the CO_2 vs room air group (P < .02). While other complications were less in the CO2 group, visual disturbances were not significantly different, but conclusion are limited by the small sample size.

Willenburg et al[205] conducted a systemic review evaluating visual disturbance (VD) following sclerotherapy of varicose veins, reticular veins and telangectasias. While the prevalence of VD was difficult to determine, two RCTs reported no VDs (95 and 75 patients treated, respectively). In large case series (>500 patients), the prevalence of VD ranged from 0.09% to 2%. In a meta-analysis that included over 9000 patients, Jia et al[10] found the median rates of VDs and headache were 1.4% and 4.2%, respectively. Chest tightness and coughing occurred in less than one percent. Room air and CO_2-created foams were included in this meta-analysis. Gillet et al[206] evaluated the side-effects and complications of foam sclerotherapy in a prospective, multicenter study of room air vs oxygen foam sclerotherapy in 1025 patients. The incidence of migraine was 0.78% (with aura 0.59%, 0.19% without aura), VD 0.68%, chest tightness 0.68%, chest tightness with visual disturbance 0.49% and transient ischemic attack occurred in 0.1%.

In summary, while theoretically CO2 foam is supposed to improve the safety profile compared to room air, the data is limited, and the studies support both methods of foam

sclerotherapy. In addition, room air foam is more stable than CO2 making both the delivery method and the physician's skill important in achieving the desired outcome.

Table. 18. Comparison of using room air and CO2 for foam sclerotherapy

1st Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Jia, 2007 [10]	69 studies, >9000 patients	Foam sclerotherapy	Liquid sclerotherapy, surgery	Serious adverse events were rare; insufficient evidence for meaningful comparison to other minimally invasive therapies	Systematic review
Willenberg, 2013 [205]	Over 20,000 patients from 4 RCT, 18 case series and 3 case reports	Sclerotherapy	CO2 based foam, liquid sclerotherapy	Visual disturbance following sclerotherapy is an uncommon event with no long-term neurological deficit	Systematic review
Morrison, 2008 [204]	177 patients	UGFS with 1% Polidocanol foam mixed with room air	CO2 based foam,	Visual disturbances CO2 : 3.1% (4/128), Room air : 8.2% (4/49) (*P* = .15). Chest tightness (3.1% vs 18%), dry cough (1.6% vs 16%), or dizziness (3.1% vs 12%) were lower in the CO_2 vs air groups (*P* < .02). The proportion of patients with side effects decreased from 39% (19/49) to 11% (14/128) as CO_2 replaced air for foam preparation (*P* < .001).	Prospective observational study
Gillet, 2009 [206]	1025 patients	UGFS for GSV or SSV reflux	None	30-day saphenous occlusion: 90.3%. Side effects : n=27 (2.6%), migraine (n = 8, 4 with VD); VD alone: n= 7. Thrombo-embolic events: 10 DVTs, 1 PE,1 ischemic stroke, with complete clinical recovery in 30 minutes, 1 septicemia with satisfactory outcome	Multicenter prospective observational study

7.2.5. There is currently no clinical study of sclerotherapy with physician-compounded foam (PCF), prepared using the Tessari-method, that shows that it is less safe or effective than polidocanol endovenous microfoam (PEM).

CONSENSUS STATEMENT

Rationale. Polidocanol endovenous microfoam (PEM), used for treatment of truncal veins and varicose tributaries is a promising product that appears to be more stable and cohesive, with a narrow bubble size distribution compared to physician compounded foam, used for sclerotherapy of varicose tributaries and superficial truncal veins.

Evidence. As articulated in the statement, there is no clinical evidence that sclerotherapy with physician-compounded foam (PCF), prepared using the Tessari-method is less safe or effective than polidocanol endovenous microfoam (PEM). There are no prospective studies comparing the two techniques since the VANISH-2 RCT compared 0.5% and 1% polidocanol endovenous microfoam with placebo. [207] In laboratory testing, the polidocanol endovenous microfoam (PEM) had a narrow bubble size distribution, better stability, more cohesive properties and lower degradation rate than any physician-compounded foams. [208] Prospective randomized studies comparing PEM with physician compounded foam in patients with varicose veins are warranted.

Table. 19. Outcomes of foam, liquid and placebo sclerotherapy .

1st Author, Year (Ref.)	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Todd, 2014 [207]	232 patients (C2: 31.9%, C3-C6:68.1%)	PEM 0.5%, PEM 1% for GSV reflux	Placebo	At 8 weeks PEM 0.5% and 1% was effective and provided clinically meaningful benefit in symptoms (VVSymQ) and appearance of varicose veins vs placebo . Thrombotic complications: thrombus extension 3.9%, DVT 5.6%, isolated gastrocnemius or	RCT (VANISH-2)

				soleal vein thrombosis 0.9%. No PE.	
Todd, 2015 [56]	58 patients	1% PEM	None	PEM 1% led to durable, clinically meaningful, and ongoing improvements at 1 year in VV symptoms and appearance	Treatment arm of an RCT followed upto 1 year. (VANISH-2)
King, 2015 [209]	279 patients (C2: 49.1%, C3-C6: 50.9%)	PEM 0.125%, 0.5%, 1%, 2% for GSV reflux or varicose tributaries	Placebo	At 8 weeks administration of up to 15 mL of PEM was safe and effective. VVSymQ scores for pooled PEM group $p < .0001$) and individual dose concentrations ($p < .001$) were superior to placebo. IPRV3 and PA-V3 scores were also significantly greater. Most AEs were mild and resolved without sequelae. No PE.	RCT
Gibson, 2017 [56]	77 patients (C2: 0, C3-C5: 100%)	PEM, 1% vs placebo for symptomatic, visible varicose veins	Placebo	PEM, 1% had statistically significant improvement vs placebo in symptoms and appearance	RCT
Lal 2017 [210]	221 patients C2: 41.3%, C3-C6: 48.7%)	PEM 1%	Placebo	20-30% more patients in PEM 1% group achieved clinically meaningful functional and psychological improvement vs placebo	Pooled data from 2 RCTs
De Avila Oliveira, 2021 [128]	4278 patients with varicose veins	sclerotherapy (liquid, foam) for treatment of varicose veins	Placebo, different concentration of same sclerosing liquid, foam, different sclerosing solutions,	Very low-certainty evidence that sclerotherapy is effective and safe compared to placebo. Limited to no evidence for one concentration of foam to another; foam compared to liquid; foam compared to any other substance; or one technique to another.	Systematic review with 28 RCTs

Kim ,2021[129]	60 patients (C2;32, C3-C6: 28)	PEM for superficial truncal reflux	None	Closure rate 93% at 6 months. VCSS improved from 7.3 to 1.4. (P<.0001) Complications: 1 DVT; 8.3 % had thrombophlebitis, 6.6% had skin pigmentation.	Prospective observational study
Jimenez, 2022 [211]	49 patients/68 limbs (C2:15, C3-C6 :53)	PEM for symptomatic BK truncal vein reflux after previous saphenous ablation	None	At a median follow-up of 97 days, PEM ablation resulted in a 96% closure rate, symptomatic relief of 78%, two deep venous thrombus extensions, one requiring anticoagulation.	Retrospective cohort study
Deak, 2022[212]	1070 patients (C2 :469, C3-C6 :601)	EVLA (n=550)	PEM (520)	Reflux eliminated in 93.5% (514/550) after PEM and 92.8% (482/ 520) after EVLA; 3-year follow-up; no neurologic or cardiac adverse events after PEM	Retrospective non-randomized comparative study

8. TREATMENT OF VARICOSE TRIBUTARIES CONCOMITTANT OR STAGED WITH SUPERFICIAL TRUNCAL ABLATION

8.1.1. For patients with symptomatic reflux in the GSV or SSV and associated varicosities, we recommend simultaneous 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.

GUIDELINE: Grade of recommendation: 1 (strong), Quality of Evidence: C (low to very low)

8.1.2. For patients with symptomatic reflux in the AAGSV or PAGSV, we suggest simultanous ablation of the refluxing venous trunk and phlebectomy or ultrasound-guided foam sclerotherapy of the varicosities with physician-compounded foam or commercial polidocanol endovenous microfoam.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

8.1.3. For patients with symptomatic reflux in the GSV or SSV, we suggest ablation of the refluxing venous trunk and staged phlebectomy or ultrasound-guided foam sclerotherapy of the varicosities only if anatomic or medical reasons are present. We suggest shared decision-making with the patient regarding the timing of the procedure

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

8.1.4. For patients with symptomatic reflux in the AAGSV or PAGSV, we suggest ablation of the refluxing venous trunk and staged phlebectomy or ultrasound-guided foam sclerotherapy of the varicosities only if anatomic or medical reasons present. We suggest shared decision-making with the patient regarding the timing of the procedure.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

8.2. For patients with symptomatic reflux in the major superficial venous trunks and associated varicosities undergoing initial ablation alone, we recommend follow-up for ≥3 months to assess the need for staged phlebectomy or ultrasound- guided

sclerotherapy for persistent or recurrent symptoms. Longer follow-up is recommended for those with recurrence or more advanced CEAP class.

GOOD CLINICAL PRACTICE STATEMENT

For Rationale and Evidence supporting Guidelines 8.1.1. – 8.1.4. and good clinical practice statement 6.2, please see Part I. of the varicose vein guidelines.[8] The panel strongly recommended concomitant procedures to treat truncal incompetence and varicose veins at the same settings, since most patients would like to have a single operation, but the evidence supporting the efficacy of a concomitant procedure had to be downgraded to C (low to very low), because the meta-analysis by Aherne et al[213] included 12 non-randomized studies with the intrinsic associated bias. A sub analysis of 3 RCTs showed no difference in reinterventions between the groups. In addition, 63.9% of the patients with planned staged intervention never had a second procedure. The study counted the 2nd operation of a staged procedure "re-interventions" and the percent of reinterventions after the staged procedures was not investigated. In one of the RCTs,[152] the need for staged treatment of varicose tributaries was only 17% in those patients who underwent extended EVLA for axial, below-knee saphenous incompetence.

9. MANAGEMENT OF RECURRENT VARICOSITIES

9.1.1. For patients with symptomatic recurrent varicosities, clinical evaluation and DUS should be performed before treatment to determine the potential source of recurrence.

CONSENSUS STATEMENT

Rationale. Mandatory follow-up for C2 patients for several years post intervention is costly and not indicated. Patients who present with recurrent symptoms are common, however, and require thorough evaluation to determine the source of recurrence.

Evidence. Evaluation of symptomatic recurrent varicose veins should be performed after a careful clinical exam of the patient in the standing position and with DUS to assess the etiology, source, type, and extent of recurrent varicose veins. Sites of reflux at the SFJ or SPJ and at sites of potential incompetent perforating veins should be investigated. DUS can identify residual saphenous stumps but has a sensitivity of 62% and a positive predictive value of only 26% to correctly identify neovascularization.[214]

Recurrent varicose veins after surgery (REVAS) have been reported to occur between 6.6% to 37% at 2 years and upwards of 50% at 5 years.[7] We 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 and interval healing has occurred. Any residual symptoms or problematic residual varicose veins should be reassessed and documented. Reevaluation after 3-months may be patient initiated based on recurrent symptoms.

9.1.2 For patients with symptomatic recurrent varicosities due to persistent or recurrent reflux of the GSV or AAGSV, treatment with either open surgical or endovascular techniques may be performed, with good outcomes expected.

CONSENSUS STATEMENT

Rationale and evidence.

Theivacumar and colleagues treated 64 patients with EVLA of the above knee (AK) GSV. AK-GSV EVLA improved symptoms regardless of persisting BK reflux, the latter,

however, was responsible for residual symptoms and a greater need for sclerotherapy for residual varicosities.[153] A systematic review in 2021 investigated the incidence of below knee (BK) residual reflux in patients who underwent ablation of the GSV[33]. High ligation and stripping (HLS) in the AK GSV (6 studies, 525 limbs), as well as EVLA, AK only (7 studies, 696 limbs) and AK+BK ablation (2 studies, 147 limbs), were included. The authors found that AK+BK EVLA was associated with significantly lower odds of BK reflux recurrence compared to AK-EVLA alone (OR 0.1857; 0.076-0.4734; P < .0001). No statistically significant difference was observed in BK-GSV reflux recurrence between patients receiving AK-EVLA and those receiving AK-HLS.

Endovenous treatment of BK refluxing segments of GSV was investigated in a 2018 retrospective review of 37 limbs utilizing RFA and EVLA[215]. Complete closures were found in 35/37 limbs and VCSS was reduced in both groups. Ecchymosis scores were significantly lower after RFA vs EVLA with a 980 nm system, but no difference was reported when compared to a group where a 1,470 nm fiber was used. Gifford et al also reported good outcomes with few complications in a retrospective series of BK-GSV ablation mainly with EVLA (77 limbs) with only about half of the cohort including patients with C1-3 classification and concomitant ambulatory phlebectomies being performed in 75% of cases[151].

Catheter-directed foam sclerotherapy has also been investigated as a treatment modality for recurrent GSV reflux in a small prospective analysis of 21 patients in Brazil with mostly C2 disease[216]. Foam sclerotherapy was performed as a pull-back procedure developed by Parsi with either 3% sodium tetradecyl sulfate or polidocanol 3%, using ultrasound guided tumescent anesthesia. Closure rate was 100% up to six months and 86% at one year. There were no complications.

Bradbury et al studied 1252 legs with C2-C6 disease[217]. They were treated with ultrasound-guided foam sclerotherapy (UGFS). There were 868 C2 and C3 patients. The authors found that out of 1031 patients with initially treated for great saphenous vein reflux, only 11.8% required a second UGFS for recurrent reflux. Of the 139 patients with AAGSV reflux, 10.1% required a second UGFS for recurrent reflux. Of the 239 patients with SSV reflux, 10.5% required retreatment for axial vein reflux. New reflux rates found in follow up included 3.4% GSV, 6.5% AASV, and 3.4% SSV.

Hernando et al, treated 21 patients 16 with C2 disease, for recurrent symptomatic varicose veins.[216] Previous interventions included CHIVA, mechanochemical ablation, thermal ablation, and cyanoacrylate closure. The patients were treated with catheter directed foam for the refluxing axial veins, and phlebectomy for the varicose tributaries. Catheter-directed sclerotherapy was performed in 18 GSVs. Closure at 1 week and at 6 months was 100%, and at1 year it was 86%.

Turtulici et al studied 37 patients with recurrent varicose veins.[218] Ten patients had reflux in the SFJ, 21 had single or multiple recanalized and refluxing perforator veins, and 6 had a combination of SFJ reflux and perforator vein reflux. All patients were treated with RFA. Recanalized axial veins were found in 4%, but no retreatment was required. The vein diameters were small and the Aberdeen Varicose Vein Severity scores of the limbs decreased. [219].

9.1.3. For patients with symptomatic recurrent varicosities due to persistent or recurrent reflux at the groin, either EVLA or RFA can be used if there is a straight GSV stump and long enough segment for thermal ablation. **. Sclerotherapy or phlebectomy should be performed for recurrence due to neovascularization.**

CONSENSUS STATEMENT

Rationale. Groin recurrence can be due to recanalized or enlarged remnants of the GSV or tributaries due to neovascularization or disease progression from other vein segments.

Evidence. The Edinburgh group[220] has classified recurrence into the following subtypes: residual GSV (Type 1A), residual tributaries that have enlarged (1B), or neovascularization (1C). The disease from new segments, Type 2 is subdivided into cross-groin connections (2A) and thigh perforators (2B). Recurrent veins are often difficult to classify [221] and difficult to treat and there is no preferred mode of treatment. Options include surgical removal, sclerotherapy, and thermal ablation. All modalities have their challenges, including easy tearing and bleeding in the presence of scarring from previous procedures. Ultrasound guided foam sclerotherapy is used

with increasing frequency.[222] EVLA can be performed if there is a straight stump but it can also be challenging in patients with tortuous or short GSV stumps.

9.1.4. For patients with symptomatic recurrent varicosity due to persistent or recurrent reflux of the SSV, ultrasound-guided foam sclerotherapy should be performed.

CONSENSUS STATEMENT

Rationale and Evidence. SSV recurrence is rare but can occur following incomplete obliteration distal to the SPJ and in patients with persisting reflux in tributaries associated with the saphenous stump. Recurrence can also occur if there is neovascularization that reconnects the popliteal vein to the superficial network or if there are other sources of proximal reflux connecting to the SSV, not treated initially. Currently ultrasound-guided foam sclerotherapy appears to be the preferred treatment[222].

Table. 20. Treatment of patients with recurrent and residual axial reflux of superficial truncal veins.

Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Theivacumar, 2009[153]	64 patients	EVLA in AK GSV	none	Persistent BK reflux of the GSV was associated with residual symptomatology	Prospective
Sussman, 2022[33]	15 studies 1368 patients	Ablative/surgical GSV interventions	none	BK reflux recurrence shown to be lower in AK+BK-EVLA over AK-EVLA or AK-HLS	Systematic review
Hwang, 2018[215]	37 limbs	BK-GSV RFA or BK-GSV EVLA plus minus stripping	none	94.6 % closure at 12 months	Retrospective
Gifford, 2014[151]	14 limbs	BK-GSV RFA BK-GSV EVLA	none	No residual or recurrent disease following repeat ablation	Retrospective
Hernando, 2022[216]	21 patients	Catheter directed	none	100% closure up to 6 months,	Prospective

		sclerotherapy and phlebectomy		86% closure at 1 year	
Bradbury, 2010[217]	Primary disease: 977 (868 C2/3 disease) patients, 1252 limbs Recurrent disease: 372 patients GSV (n=286) SSV (n=50) AASV (n=46)	Foam sclerotherapy	none	No significant difference in retreatment rates between UGFS for GSV and SSV reflux or between UGFS for primary or recurrent disease	Prospective
Turtulici[223], 2017	37 patients with recurrent disease	RFA	none	SFJ and perforator treatment failure at one year was 17% and 23%	Prospective
Theivacumar, 2008[219]	27 patients with recanalization, 3 patients with repeated EVLA	EVLA	none	Successful EVLA causes GSV shrinkage. remains small with minimal reflux and persisting clinical benefit	Prospective

10.1.5. For patients with residual or recurrent varicosity due to incompetent perforator veins, treatment with both open and endovascular techniques may be used depending on the physician experience, who is specialized in vein care, patient choice and availability of technology.

CONSENSUS STATEMENT

Rationale. There are no high-level data to compare outcome of different techniques to treat IPVs responsible for recurrent/persistent varicose veins. One should rely on experience, patient wishes, and the availability of the various techniques reviewed above.

Evidence. A 2016 prospective trial with 296 IPV closures on 112 patients compared three methods of IPV closure (RFA, EVLA and FS) in mostly C5-6 patients[224]. Closure success was significantly better with RFA (73% P= .05) versus FS (57%) but failed to reach significance vs EVLA (61% P = .09). Interestingly, when patients failed FS and were subsequently treated with thermal ablation, RFA success improved to 89% (P = .003) and EVLA success improved to 85% (P = .03). The authors concluded that RFA was found to be the most reliable means of IPV closure. After failed FS attempts, IPV closure was enhanced when thermal ablation was used as a secondary technique. A common factor leading to increased failure in all groups was morbid obesity. Although C2-6 patients were enrolled in this study, only 3 with C2 disease were included and all three were treated with foam initially, thereby significantly limiting the applicability of the findings to C2 disease. More recently, a technique for cyanoacrylate closure of perforating veins has been described in a retrospective series of 83 patients with C2-6 disease (27% C2 patients) showing a success rate of 86.5% at 72 days with complications of mainly superficial phlebitis in about 16% of treated veins recorded within 4 weeks[225]. For further evidence on efficacy of IPV ablation, see Guideline 10.

10. ABLATION OF INCOMPETENT PERFORATING VEINS

10.1.1. For patients with varicose veins (CEAP class C2) who have significant, symptomatic axial reflux of the GSV or SSV, we recommend against treatment of

incompetent perforating veins concomitant with initial ablation of the saphenous veins.

GUIDELINE: Grade of recommendation: 1 (strong), Quality of Evidence: C (low to very low)

10.1.2. For patients with varicose veins (CEAP class C2) who have significant, symptomatic axial reflux of the AAGSV or PAGSV, we suggest against treatment of incompetent perforating veins concomitant with initial ablation of the superficial truncal veins.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

For Rationale and Evidence supporting Guidelines 10.1.1.and 10.1.2, please see Part I. of the varicose vein guidelines.[8]

10.2. For patients with symptomatic residual or recurrent varicose veins due to incompetent perforator veins, either open or endovascular techniques can be used to treat the perforator veins.

CONSENSUS STATEMENT.

Rationale. Since incompetent perforating veins (IPVs) are potential sources of recurrence, occlusion of relevant IPVs is indicated in C2 patients who have symptomatic recurrent or residual varicose veins after previous superficial truncal ablation and tributary treatment.

Evidence. Various techniques have been used to treatment of IPV, from the Linton procedure to SEPS and to less invasive techniques of ligation through mini phlebectomy and endovenous procedures.[226] The Linton and the SEPS procedures today are of historic interest only, but SEPS

was useful to gain insight into the efficacy of occlusion of IPVs.[227] In an RCT by Kianifard et al [228] 72 patients with C2 disease were treated with HL&S ± phlebectomy, 38 also underwent the SEPS procedure. At 1 year, no additional clinical benefit could be observed, when SEPS was added to HL&S. It should therefore be emphasized that SEPS or any other technique for perforator treatment concomitant with initial superficial axial reflux treatment in C2 disease is not recommended.[8]

For treatment of recurrent or residual veins due to IPVs, several techniques of IPV occlusion were reported. Park et al used EVLA to occlude the saphenous vein that had retrograde flow from an IPV of the thigh in 69 patients. [229] This RCT concluded that direct IPV treatment was not justified since the technical success of the perforator ablation was significantly lower than just closure of the GSV (76.5% vs 100%). The outcomes were not different for either clinical success or complications between the 2 groups (one with direct IPV treatment, one without). Foam sclerotherapy (FS) for IPVs has also been analyzed in conjunction with GSV ablation in a prospective trial[230]; at 6 months it showed a closure rate of 75% for IPVs vs a 98% closure of GSV. A prospective trial on 296 IPV closures in 112 patients compared three methods (RFA, EVLA and FS); most patients had C5-6 disease. [224] Closure success was significantly better with RFA (73% P= .05) versus FS (57%) but failed to reach significance vs EVLA (61% P = .09). More recently, a technique for cyanoacrylate closure of perforating veins was described in a retrospective series of 83 patients with C2-6 disease (27% C2 patients). IPV closure rates were excellent, 96 % at 16 days and 86% at 72 days. There were no DVTs, but one patient needed antibiotic treatment for septic thrombophlebitis.[225]

In summary, there is little to no randomized data for the perforator treatment of choice for patients with recurrent/persistent C2 disease, with an associated IPV. When treatment of an IPV

in a C2 patient is desired, one should rely on experience, patient wishes, and the availability of the various techniques reviewed above.

Table. 21. Technique and outcome of perforator ablation in recurrent C2 disease

Author, Year	Patients/ Limbs	Intervention	Comparison	Outcome	Study design
Kianifard, 2007[228]	72 patients	38 patients had standard surgery + SEPS (71% C2 disease)	32 patients with standard surgery (75% C2 disease)	Reduction in 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
Park, 2012[229]	69 patients (C2, C3) without SFJ reflux but with IPV reflux into GSV	EVLA of IPVs in the thigh followed by ablation of the GSV below the IPV (n=34)	EVLA of the GSV starting just proximal to the thigh IPV without ablation of the IPV itself (n=35)	Technical success was significantly lower with IPV ablation (76.5%) compared to GSV ablation alone (100%) [p = .002]. No significant difference in closure of treated vein. No significant difference in occurrence and degree of complications between the groups.	Randomized control trial
van Neer, 2006,[231]	62 limbs with C2	HL/S of the GSV to knee	none	No difference in 6-month outcome based on preoperative IPV presence.	
Koroglu, 2011[232]	60 limbs in 55 patients	EVLA + foam sclerotherapy (FS)	EVLA of venous varicosities + FS of IPV	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 ($p<0.05$)	

11. MANAGEMENT OF ABLATION RELATED THROMBUS EXTENSION (ARTE) AND DEEP VEIN THROMBOSIS (DVT) AFTER ENDOVENOUS ABLATIONS

11.1. Post-procedure DUS

11.1.1. In an average-risk patient who is asymptomatic after thermal ablation of the saphenous vein, we recommend against routine early post-procedural DUS for ablation-related thrombus extension (ARTE), formally known as Endovenous Heat Induced Thrombosis (EHIT) **or deep vein thrombosis (DVT).**

GUIDELINE. Grade of recommendation 1 (strong), Quality of Evidence B (moderate)

11.1.2. In an average-risk patient, who is asymptomatic following non-thermal ablation of the saphenous vein, routine early post-procedural DUS may be performed to detect ablation-related thrombus extension (ARTE).

CONSENSUS STATEMENT

11.1.3. In a high-risk patientwho is asymptomatic after thermal or non-thermal saphenous ablation, early DUS to exclude ablation-related thrombus extension (ARTE) or DVT should be performed.

CONSENSUS STATEMENT

11.1.4. In symptomatic patients who have undergone either thermal or non-thermal ablation, we recommend early DUS to exclude ablation-related thrombus extension (ARTE) or DVT.

GUIDELINE. Grade of recommendation 1 (strong), Quality of Evidence A (high)

Rationale. Based on early reports of a high incidence of thrombus extension at the SFJ[233] (endothermal heat induced thrombosis – EHIT) following thermal ablation of the GSV as well as ready access to ultrasound in most venous clinics, screening for EHIT and deep venous thrombosis (DVT) with early DUS has become a common practice. EHIT is commonly classified as thrombus extension to the saphenofemoral or SPJ (I), involvement of < 50% of the deep venous lumen (II), involvement of > 50% of the deep venous lumen (III), or occlusive deep venous thrombosis (IV). [234] As technology has evolved over the last two decades, it has become clear that junctional thrombus extension can occur after non-thermal as well as thermal ablation. Accordingly, we suggest that the term "endovenous heat-induced thrombosis (EHIT)" be replaced by "ablation-related thrombus extension (ARTE)". To ensure consistency with previous reports, this should probably be classified similar to EHIT (I – IV), although it must be acknowledged that the clinical relevance of ARTE I and likely even ARTE II is minimal. In the following discussion, the preferred terminology "ARTE" will be used whenever possible, although the term "EHIT" will still be used for studies specifically reporting this as an outcome.

Previous guidelines from the American Venous Forum (AVF) and Society for Vascular Surgery (SVS) have suggested that venous DUS be performed within 1 week of the index procedure as an ungraded best practice recommendation. [234] The European Society for Vascular Surgery (ESVS) has similarly considered ultrasound surveillance after treatment of a saphenous

trunk as a consensus recommendation. [59] However, despite this guidance, most evidence suggests that the incidence of thromboembolic complications after saphenous ablation is low, with the combined incidence of ARTE, DVT, and pulmonary embolism (PE) being 1.3 – 1.7%. [235] [236, 237] Given this low incidence, the potential magnitude of effect of any intervention such as routine ultrasound surveillance after venous ablation would be classified as "Trivial" to "Small" (fewer than 5 events per 1000 subjects to 5 – 20 events per 1000 people) according to criteria developed by a CHEST expert panel. [238] No trials randomizing patients to early ultrasound screening versus observation have been performed, and are unlikely to be done, given the large number of patients such a trial would require achieving adequate power in the setting of this low event rate. Assuming a pooled incidence of all venous thromboembolic (VTE) events of 1.5%, a randomized clinical trial evaluating the ability of screening DUS to reduce the incidence to 1% would require approximately 15,500 patients. [239] Furthermore, routine ultrasound screening is not recommended even in populations at higher risk for venous thromboembolism, including critically ill patients with coronavirus 2019 (COVID-19 – ungraded consensus recommendation)[240]; those undergoing orthopedic surgery (Grade 1B against)[241], non-orthopedic surgery(Grade 2C against)[242]; and major trauma patients(Grade 2C against).[242] Based on the low incidence of thromboembolic complications in asymptomatic patients, the high cost of routine DUS, the futility of performing randomized trials evaluating the utility of routine DUS, and recommendations against screening in other higher-risk populations, in average risk patients we recommend against routine ultrasound surveillance following thermal ablation of the saphenous vein. . Although evidence in randomized trials of routine ultrasound screening is lacking, the strength of our recommendation is 1 (strong) against screening, given the futility of performing such studies.

Evidence. A systematic review of 39 randomized controlled trials and 33 observational studies (31,663 patients in total) undergoing routine DUS within 4 weeks of thermal or non-thermal ablation of the GSV, SSV, or accessory veins, found a very low incidence of EHIT (2.9%), DVT (0.26%), and PE (0.03%). [235] Most EHITs were Types I-II, with the incidence of EHIT III – IV being only 0.5%. Thrombus extension after non-thermal ablation was not studied in this review. The pooled incidence of any VTE event (EHIT II – IV, DVT, and PE) was 1.32% (95% CI 0.75 – 2.02%) with significant heterogeneity. The cost of routine ultrasound screening was estimated to be $61,292 per EHIT III-IV or DVT prevented.

A second, large systematic review (52 studies, 16,398 patients) evaluated only observational studies or randomized trials including patients undergoing thermal ablation of the GSV and having ultrasound surveillance within 1 month of the procedure. [236] The pooled incidence of EHIT II - IV or DVT was 1.7% (95% CI .9 – 2.7%), for EHIT II - IV 1.4 % (0.8 – 2.3%), for DVT 0.3% (0.2 – 0.5%), and for PE 0.1% (0.1 - .02%). Significant heterogeneity was noted for EHIT II - IV + PE and EHIT II - IV, but not for DVT or PE.

A third systematic review including 75 studies (23,265 patients) included both RCTs and case series and found very similar incidences of EHIT II – IV (1.27%, 96% CI 0.74 – 1.93%), DVT (0.28%, 0.18 – 0.4%), and PE (0.11%, 0.06 – 0.18%). [237] Other systematic reviews have found the majority of DVTs to be confined to the calf veins, with the incidence of proximal DVT varying between 0% and 0.4%. [243] None of these reviews studied thrombus extension after non-thermal ablations.

Although randomized trials evaluating screening DUS versus no ultrasound in asymptomatic patients after saphenous ablation have not been done, two such trials have been performed in

orthopedic patients. [241] These trials failed to demonstrate a benefit to routine post-operative screening, although major bleeding rates were higher in the screening arms.

In one of the systematic reviews,[235] non-thermal techniques were associated with a higher incidence of DVT than thermal techniques (0.43 versus 0.23%, p = .02), although this difference was due to a higher incidence of DVT in patients undergoing sclerotherapy. Although total VTE events were higher among patients undergoing RFA in comparison to endovenous laser ablation (EVLA) (3.1% versus 2.2%, p < .001), EHIT was higher in patients undergoing EVLA than after RFA(4.4% versus 3.0%, p < .001). However, a second large meta-analysis found the incidence of thrombotic events to be similar for both, RFA and EVLA. [236]

Although some data suggests that the incidence of thromboembolic complications has decreased since 2009[244], older meta-analyses[245] have demonstrated a similarly low incidence of thromboembolic complication after thermal ablation or foam sclerotherapy of the GSV. Among studies evaluating the incidence of thromboembolic complications after thermal ablation (12 randomized controlled trials, 19 case series) or foam sclerotherapy (12 randomized controlled trials, 6 case series), the individual incidence of EHIT, DVT, and PE was less than 1% for all treatment modalities (RFA, EVLA, UGFS). Differences between treatment modalities were judged not to be clinically meaningful.

While thrombotic complications after isolated endovenous ablation are uncommon, the incidence in patients undergoing open procedures such as high ligation and stripping and/or phlebectomy may be as high as 6.25% [39, 246]. Phlebectomy of tributaries concomitant with saphenous ablation has been identified as an independent risk factor for VTE development [244]. These patients may not identify VTE symptoms due to pain and swelling associated with

phlebectomy and many VTE are asymptomatic [246]. Thus, the role, or lack thereof, of surveillance DUS in this patient population remains to be defined.

While we recommend against routine ultrasound screening in asymptomatic, average-risk patients, clinicians should have a low threshold for obtaining such studies in patients with post-operative symptoms suggestive of DVT and should also consider such studies in selected high-risk patients. The recommendation for DUS in patients with post-procedure symptoms suggestive of DVT (1A) is based on a meta-analysis performed by the American Society of Hematology in support of their guidelines for evaluation of patients with a high pre-test probability of DVT. [247] As discussed below (guideline 11.2.1.), consistently defining the risk factors constituting a "high-risk" patient is more difficult and requires clinical judgement. With respect to ablation technique, some randomized trials[248, 249]and meta-analyses have suggested a higher thrombotic risk with foam sclerotherapy, although such reports are not consistent across studies[245]. The clinical relevance of these ultrasound-detected events in asymptomatic patients is unclear and requires further study. Data from at least one RCT of polidocanol endovenous microfoam demonstrated no difference in outcome among patients with ultrasound-detected post-procedural thrombotic events regardless of whether they were treated with anticoagulants or not. [248] More studies are needed to define the main risk factors for thrombotic complications, but increased risk of EHIT was reported by Hicks et al[250] in patients who underwent simultaneous RFA and phlebectomy, (odds ratio, 3.46; 95% confidence interval, 1.36-10.8) and in those who had a history of VTE (odds ratio, 3.48; 95% confidence interval, 1.22-9.25) (P = .02). In a Vascular Quality Initiative (VQI) study of 4881 patients who underwent thermal ablation of superficial truncal veins, those

with deep vein reflux had significantly higher rate of proximal thrombus extension (3.1% vs. 1.1%; P<.001). Age and large GSV diameter,[251] a higher Caprini score and male gender [252] were also found to increase the risk of EHIT in some studies, although others failed to confirm these associations.[253, 254]

Table 22. Venous thromboembolism (VTE) after endovenous ablations

First author, year	Patient	Intervention/ exposure	Comparison	Outcomes	Study design	Possible explanations of heterogeneity (factors to be used to stratify analysis)
Suarez, L.B. (2022) [235]	Patients undergoing thermal or non-thermal ablation of the GSV, SSV, or accessory veins	-	-	Pooled incidence of EHIT I-IV, EHIT II-IV, and DVT. Pooled incidence of EHIT II-IV, DVT, and PE together.	Systematic review of observational studies and RCTs with at least 150 patients.	Timing of DUS after ablation
Healy, D.A. (2108) [236]	Patients undergoing thermal ablation of the GSV	-	-	1. EHIT II – IV + DVT 2. EHIT II – IV, DVT, and PE	Systematic review of observational studies and RCTs with at least 100 patients	Timing of DUS after ablation
Healy, DA (2021)[237]	Patients undergoing thermal ablation of the GSV with DUS within 30 days	-	-	1. EHIT I – IV 2. DVT 3.PE 4. EHIT II – IV + PE	Systematic review of RCTs (17) and case series (58) with at least 100 patients	Timing of DUS after ablation Variable thromboprophylaxis

11.2. Pharmacological thromboprophylaxis

11.2.1. For high-risk patients undergoing endovenous ablation, we suggest pharmacological thromboprophylaxis.

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

Rationale. This guideline is consistent with that previously suggested by the AVF / SVS. [234] Other guidelines include those from the UK Royal Society of Medicine which suggest pre-operative assessment of all patients for both VTE and bleeding risk with pharmacological prophylaxis for 7 – 14 days in intermediate-risk patients and for 4 – 6 weeks in high-risk patients. [255] The European Society for Vascular Surgery recommends VTE risk assessment in all patients with consideration of individualized thromboprophylaxis (Class IIa, Level B). [59]

Although the weight of the evidence does suggest some benefit to pharmacological thromboprophylaxis, the evidence is difficult to generalize due to the limited magnitude of effect among those systematic reviews reporting a benefit of routine thromboprophylaxis (number needed to treat 25.4 – 172.4 for the prevention of DVT), lack of risk stratification in most studies, and significant heterogeneity in the results. In addition to the uncertain value of routine thromboprophylaxis, there is little data regarding optimal agents, dose, or duration of thromboprophylaxis if used. We therefore suggest pharmacoprophylaxis in high-risk patients, but with a low certainty of evidence.

Evidence. Despite the very low incidence of thromboembolic events among patients undergoing endovenous ablation, one large systematic review did find a significantly lower incidence of EHIT among those receiving pharmacological prophylaxis (1.63 % versus 3.04 %, $p < .001$).[235] However, this was not a uniform finding across individual studies and there was heterogeneity in the prophylactic regimes used. Another systematic review included 8 studies (3 randomized controlled trials, 5 cohort studies, 6479 patients) comparing pharmacoprophylaxis to no

prophylaxis following a variety of varicose vein procedures. [243] Five studies evaluated prophylaxis after open surgery and 3 after EVLA. The risk of DVT was lower for endovenous procedures than for open surgery. Prophylaxis was associated with a non-significant reduction in the composite risk of DVT, PE, and superficial venous thrombosis (pooled risk ratio – 0.63, 95% CI 0.04 – 10.43, p = .74) and of DVT alone (pooled risk ratio 0.59, 0.08 – 4.60, p = .61). There was significant heterogeneity in both results. Notably, confining the analysis to randomized trials did show a significant reduction in the risk of DVT (0.22 versus 4.15%: risk ratio = 0.05, 95% CI 0.02 – 0.13, p < .00001). Among the 2 studies reporting bleeding risk, there was no difference among those receiving or not receiving prophylaxis. Although a few included studies evaluated the efficacy of fondaparinux and rivaroxaban as well as short versus extended courses of prophylaxis, conclusions based on the available data are difficult.

A second broader meta-analysis included 47 randomized trials, 105 prospective cohort studies, 67 retrospective cohort studies, and 2 case control studies including a total of 476, 266 patients undergoing a variety of superficial endovenous interventions with exclusion of open venous surgery. [32] Notably, most studies excluded patients with a history of DVT. Although significant heterogeneity precluded analysis of all study arms, among prospective studies additional pharmacological prophylaxis reduced the incidence of DVT to 0.73% (95% CI 0.52 – 1.02%) from 1.31% (1.15 – 1.48%) for mechanical prophylaxis alone (compression stockings / bandages). No significant difference was noted between single-dose and extended pharmacoprophylaxis[i]. LMWH, as a single dose and/or as an extended dose with 3 to 14 days of prophylaxis was used most often. Other drugs for 3 to 14 days prophylaxis included Vitamin K antagonists or direct oral anticoagulants (DOACs). There were no significant differences in PE (0.14%, 0.07 – 0.28% versus 0.16%, 0.15 – 0.18%) or EHIT III – IV (0.35%, 0.09 – 1.40%

versus 0.88%, 0.28 – 2.70%) in comparing pharmacoprophylaxis to mechanical prophylaxis alone. Major bleeding was quite rare (1 case) while minor bleeding was observed in 0 – 10% of patients. Risk of bias was estimated to be high, and the quality of evidence was moderate among randomized trials and very low among non-randomized trials.

A systematic review included in the AVF / SVS EHIT guidelines, which included only retrospective observational studies, failed to show a lower incidence of EHIT with pharmacological thromboprophylaxis. [234]

Table 23. Pharmacologic thrombosis prophylaxis

First author, year	Patient	Intervention/ exposure	Comparison	Outcomes	Study design	Possible explanations of heterogeneity (factors to be used to stratify analysis)
Turner (2022)[32]	Patients with superficial reflux undergoing endovenous intervention (open surgery excluded)	Mechanical + Pharmacoprophylaxis (single dose – 12 studies, extended – 29 studies, combination – 2 studies)	Mechanical prophylaxis (compression stockings or bandages)	DVT (randomized trials) EHIT III-IV PE Major / minor bleeding	Systematic Review and Meta-analysis	Failure to distinguish EHIT from DVT in some studies Confounding by indication (observational studies) Poor reporting of mechanical (compression) prophylaxis Differences in anticoagulation regimens (agents, dose, duration)
Alameer (2022) [243]	Patients undergoing varicose vein intervention (open or endovenous)	Pharmacoprophylaxis	Compression	All Thrombotic Events DVT Bleeding	Systematic Review and Meta-analysis	Variable anticoagulation agents and duration Lack of risk stratification

11.2.2. For patients undergoing endovenous ablation routine risk stratification should be performed to assess the need for peri-procedural thromboprophylaxis.

CONSENSUS STATEMENT

Rationale and Evidence. The literature reflects great uncertainty regarding the value of risk assessment in determining the need for thromboprophylaxis in patients undergoing superficial venous interventions. [32] Defining the risk factors for DVT / EHIT after saphenous ablation is unfortunately difficult due to the very low number of events and limited statistical power. Although inconsistent across studies, suggested risk factors for EHIT / DVT have included age, male gender, CEAP class, personal or family history of VTE, known thrombophilia, reduced mobility, obesity, hormone therapy, active cancer, concomitant procedures including sclerotherapy and mini-phlebectomy, large GSV diameter, and a history of SVT. [234, 243, 244, 252, 255] Given such uncertainty, deciding who constitutes a high-risk patient requires some degree of clinical judgement at present. Although one single-center study has shown the Caprini risk assessment score to be associated with the development of EHIT (odds ratio 1.58, 95% CI 1.24 – 2.0, p = .0002), only ultrasound identified EHIT I – II were found in this study and it remains unclear whether the Caprini score is predictive of clinically relevant thrombotic events after superficial venous intervention. [252]

Currently, no specific guidelines address the role of VTE risk stratification in the ambulatory surgery setting. Data from patients undergoing both inpatient and outpatient procedures suggests that identification of patient and procedural related risk factors allows for identification of 15-20-fold variation in VTE risk. Individualized risk stratification allows for the identification of low-risk patients in whom the risk-benefit ratio is unfavorable, and potentially for the identification of patients at high VTE risk in whom the benefit of receiving chemical chemoprophylaxis outweighs the attendant bleeding risk. A widely accepted risk threshold is a calculated VTE risk of 3%, assuming a 2-fold reduction in VTE events compared to expected bleeding events from administration of an anticoagulant [242]. Currently, no VTE risk assessment model (RAM) has been validated in patients undergoing varicose vein procedures.

Indirect evidence suggests that risk stratifying patients undergoing varicose vein procedures may have potential benefits. Namely, amongst patients undergoing a variety of ambulatory surgical procedures, those undergoing procedures for varicose vein procedures are at the highest risk for development of VTE [256]. Secondly, variations in VTE rate amongst patients undergoing venous procedures have been identified according to patient and procedure related characteristics. For instance, patients undergoing open surgery or longer operations are at greater risk at developing VTE [257]. Third, limited evidence suggests that those with a higher composite VTE risk assessment model (RAM) score, such as that used in the Caprini RAM, have an increased VTE and ARTE risk [258]. Finally, a recent meta-analysis suggested that in patients undergoing inpatient and outpatient surgical procedures (including those undergoing venous procedures) with a Caprini score of ≥ 7 benefited from chemoprophylaxis in terms of VTE risk reduction without an increase in bleeding [259]. This data highlights the critical need to determine from a specific VTE RAM the threshold at which chemical thromboprophylaxis is favorable for the patient undergoing outpatient axial and/or tributary bed treatment. Future studies should likely focus on clinically relevant venous thromboembolic events (DVT, PE) and should include some measure of risk.

11.3. Treatment of **varicose vein procedure related** DVT and ARTE

In patients with DVT after endovenous ablation, we endorsed the recommendations of Stevens et al, Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. Chest. 2021;160(6): e545-e608. [260] The evidence base for these guidelines was adopted without review.

11.3.1. For patients with acute isolated distal DVT after varicose vein procedure, without symptoms **or risk factors for extension we suggest serial imaging of the deep veins for 2 weeks.**

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: B (moderate)

11.3.2. For patients with isolated distal DVT after varicose vein procedure, and symptoms **or risk factors for extension we suggest anticoagulation.**

GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low)

11.3.3. For patients with acute proximal DVT after varicose vein procedure we recommend anticoagulation with a direct oral anticoagulant (over a vitamin K antagonist)

GUIDELINE: Grade of recommendation: 1 (strong), Quality of Evidence: B (moderate)

11.3.4. For patients with symptomatic ARTE after endovenous ablation, we recommend anticoagulation with a direct oral anticoagulant (over a vitamin K antagonist)

GUIDELINE: Grade of recommendation: 1 (strong), Quality of Evidence: C (low to very low)

11.4.1. For patients with asymptomatic ARTE III and IV after endovenous ablation, anticoagulation with a direct oral anticoagulant (over a vitamin K antagonist) should be performed.

CONSENSUS STATEMENT

11.4.2. For patients who receive anticoagulation for ARTE following endovenous ablation, treatment should be continued until the thrombus retracts.

CONSENSUS STATEMENT

Rationale. As discussed above, routine screening of asymptomatic, average-risk patients for ARTE / DVT is not recommended and asymptomatic ARTE / DVT in these patients should rarely be diagnosed. The majority of ARTEs are ARTE I and II,[235]which is of minimal clinical relevance. Although previous guidelines[234] have recommended either no treatment (EHIT I), weekly surveillance (EHIT II), or consideration of antiplatelet versus anticoagulant therapy (high-risk patients with EHIT II), these should be rarely encountered in the absence of routine ultrasound surveillance. When ARTE I or II are identified, we suggest no treatment or follow-up for ARTE I and weekly surveillance until resolution of the thrombus with ARTE II.

ARTE III and IV are presumably more likely to be symptomatic and to be suspected based on accepted clinical indications. Although it is not entirely clear that the natural history of ARTE III – IV is the same as DVT[234], a conservative approach would suggest treatment similar to established guidelines for DVT treatment[260]. However, as the natural history of ARTE is not well documented, the value of alternative approaches such as anticoagulation until thrombus resolution as observed by ultrasound cannot be entirely excluded. Given the uncertain benefit, treatment of symptomatic ARTE according to established guidelines for acute DVT is a weak suggestion. Furthermore, as this evidence is extrapolated from current guidelines for the management of DVT and is therefore indirect, for the management of ARTE the level of evidence has been downgraded to C.

Further research is needed regarding the natural history of ARTE. More data is particularly needed regarding the value of anticoagulation versus serial follow-up and the duration of anticoagulation in treated patients. Given the uncertainty of the evidence, at present, duration of anticoagulation should be at the judgment of the clinician.

Evidence. The management of symptomatic DVT is generally guided by the CHEST guidelines for Antithrombotic Therapy for VTE Disease [260] and the reader is referred to that manuscript for the supporting evidence.

Unfortunately, the data regarding the management of ARTE is substantially less robust. The evidence regarding the treatment of ultrasound detected (most presumably asymptomatic) ARTE is derived from small case series and retrospective studies and is accordingly quite variable. One systematic review evaluated the management of ARTE detected by routine ultrasound screening in 24 studies for which the treatment was described. [237] Among the 25 included studies, anticoagulation was the most common treatment for EHIT, with 2 studies reporting selective use of antiplatelet therapy and 7 studies reporting observation only. Irrespective of treatment, there were no reports of propagation or embolization of EHIT II – IV once identified. The authors concluded that the natural history of EHIT is generally benign.

Table 24. Evidence for treatment of EHIT

First author, year	**Patient**	**Intervention/ exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Healy, D.A. 2021[236]	Patients developing EHIT II-IV after thermal ablation of the GSVGSV ablation	-	-	1. EHIT treatment modality 2. EHIT propagation or embolization	Systematic review (24 studies)	Lack of standardized treatment for EHIT

12. MANAGEMENT OF SUPERFICIAL VEIN THROMBOSIS (SVT) IN PATIENTS WITH VARICOSE AND NON-VARICOSE VEINS

Guidelines 12. address the management of SVT in patients who have not recently undergone superficial venous interventions. The management of EHIT and other thrombotic complications of superficial venous interventions were presented in Guidelines 11.

12.1.1. For patients with SVT of the main saphenous trunks and tributaries above the knee > 3cm from the SFJ and ≥5 cm in length, whether or not associated with varicose veins, we recommend fondaparinux 2.5mg subcutaneously daily for 45 days; alternatively, rivaroxaban 10 mg daily for 45 days may be appropriate for patients unwilling or unable to perform subcutaneous injections.

GUIDELINE. Grade of recommendation: 1 (strong), Quality of Evidence: A (high)

12.1.2. For patients with SVT of the main saphenous trunks≤ 3 cm from the SFJ, treatment with full anticoagulation for a minimum of 6 weeks should be continued.

CONSENSUS STATEMENT

12.1.3. For patients with SVT of the main saphenous trunks we suggest against using prophylactic or therapeutic dose low-molecular weight heparin (LWMH) and non-steroid anti-inflammatory drugs (NSAIDs). While both have been found to reduce SVT pain and extension, they have failed to prevent VTE. If NSAIDs are used for treatment of short

segment distal SVT, surveillance with DUS for VTE extension is recommended due to the high prevalence of concomitant DVT.

GUIDELINE. Grade of recommendation: 1 (strong), Quality of Evidence: A (high)

12.1.4. For selected patients with isolated thrombosis of varicose tributaries or limited involvement of the GSV, we suggest phlebectomy as a safe alternative.

GUIDELINE. Grade of recommendation: 2 (weak), Quality of Evidence: B (moderate)

12.1.5. In patients with saphenous thrombophlebitis, ablation should be performed once the inflammation has resolved if there is evidence of pathologic reflux on DUS.

CONSENSUS STATEMENT

Rationale. Despite recognition that superficial thrombophlebitis, also known as superficial vein thrombosis (SVT), is more common than DVT, there is less awareness of its associated morbidity and little consensus on its management. [261] While traditionally thought of as benign, recent studies have highlighted its association with DVT and PE if left untreated. Studies show that SVT may progress to DVT in 6% to 44% of patients; 20% to 33% may have asymptomatic pulmonary embolism (PE); and 2% to 13% may have symptomatic PE. Superficial venous thrombosis involving the saphenous trunk has the greatest association with VTE. [34] Although the majority of SVT occurs in varicose veins, SVT in non-varicose veins confers greater morbidity and few studies have stratified treatment based on this distinction. [34] Several therapies including surgery, compression stockings, and non-steroidal anti-inflammatory drugs (NSAIDs) aim to reduce pain and inflammation, however, given the associated progression to VTE,

anticoagulation is recommended. Of note, the application of warm compresses to the site of SVT has never been evaluated in any study.

Evidence. These recommendations are supported by two recent systematic reviews. [34, 35] The 2018 Cochrane review included 33 studies involving 7296 patients with SVT of the legs. [34] Treatments evaluated included fondaparinux, rivaroxaban, low molecular weight heparin (LMWH), unfractionated heparin (UFH), non-steroidal anti-inflammatory drugs (NSAIDS), compression stockings, and topical, intramuscular, or intravenous treatment as well as surgical thrombectomy or ligation. A minority of studies compared treatment to placebo and most studies were small and of poor quality. Further, most studies excluded patients with SVT that was within 3 cm of the SFJ. The recommendations are primarily based on one large placebo controlled RCT of 3002 participants who received fondaparinux and demonstrated a significant reduction in symptomatic VTE, SVT extension, and SVT recurrence in comparison to placebo. Major bleeding was infrequent in both groups. A second systematic review and meta-analysis included seventeen studies and 6862 patients with SVT and confirmed that fondaparinux achieved the lowest rate of progression to DVT and PE without conclusions about other treatment due to low quality evidence. [35] In the Surprise study, patients with SVT and one or more risk factors for VTE were randomized to 45 days of fondaparinux or rivaroxaban 10 mg. [262]. The results suggested that rivaroxaban was as effective as fondaparinux, however, the study was not powered to prove non-inferiority. A call for further studies was prompted by the non-significant increase in the primary composite outcome as well as by an increase in clinically relevant non-major bleeding in the rivaroxaban group.

Low quality evidence in one study found that prophylactic LMWH reduced extension of SVT (statistically significant), but did not reduce symptomatic VTE, while therapeutic LMWH

evaluated in one study reduced both SVT extension (statistically significant) and VTE progression, but improvement was less significant at 3 month follow up due to a catch-up phenomenon that showed increased VTE similar to comparator group, after LMWH treatment was completed. [34] NSAIDS were also found in one study to reduce SVT extension (statistically significant). [263] However, there were no differences in the incidence of VTE or in the resolution of local symptoms and signs. While there were no major bleeding episodes recorded in either the NSAID or placebo groups, indomethacin increased the rate of adverse effects. [264] NSAIDs have also been found to increase the risk of gastric pain three-fold compared with placebo. [263, 264]

Compared with elastic stockings alone, one study showed that high ligation and stripping plus elastic stockings reduced the risk of SVT extension and recurrence (RR 0.09, 95% CI 0.01 to 0.64) and was associated with a lower, non-significant, incidence of VTE (RR 0.37, 95% CI 0.08 to 1.78). [265] However, most studies evaluating surgery and topical treatments did not report SVT progression, VTE or adverse events. [34]

A recent analysis from the RIETE registry of patients with thrombosis involving main trunk of the GSV within 3 cm of the SFJ compared those treated with full dose fondaparinux or LMWH followed by VKA (227 patients) to those (147 patients) who received preventative doses of fondaparinux or intermediate dose LMWH. [266] Those receiving full dose anticoagulation received a longer course of treatment and all patients were followed for 3 months. There was no difference in VTE or recurrent SVT between the groups or in the safety outcomes of major bleeding or clinically nonmajor bleeding. The authors concluded that these findings are hypothesis generating and support a trial evaluating the efficacy of preventative dose anticoagulation in comparison to therapeutic anticoagulation for treatment of SVT approaching the SFJ.

There is a paucity of studies specifically evaluating the management of SVT in patients with varicose veins. In a prospective observational study of 195 limbs with SVT and varicose veins treated with surgery or anticoagulation, there was no difference in the primary composite outcome of SVT extension/recurrence, DVT or symptomatic PE. [267] The authors concluded that urgent surgery is not associated with reduction in VTE compared to anticoagulation alone but could be safely performed in selected patients with isolated thrombosis of varicose tributaries or limited involvement of the saphenous trunk.

A single center randomized trial of 73 patients compared the use of thigh high 23-32 mmHg compression stockings to no compression stockings for 3 weeks in patients with isolated SVT of the legs who all received prophylactic dose LMWH with or without NSAIDS. [268] The addition of compression stockings resulted in no significant difference in reduction of pain, consumption of analgesics, thrombus length, skin erythema, D-dimer, or quality of life. However, patients wearing compression had significantly faster thrombus regression at 7 Days.

Historically, SVT was recognized as a disease with a 10-20% recurrence rate. One large case series of SVT patients described a recurrence rate of 15% amongst 221 patients [269]. In modern times with widespread application of anticoagulant therapies, the risk of recurrence or VTE is ~6%, with the highest risk occurring amongst patients with previous episodes of SVT and long segment thrombosis [270]. Although not addressed by a randomized control trial, best practice would include informing patient of the risk of recurrence and offering surgical or endovascular therapy for the treatment of symptomatic recanalized varices and axial reflux (if present in the recanalized saphenous vein after completion of evidence based antithrombotic therapy).

Table 25. Treatment of Superficial Venous Thrombosis

1st Author, Year	Patients /Limbs	Intervention	Comparison	Outcome	Study design
DiNisio 2018[34]	7296	Fondaparinux, rivaroxaban, LMWH, UFH, NSAIDS, compression, topical, IM, IM, surgical	Placebo (few)	SVT extension, VTE, pain, bleeding	RCTs for systematic review
Duffett 2019[35]	6862	NSAIDs, anticoagulant therapies, surgical therapies	Placebo, No therapy (few)	DVT, PE	RCT, cohort for Systematic review
Prandoni, 2022[266]	374	LMWH, fondaparinux, VKA, DOAC (Full anticoagulation)	Preventive anticoagulation	SVT extension, VTE, bleeding	Retrospective, registry
Casian, 2022[267]	190/ 195	Anticoagulation, surgery	None	SVT recurrence, extension, VTE	Prospective observational

13. MANAGEMENT OF BLEEDING VARICOSE VEINS

13.1. For patients with bleeding due to varicose veins, prompt referral to a venous specialist should be done.

CONSENSUS STATEMENT

13.2. For patients presenting with acute bleeding from varicose veins, direct compression and sclerotherapy should be attempted before suture ligation to control bleeding.

CONSENSUS STATEMENT

13.3. For patients who presented with bleeding from varicose veins, after the bleeding has been controlled, evaluation for superficial venous incompetence and appropriate intervention on the responsible veins should be done to control venous hypertension and reduce the risk of recurrent bleeding.

CONSENSUS STATEMENT

13.4. Patients with varicose veins or venous ulcerations should be counseled on the possibility of venous bleeding and their families, caregivers, or friends educated regarding simple compression techniques to control severe bleeding.

CONSENSUS STATEMENT

Rationale. The true incidence of bleeding from varicose veins is unknown due to under-reporting but appears to occur in approximately 4% of patients presenting with varicose veins. [271, 272] Bleeding often arises from small veins at the ankle with surrounding skin pigmentation and induration or following exacerbation of a venous ulcer leading to erosion of veins underlying the ulcer bed. [273] Patients may report bleeding when the varicosities are exposed to warm water (in the shower or bathing), causing the veins to vasodilate, or bleeding can occur because of minor trauma. Patients with right heart failure or cardiomyopathy may also experience intermittent, often heavy, bleeding from dilated veins. Regardless of the cause, when a varicose vein ruptures, profuse bleeding can occur due to associated venous hypertension.

Although most bleeding associated with varicose veins is not associated with hypotension and does not require transfusion[274], fatal hemorrhage is an uncommon, but not entirely rare event[273]. Most cases of fatal variceal hemorrhage have come from autopsy reports. A 2011 report documented less than 100 fatalities over several decades. [275] Twenty-three fatalities were

reported in England and Wales in 2001. [273]. A systematic review including 17 articles found that deaths secondary to bleeding varicose veins accounted for 0.01% of autopsy cases. [276] The victims were patients aged 60-90+ years of age with no gender discrimination. Deaths due to hemorrhage occurred in older persons who lived alone, were mobility impaired, had skin fragility or an ulcer located near the malleolus, were on anticoagulation or antiplatelet medication, or had a comorbidity such as dementia or liver failure. These rare case reports describe pulsatile bleeding both from the thin-wall veins themselves and from exposed veins in a venous ulcer bed leading to hypovolemic shock and death, especially in the presence of ischemic heart disease. [277] Another single-center study found that patients with bleeding episodes had decreased access to basic first aid or hemorrhage control techniques. [271]

As many of the fatal hemorrhagic events can be prevented, it is critical that patients be asked about prior bleeding episodes, be warned about the possibility, and be instructed in first aid and hemorrhage control techniques. The danger of applying venous tourniquets and increasing venous pressure has often been emphasized in the literature. [273]

Evidence. Both because of the infrequency of bleeding events and the difficulty in leaving such patients untreated, no studies comparing intervention to conservative management have been performed. However, very limited evidence does suggest that fatal hemorrhage usually occurs after a previous untreated episode of bleeding[273] and there is general consensus that patients should be treated after the first episode of hemorrhage[274, 278]. Furthermore, there is evidence from single-center series that superficial venous intervention results in a low incidence of recurrent hemorrhage. Selection of an appropriate treatment modality is somewhat dependent of the patient's venous anatomy and size of the bleeding vein. Among 5 patients reported in one series, acute control of venous hemorrhage was successfully achieved with direct injection of 1%

polidocanol foam into the bleeding varicosity with or without foam sclerotherapy (3% polidocanol) of the associated saphenous trunk. No recurrent bleeding was noted after a mean follow-up of 17.4 months. [279]. A larger series reported successful acute control of bleeding in 72 patients treated with foam sclerotherapy. [278] In comparison to 52 patients treated with simple suture ligation, foam sclerotherapy was associated with faster wound healing (7 versus 14 days, $p < .001$) and a lower risk of recurrent bleeding at 12 months (0% versus 23%, $p < .001$). Others have similarly reported excellent control of bleeding from smaller veins (< 1 mm) with sclerotherapy, while bleeding from larger veins was successfully controlled with high ligation, stripping, and phlebectomy. Recurrent bleeding was noted in only 1 of 14 patients (7%) after a mean follow-up of 21.3 months. [274] Venous ablation has been used more recently in patients with varicosities, with small series (n = 13) demonstrating 85% of patients to be free from recurrent bleeding at a mean follow-up of 2.26 years. [272]

Although the supportive evidence is quite limited, the literature does suggest that acute bleeding is optimally managed with sclerotherapy, while prevention of recurrence may warrant ablation of any truncal venous incompetence.

14. MANAGEMENT OF SUPERFICIAL VEIN ANEURYSMS

14.1. For patients with superficial truncal vein aneurysm, located within 3 cm of the SFJ or SPJ, open surgical excision, with high proximal and distal ligations should be performed. If symptomatic saphenous reflux is present, endovenous or open surgical ablation (phlebectomy or limited stripping) of the distal saphenous vein should be performed.

CONSENSUS STATEMENT

14.2. For patients with asymptomatic superficial truncal vein aneurysm, located >3 cm distal to the SFJ, endovenous ablation alone should be performed. Thrombo-prophylaxis in these patients reduces the risk of VTE.

CONSENSUS STATEMENT

14.3. Patients with symptomatic, thrombosed or large (> 3cm) aneurysms in the superficial veins should be treated with surgical excision.

CONSENSUS STATEMENT

Rationale. Focal dilation of the saphenous veins (GSV, SSV, AAGSV or PAGSV) that measures at least 20 mm for GSV and 15 mm for SSV, or has a diameter that is three times the upper limit of the average saphenous diameter is considered an aneurysm.[280] Most patients are asymptomatic or have a palpable lump at the groin or in the popliteal fossa.[281] Many patients present only with symptoms of varicosity or chronic venous insufficiency.[158, 282, 283] Patients occasionally complain of a tender lump,[284] that can be firm, if the aneurysm is thrombosed.[285] Evaluation with DUS is usually satisfactory to assess the aneurysm, but congenital superficial truncal vein aneurysms may occur in patients with venous malformations (Klippel-Trenaunay syndrome)[286] and saphenous aneurysms may occasionally mimic femoral hernias,[281] synovial[287, 288] or Baker cysts[289] or a venous leiomyosarcoma.[290] In these patients further evaluation with computed tomography or magnetic resonance imaging is warranted. When the saphenous aneurysm is near the femoral or popliteal vein, open surgical excision is indicated, with ligation or oversewing of a dilated proximal saphenous stump. In patients with associated symptomatic

saphenous reflux, endovenous ablation, tumescent anesthesia aided phlebectomy or limited stripping of the distal segment should also be performed. If the aneurysm is located > 3 cm distal to the SFJ or SPJ, permitting safe proximal occlusion with endovenous techniques, endovenous ablation alone is frequently possible and safe, although most large (>3cm) or symptomatic, thrombosed aneurysms are better treated with surgical excision at any location. There is also significant risk of sural nerve injury, when thermal ablation is used to treat a distal SSV aneurysm. Ablation of saphenous aneurysms within 3 cm. of the SFJ and SPJ should not be treated with UGFS due to the increased risk of propagation of larger amount of foam into the deep venous system.

Evidence. Similar to deep vein aneurysms,[291-293] there is evidence that saphenous vein aneurysms carry a risk of venous thromboembolism (VTE).[294-296] Treatment therefore is recommended to all aneurysms, whether or not there is thrombus in the aneurysm sac. Most reports describe open surgical excision of saphenous aneurysms, with proximal and distal ligation or distal saphenous ablation.[281, 284, 285, 294-297] In two smaller series of mostly small GSV aneurysms (< 3 cm in size), located close to the SFJ, endovenous ablation alone was used, without proximal high ligation.[158, 283]

Pavlović, et al[283] treated 11 limbs of 8 patients with RFA alone, without high ligation. All GSV aneurysms were located near the SFJ, distal to the preterminal valve. Median aneurysm diameter was 21 mm (IQR 17.2-23.4), all patients had incompetent GSV and chronic venous disease. The catheter tip was placed at 1 to 2cm from the SFJ, within the aneurysmal segment. Extra tumescent anesthetic and compression was used, and the first segment was treated with three cycles using RFA. Thromboprophylaxis was given for 7 days. At a median follow up of 8 years median saphenous diameter was reduced to 5.8 mm, the aneurysmal segment was either

completely or partly obliterated, and, if partly patent, always had an antegrade flow. One patient (9.1%) had EHIT III despite thrombosis prophylaxis.

In a prospective study, Hamann, et al[158] treated 15 limbs of 13 patients with GSV aneurysm, located within 2 cm of the SFJ. Four aneurysms were surgically excised, with proximal ligation, because they were located near the SFJ and had a diameter >3 cm. The other 11 were treated with endovenous ablation alone. A generous amount of tumescent anesthesia was used to diminish the aneurysm diameter as much as possible. Additional energy was applied in the aneurysmal segment, either 100 Joules/cm for EVLA or 3 energy cycles for RFA. No patient had DVT or thrombus extension into the femoral vein. At 1 year, none of the aneurysms were visible on DUS. Three patients needed retreatment for partial or segmental recanalization, with good result. Thromboprophylaxis was given to patients with a history of VTE or SVT.

Further experience with larger number of patients is needed to recommend endovenous ablation alone for treatment of large aneurysms or for those located <3 cm to the SFJ or SPJ. One of the main reasons for this needed study is that current North American guidelines suggest placement of the tip of thermal ablation catheters at least at 2 cm distal to the SFJ.[7]

15. FUTURE RESEARCH

The writing committee of the Varicose Veins Guidelines identified several gaps in our knowledge on the natural history, evaluation, prevention and treatment of patients with varicose veins. Table 26. includes the top 20 recommended topics on future research on varicose veins, in order of importance.

Table 26. Top 20 topics for future research on varicose veins

N.	Topic of Research
1.	Comparative studies of polidocanol endovenous micro-foam vs. physician compounded foam for treatment of varicose tributaries.
2.	Comparative studies of polidocanol endovenous micro-foam vs. other techniques of thermal and non-thermal ablations of incompetent superficial truncal veins.
3.	Best metric of axial reflux to determine ablation of superficial truncal veins: vein diameter, reflux time, reflux volume or combination of these metrics.
4.	Longitudinal studies to identify risk factors for progression of C2 to C4 disease.
5.	Comparative studies of thermal vs. non-thermal ablations.
6.	Studies to identify patients who need peri-procedural thrombosis prophylaxis and define optimal drugs (LMWH, DOACs), dose, and duration of prophylaxis.
7.	Cost and quality of life comparisons between staged vs. concomitant phlebectomy after saphenous ablation.
8.	Clinical trial to evaluate efficacy and cost effectiveness of 20-30 mmHg compression stockings vs. venous ablation as initial treatment of patients with C2 disease.
9.	Outcome of thermal vs non-thermal ablation of saphenous veins >10 mm in diameter.
10.	DOAC for treatment SVT of the GSV ≤ 3 cm from the saphenofemoral junction.
11.	Comparative studies of varicose vein treatment in patients with and without proximal deep vein occlusion.
12.	Best treatment option for varicose vein tributaries: mini-phlebectomies vs foam sclerotherapy
13.	Best treatment options for telangiectasia and reticular veins: foam vs liquid sclerotherapy vs surface laser.
14.	Comparative study of cyanoacrylate vs thermal closure of perforating veins.
15.	Appropriate training for treatment of varicose veins.
16.	Treatment of superficial thrombophlebitis affecting varicose veins.
17.	Adjuvant medical treatment of patients with C2 varicose veins.
18.	Long-term outcome after SSV and AAGSV ablations.
19.	Treatment of saphenous aneurysms < 3 cm in size ≤ 3 cm from the SFJ with thermal ablation vs open surgery.
20.	Management of intravenous line related thrombophlebitis: role of NSAIDS and warm compresses.

APPENDIX

1. VENOACTIVE DRUGS FOR CHRONIC VENOUS DISEASE

This section reviews briefly the scientific evidence supporting the clinical benefit of Hydroxyethylrutosides, Calcium dobesilate, Horse chestnut extract, Red vine leaf extract and Sulodexide for patients with varicose veins and CVD. None of these products are approved by the U.S. Food and Drug Administration for use in patients with venous disease.

Clinical benefit of Hydroxyethylrutosides

Rationale: Hydroxyethylrutosides (HR) are composed by one or several bioflavonoids obtained from hydroxyethylation of rutoside (a combination of flavonol quercetin and disaccharide rutinose). HR is a potent inhibitor of inflammation-related gene expression, and production of inflammatory cytokines (NO, TNF-alpha, IL-1, IL-6) in macrophages and neutrophils[104].

Evidence. A systematic review and meta-analysis of 15 trials with 1643 patients[17] evaluated the effect of HR, with or without compression bandaging vs. placebo, with or without compression bandaging, and HR vs. compression bandaging alone. Compared with placebo, a significant but modest reduction of pain, leg heaviness and cramps were reported. The trials were of limited quality.

Table 26. Clinical benefit of Hydroxyethylrutosides

First author, year	Patient	Intervention/exposure	Comparison	Outcomes	Study design	Possible explanations of heterogeneity (factors to be used to stratify analysis)
Aziz Z, 2015[17]	Adults with CVI including CEAP C2	Hydroxyethylrutosides (HR) with or without compression bandaging	Placebo with or without compression bandaging, compression	Pain, heavy legs, and cramps. Safety analysis. **Modest improvement in**	Systematic review and meta-analysis of 15 RCT.	Age, sex, different stages of CVD in patients with varicose veins

			bandaging alone in one RCT	**several symptoms of CVI (pain, heaviness, cramps)**		
Allaert FA, 2012[116]	Adults with lower extremity venous edema	Hydroxyethyl-rutosides, Ruscus extracts, MPFF, and diosmin	Placebo or other VAD	Reduction of ankle edema **Third best VAD for reduction of ankle circumference**	Systematic review and meta-analysis of 10 double-blind, randomized, placebo or other VAD-controlled trials	Age, sex, different stages of CVD in patients with varicose veins
Pompilio G, 2021[15]	Adults with Chronic Venous Disease	Hydroxyethyl rutosides, Ruscus extracts, MPFF, sulodexide, calcium-dobesilate, horse chestnut extracts and pentoxifylline	Placebo in 45 RCT	Ulcer healing, leg volume, ankle circumference, symptoms such as pain assessed by VAS, feeling of swelling, heaviness, as well as QoL (CIVIQ-20 score) **First top rank to be the better treatment for pain, cramps, swelling sensation and heaviness score measured by Likert scale**	Systematic review and meta-analysis of 45 RCTs and separated analysis of 17 observational studies with sulodexide	Age, sex, different stages of CVD in patients with varicose veins

Clinical benefit of Calcium dobesilate

Rationale. Calcium dobesilate (calcium 2,5-dihydroxybenzene-sulphonate) is a synthetic drug used for CVI, hemorrhoids, and diabetic retinopathy. Experimental studies claimed a protective action against oxidative stress in varicose veins[298] and other beneficial effects such as regulation of apotosis,[299] increased NO-synthase activity, inhibition of prostaglandin synthesis, diminished capillary fragility and hyperpermeability, reduction of platelet aggregation and blood viscosity.[104]

Evidence. An RCT[300] demonstrated improvement of plethysmographic measurements after 6-month treatment. However, comparison versus placebo in another 3-month trial[301] failed to show

a significant difference for edema, symptoms of Chronic Venous Disease, and Quality of Life (QoL), with exception of QoL at 12-month follow up, better in Calcium dobesilate group. A more recent trial with Calcium dobesilate versus MPFF[302] reported similar and significant pain reduction in both groups. In an RCT versus placebo in patients with CEAP C3-4,[303] Calcium dobesilate significantly decreased leg volume ($p=0.0002$) and improved symptoms (discomfort, heavy legs, tired legs, tingling, itching and cramps ($p<0.05$)).[304]

A meta-analysis performed in 2004[18] found 10 RCTs (778 patients) comparing calcium dobesilate with placebo for CVI. The methodological quality was good in 3 RCTs (608 patients). Calcium dobesilate decreased night cramps and discomfort more than placebo with number of patients needed to be treated [NNT] of 4 (95% CI 3-7) vs 8 (95% CI 4-50). Greater improvement was reported in severe CVD as compared with the mild disease, for leg volume decrease, pain, heaviness, malleolar swelling, and paresthesia. Interestingly, no dose effect was noticed: 1000 mg was as effective as 1,500 mg daily. A meta-analysis[15] found Calcium dobesilate effectiveness comparable to Ruscus extracts in reducing foot volume and ankle circumferences. Data from a post-marketing surveillance (PMS) report 1974-1998, the international literature (1970-2003) and periodic safety update report (PSUR) 1995-2003 from the French Regulatory authorities, was reviewed to assess the safety profile of Calcium dobesilate.[305] Adverse events included fever (26%), gastrointestinal disorders (12.5%), skin reactions (8.2%), arthralgia (4.3%), and agranulocytosis (4.3%). No death was related to Calcium dobesilate administration. The authors concluded that the adverse events' risk with Calcium dobesilate is low despite 13 known cases of agranulocytosis in patients treated by Calcium dobesilate.

2220 **Table 27. Clinical benefit of Calcium dobesilate**

First author, year	**Patient**	**Intervention /exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Ciapponi A, 2004[18]	Adults with CVI including CEAP C2	Calcium dobesilate	Placebo	Pain, heaviness, night cramps, discomfort, paresthesia, malleolar swelling **Calcium dobesilate suggested as more effective than placebo in improving symptoms. Higher efficacy in more severe disease.**	Systematic review and meta-analysis of 10 RCTs	Age, sex, different stages of CVD in patients with varicose veins
Pompilio G, 2021[15]	Adults with Chronic Venous Disease	Calcium-dobesilate, Hydroxyethyl rutosides, Ruscus extracts, MPFF, sulodexide, horse chestnut extracts and pentoxifyllin e	Placebo in 45 RCTs	Ulcer healing, leg volume, ankle circumference, symptoms such as pain assessed by VAS, feeling of swelling, heaviness, as well as QoL (CIVIQ-20 score) **Calcium dobesilate the most effective treatment in reducing leg volume**	Systematic review and meta-analysis of 45 RCTs and separated analysis of 17 observational studies with sulodexide	Age, sex, different stages of CVD in patients with varicose veins
Allain H, 2004[305]	Adults with CVD, diabetic retinopathy, and hemorrhoids	Calcium dobesilate	NA	Adverse events **The risk of an adverse event with calcium dobesilate is low. 13 known cases of agranulocytosis, less than incidence in**	Review of the adverse events and safety profile	Age, sex, different stages of CVD and different diseases

				general population		

Clinical benefit of Horse chestnut extract

Rationale: Horse chestnut extract (HCSE) contains escin, a mixture of triterpene saponins, and some benzopyrones. Escin has a veno-contractile properties and a protective effect on endothelium, through the increased production of nitric oxide.[306]

Evidence. A Cochrane review[307] covered electronic data bases search and material collected from manufacturers of HCSE products with published and unpublished studies and non-English articles. The included RCTs in patients with CVI compared efficacy and safety of oral HCSE mono-preparations with placebo, or reference therapy. Assessment of symptoms shown significantly better than placebo efficacy in improvement of leg pain (7 RCT). Evaluation of the leg volume change in 6 placebo-controlled trials reported a 32.1 ml weighted mean difference (95% CI 13.49 -50.72) in favor of HCSE. This efficacy was found comparable to compression stockings in another trial.[308] The treatment safety was excellent. The authors concluded that "HCSE is an efficacious and safe short-term treatment for CVI." The most recent systematic review and meta-analysis on VAD effectiveness[15] confirmed value of HCSE therapy, although the other VAD were found more effective, MPFF in reducing leg volume and pain, and improving QoL; Calcium dobesilate and Ruscus extracts in reducing foot volume and ankle circumference.

Table 28. Clinical benefit of Horse chestnut extract

First author, year	**Patient**	**Intervention /exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be

						used to stratify analysis)
Pittler MH, 2012[309]	Adults with CVI including CEAP C2	Horse chestnut extract	Placebo	CVI related signs and symptoms: pain, leg volume. **Overall improvement of pain, edema and pruritus. Mild and infrequent adverse events**	Cochrane Database Systematic review	Age, sex, different stages of CVD in patients with varicose veins
Pompilio G, 2021[15]	Adults with Chronic Venous Disease	Horse chestnut extracts, Calcium-dobesilate, Hydroxy-ethyl rutosides, Ruscus extracts, MPFF, sulodexide, and pentoxifyllin e	Placebo in 45 RCTs	Ulcer healing, leg volume, ankle circumference, symptoms such as pain assessed by VAS, feeling of swelling, heaviness, as well as QoL (CIVIQ-20 score) **Only one study could be used for VAD comparisons.**	Systematic review and meta-analysis of 45 RCTs and separated analysis of 17 observational studies with sulodexide	Age, sex, different stages of CVD in patients with varicose veins

Clinical benefit of Red vine leaf extract

Rationale. Red vine leaf extract was found to improve cutaneous microcirculation in patients with CVI, thanks to the increased nitric oxide synthase and decreased oxidative stress.[310]

Evidence. A review paper estimated a statistically significant and clinically relevant efficacy of Red-vine-leaf-extract .[311] on leg edema reduction assessed by volumetry, and on symptoms (heaviness, tingling and pain). Three double-blind versus placebo RCTs support these findings. One[312] crossover trial versus placebo, in 71 patients with CVI Widmer grade I to II, reported a significantly decreased leg circumference ($p<0.0001$) and an increased cutaneous microvascular blood flow ($p<0.0001$) as well as transcutaneous oxygen pressure ($p<0.0001$). Another RCT, in 260 patients CEAP C2 to C4,[313] evaluated leg volume by water displacement volumetry and

noted marked dose-dependent difference favoring AS 195 group ($p<0.001$), parallel to the ankle/calf circumference pattern ($p<0.001$). The third trial confirmed previous results in 248 patients with varicose veins and CEAP C3-C4a.[314] Pain improvement and decrease of the leg volume assessed by water displacement volumetry versus placebo were significant, $p=0.047$ and $p=0.0268$ respectively. Safety of AS 195 treatment was excellent. In a recent systematic review[315] significant improvement of symptoms and edema was observed in some studies. The safety of Red-vine leaf extract treatment was excellent.

Table 29. Clinical benefit of Red vine leaf extract

First author, year	**Patient**	**Intervention /exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Azdhari M, 2020[315]	Adults with CVI	Red-vine-leaf-extract	Placebo?	Leg volume, calf circumference, tired and heavy legs, sensation of tension, tingling and pain. In some trials significant improvement of leg volume, calf circumference, tired and heavy legs, sensation of tension, tingling and pain, cutaneous microcirculation and O2 pressure.	Systematic review. 5 trials	Age, sex, different stages of CVD in patients with varicose veins
Stucker M, 2019[311]	Adults with CEAP C1s to C4	Red-vine-leaf-extract	Placebo	Leg edema reduction assessed by volumetry, and venous symptoms (heaviness, tingling and pain).	Review	Age, sex, different stages of CVD in patients with varicose veins

				Significant and relevant clinical efficacy over placebo in patients CEAP C1s to C4, on edema, tension, heaviness, tingling and pain		
Kalus U, 2004[312]	Adults with CVI grade I or II of Widmer classification. N=71	Red-vine-leaf-extract	Placebo	Cutaneous microvascular blood flow, transcutaneous oxygen pressure, leg edema Improvement of microvascular blood flow, oxygen pressure and leg circumference ($p<0.0001$)	Crossover RCT versus placebo	Age, sex, different stages of CVD in patients with varicose veins
Rabe E, 2011[314]	Adults with varicose veins and CEAP C3-C4a N=248	Red-vine-leaf-extract	Placebo	Leg volume by water plethysmography Symptoms (10-cm VAS). Global efficacy evaluations. Significantly reduced limb volume ($p=0.0268$) and improved pain ($p=0.047$)	RCT	Age, sex, different stages of CVD in patients with varicose veins

Clinical benefit of Sulodexide

Rationale. Sulodexide contain a purified glycosaminoglycan mixture of low molecular weight heparin (80%) and dermatan sulfate (20%), components of glycocalyx glycoproteins.[104] Protection of glycocalyx integrity is essential in the preservation of the vascular endothelial function and mitigation of the inflammatory reaction.

Evidence. A systematic review and meta-analysis of 13 studies with sulodexide[19] included 1901 participants with CVD at any stage of the disease, classified or non-classified, was considered.

Sulodexide decreased the intensity of pain, cramps, heaviness, edema, total symptom score and reduced inflammatory mediators in patients with CVD.

In a meta-analysis comparing efficacy of different venoactive drugs[15] sulodexide was included only in a single network meta-analysis for the proportion of patients with complete ulcer healing and it showed to have the highest probability of being the best treatment (48%) compared with pentoxifylline (37%) and MPFF (16%). The assessment of the sulodexide efficacy on venous symptoms was done in the meta-analysis of 18 observational studies showing a significant improvement of pain, feeling of swelling, heaviness and paresthesia measured by Likert scales.

In one randomized trial endovenous laser treatment of the great saphenous vein and phlebectomy were followed by sulodexide twice daily for one month and compared to the control group with no adjunctive pharmacotherapy. Compared to the control group, in the main group there was a statistically significant decrease in VCSS and improvement in the quality of life assessed by CIVIQ-20. The microcirculation of the skin was assessed by laser Doppler flowmetry. Laboratory examinations measured markers of endothelial dysfunction (homocysteine, von Willebrand factor, PAI1, soluble (s)E-selectin, sP-selectin, sICAM-1, and sVCAM-1). An increase in tissue perfusion, and an improvement in the microcirculation was found in the sulodexide group.[316]

A prospective, multicenter, randomized controlled trial assessed sulodexide as adjunctive treatment to the sclerotherapy. Group A (n= 354 patients) received sulodexide twice a day for 7 days before sclerotherapy and Group B (n=366 patients) received standard sclerotherapy alone. Polidocanol and 20 to 30 mmHg compression stockings were used in both groups for 7 days. After 1 month, the incidence of hyperpigmentation was 8.7% in group A and 14.8% in group B

(p= .01). Group A developed an average area of hyperpigmentation of 10.7% compared with 18.2% in group B (p=.01), and the skin tone of the hyperpigmented area was lower in group A than in group B (p=.02). However, the latter difference was not significant after 3 months. The overall vein disappearance rate was similar in both groups.[317]

Table 30. Clinical benefit of Sulodexide

First author, year	**Patient**	**Intervention/ exposure**	**Comparison**	**Outcomes**	**Study design**	**Possible explanations of heterogeneity** (factors to be used to stratify analysis)
Bignamini AA, 2020[19]	Adults with CVD any stage n=1901	Sulodexide	None or heparan sulphate	Leg edema reduction assessed by volumetry, and venous symptoms (heaviness, tingling and pain). Decrease of pain, cramps, heaviness, edema and total symptoms score. Reduced inflammatory mediators. Low risk of adverse events (3%)	Systematic review and meta-analysis of 13 studies	Age, sex, different stages of CVD in patients with varicose veins
Pompilio G, 2021[15]	Adults with Chronic Venous Disease	Sulodexide,Horse chestnut extracts, Calcium-dobesilate, Hydroxy-ethyl rutosides, Ruscus extracts, MPFF, and pentoxifylline	Placebo in 45 RCTs	Ulcer healing, leg volume, ankle circumference, symptoms such as pain assessed by VAS, feeling of swelling, heaviness, as well as QoL (CIVIQ-20 score).	Systematic review and meta-analysis; 45 RCTs ; 18 observational studies with sulodexide	Age, sex, different stages of CVD in patients with varicose veins

				Sulodexide at least as effective as pentoxifylline for ulcer healing. Based on observational studies it is effective in improving venous symptoms and signs.		

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2. EVIDENCE TO DECISION TABLES

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Table 31. Evidence to decision framework: Compression therapy vs. intervention

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Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	Overall, there was insufficient high quality of evidence to determine whether compression stockings are effective as the primary treatment for symptomatic varicose veins and if one stocking is better than the other. However, some studies reported improvement in symptoms.	Probably yes
How substantial are the undesirable anticipated effects?	Reported side effects of discomfort, appearance, and application difficulty. The benefits of stockings were offset by highly variable reports of compliance, presumably due to the most common side effects of itching and irritation.	Probably yes
Do the desirable effects outweigh the undesirable effects?	Probably	Probably yes
What is the overall certainty of the evidence of effects?	Low with significant heterogeneity of data	Low

How large are the resource requirements associated with the intervention?	No available data	Unknown
How large is the incremental cost relative to the net benefit?	No available data	Unknown
What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	No data available	Probably yes
Is the opinion feasible to implement?	Yes	Yes

2315

2316 **Table 32. Evidence to decision framework: Intervention vs Compression Therapy**

Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	Recommendations for superficial venous intervention over compression for patients with symptomatic varicose veins and axial reflux in the GSV or SSV are based on the Cochrane Review for compression effectiveness and two comparative randomized trials with consistent results.	Yes
How substantial are the undesirable anticipated effects?	Possible side effects are related to the surgical interventions. However, these interventions are considered as safe with low rate of complications.	Probably yes
Do the desirable effects outweigh the undesirable effects?	Probably	Probably yes
What is the overall certainty of the evidence of effects?	Moderate	Moderate
How large are the resource requirements associated with the intervention?	No available data	Unknown
How large is the incremental cost relative to the net benefit?	No available data	Unknown

What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	No data available	Probably yes
Is the opinion feasible to implement?	Yes	Yes

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2318 **Table 33. Evidence to decision framework: Immediate intervention vs 3-months trial of**

2319 **Compression**

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Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	There is no data proving the value of a 3-month trial of compression stockings prior to intervention for patients with C2 disease, required by some Insurance companies. Compression therapy was found to be inferior to minimally invasive endovenous therapies (including UGFS and ETA) that produce better results with regards to anatomic disease extent, patient satisfaction and QoL.	Probably no
How substantial are the undesirable anticipated effects?	Reported side effects of discomfort, appearance, and application difficulty. The benefits of stockings were offset by highly variable reports of compliance, presumably due to the most common side effects of itching and irritation.	Probably yes
Do the desirable effects outweigh the undesirable effects?	Probably	Probably yes
What is the overall certainty of the evidence of effects?	Low with practically no data	Low
How large are the resource requirements associated with the intervention?	No available data	Unknown
How large is the incremental cost relative to the net benefit?	Compression therapy was found to be inferior to minimally invasive endovenous therapies (including UGFS and ETA)	Unknown

	that produce better results with regards to cost effectiveness.	
What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	No data available	Probably yes
Is the opinion feasible to implement?	Yes	Yes

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2323 **Table 34. Evidence to decision framework: Post-procedure Compression Therapy**

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Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	Application of compression for one week after any endothermal ablation with and without concomitant phlebectomies appeared to be effective in reducing pain within the first 5-10 days after endothermal ablation and phlebectomies with the greatest benefits in patients undergoing EVLA. Earlier return to daily activities was also observed.	Probably yes
How substantial are the undesirable anticipated effects?	Reported side effects of discomfort, appearance, and application difficulty. The benefits of stockings can be offset by highly variable reports of compliance, presumably due to the most common side effects of itching and irritation.	Probably yes
Do the desirable effects outweigh the undesirable effects?	Probably not	Probably not
What is the overall certainty of the evidence of effects?	Moderate	Moderate
How large are the resource requirements associated with the intervention?	No available data	Unknown

How large is the incremental cost relative to the net benefit?	No available data	Unknown
What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	No data available	Probably yes
Is the opinion feasible to implement?	Yes	Yes

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Table 35. Evidence to decision framework: MPFF and Ruscus

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Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	Overall, there was a moderate quality of evidence to determine whether Micronized Purified Flavonoid Fraction (MPFF) or Ruscus are effective in symptomatic patients with varicose veins for treatment of vein related pain, leg heaviness and/or sensation of swelling.	Yes
How substantial are the undesirable anticipated effects?	Main side effects are mild gastro-intestinal disturbances potentially alleviated by administration with a meal.	Probably no
Do the desirable effects outweigh the undesirable effects?	Probably	Yes
What is the overall certainty of the evidence of effects?	Moderate, as most of the studies address the cohort of patients with Chronic Venous Disease and varicose veins patients are only part of them	Moderate
How large are the resource requirements associated with the intervention?	MPFF or Ruscus nutritional supplements are not expensive and available in the US	Low
How large is the incremental cost relative to the net benefit?	No available data for the varicose veins	Unknown

What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	No data available	Probably yes
Is the opinion feasible to implement?	Yes	Yes

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2332 **Table 36. Evidence to decision framework: Drugs and nutritional supplements**

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Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	Overall, there was a moderate quality of evidence for Calcium dobesilate and low quality of evidence for Hydroxyethylrutosides or Horse chestnut extract or Red vine leaf extract or Sulodexide to determine whether these compounds are effective in symptomatic patients with varicose veins for treatment of vein related pain, leg heaviness and/or sensation of swelling.	Probably yes
How substantial are the undesirable anticipated effects?	Main side effects for Hydroxyethylrutosides or Horse chestnut extract or Red vine leaf extract or Sulodexide are mild gastro-intestinal disturbances potentially alleviated by administration with a meal. Calcium dobesilate adverse events included fever, gastrointestinal disorders, skin reactions, arthralgia, and agranulocytosis.	Monitor agranulocytosis with Calcium dobesilate
Do the desirable effects outweigh the undesirable effects?	Probably yes	Monitor agranulocytosis with Calcium dobesilate
What is the overall certainty of the evidence of effects?	Moderate for Calcium dobesilate, low for Hydroxyethylrutosides or Horse chestnut extract or Red vine leaf extract or Sulodexide. Most of the studies address the cohort of patients with Chronic Venous Disease and varicose veins patients are only part of them	Moderate to low

How large are the resource requirements associated with the intervention?	Only Horse chestnut extract or Red vine leaf extract are available in the US as inexpensive nutritional supplements	Low
How large is the incremental cost relative to the net benefit?	No available data	Unknown
What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	No data available	Probably yes
Is the opinion feasible to implement?	Yes	Yes

Is the opinion acceptable to key stakeholders?	No data available	Probably yes
Is the opinion feasible to implement?	Yes	Yes

Table 37. Evidence to decision framework: Routine ultrasound screening in asymptomatic average-risk patients

Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	Routine screening associated with substantial cost, resource utilization, & cost. Risk of bleeding events associated with anticoagulation for asymptomatic ultrasound identified events.	Large
How substantial are the undesirable anticipated effects?	Risk of asymptomatic thrombus progression / embolization if not identified. Incidence of these events is very low (approximately 1.5%). However, risk of progression /embolization in these patients is unclear.	Probably low

Do the desirable effects outweigh the undesirable effects?	Yes	Yes
What is the overall certainty of the evidence of effects?	High certainty regarding low incidence of thrombotic events after ablation. Low certainty regarding the natural history of rare asymptomatic events identified by ultrasound.	
How large are the resource requirements associated with the intervention?	Very high	Very high
How large is the incremental cost relative to the net benefit?	Very high	Very high
What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	No data available	Probably yes
Is the opinion feasible to implement?	Yes (resource saving)	Yes

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2343 **Table 38. Evidence to decision framework: Pharmacoprophylaxis after**
2344 **endovenous ablation**

Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	Routine thromboprophylaxis appears to reduce the risk of post-procedural thrombotic events, but the data is heterogenous and the magnitude of effect is low.	Low
How substantial are the undesirable anticipated effects?	Low risk of increased bleeding with pharmacoprophylaxis. No data regarding the cost and inconvenience of pharmacoprophylaxis.	Probably low
Do the desirable effects outweigh the undesirable effects?	Probably, but with very low magnitude of effect.	Probably yes
What is the overall certainty of the evidence of effects?	Low with significant heterogeneity and low magnitude of effect	Low

How large are the resource requirements associated with the intervention?	No available data	Unknown
How large is the incremental cost relative to the net benefit?	No available data	Unknown
What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	No data available	Probably yes
Is the opinion feasible to implement?	Yes	Yes

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2346 **Table 39. Evidence to decision framework: Treatment of symptomatic ARTE**
2347 **according to established guidelines for acute DVT**

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Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	The value of routine treatment of symptomatic DVT is well established although it is less certain that the natural history of ARTE is identical to DVT.	Probably beneficial
How substantial are the undesirable anticipated effects?	Low risk of major bleeding (approximately 1%) with direct oral anticoagulants. Inconvenience and cost of anticoagulation. High cost and inconvenience of routine ultrasound follow-up.	Low
Do the desirable effects outweigh the undesirable effects?	Probably favors anticoagulation in symptomatic patients	Probably yes
What is the overall certainty of the evidence of effects?	Low with uncertain natural history of ARTE High certainty regarding low risk of anticoagulation	Low
How large are the resource requirements associated with the intervention?	Low – Fewer resources required for anticoagulation in comparison to ultrasound follow-up	Low
How large is the incremental cost relative to the net benefit?	No available data	Unknown

What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	No data available	Unknown
Is the opinion feasible to implement?	Yes	Yes

Table 40. Evidence to decision framework: Treatment of SVT (main saphenous trunks and tributaries above the knee > 3cm from the SFJ and at least 5 cm in length)

Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	Prevention of key outcomes: SVT extension, recurrent SVT, VTE clinically and statistically significant	Large
How substantial are the undesirable anticipated effects?	Risk of clinically relative bleeding low	Low
Do the desirable effects outweigh the undesirable effects?	Yes	Yes
What is the overall certainty of the evidence of effects?	High certainty regarding low incidence of thrombotic events after treatment	
How large are the resource requirements associated with the intervention?	Low	Very high
How large is the incremental cost relative to the net benefit?	Low	Very high
What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	Similar to other guidelines	Yes
Is the opinion feasible to implement?	Yes	Yes

Table 41. Evidence to decision framework: SVT of the main saphenous trunks and treatment with LWMH and NSAIDs.

Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	NSAIDS reduce SVT pain and extension	Large
How substantial are the undesirable anticipated effects?	Low risk of increased bleeding, GI intolerance with NSAIDs Risk of VTE	Large
Do the desirable effects outweigh the undesirable effects?	Probably, especially for distal DVT	Yes
What is the overall certainty of the evidence of effects?	Moderate certainty	Yes
How large are the resource requirements associated with the intervention?	Low	Unknown
How large is the incremental cost relative to the net benefit?	Low	Unknown
What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	Yes	Yes
Is the opinion feasible to implement?	Yes	Yes

Table 42. Evidence to decision framework: treatment of isolated thrombosis of varicose tributaries or limited involvement of the GSV

Domain	Evidence / Panel Input	Judgement
How substantial are desirable effects of the strategy?	Surgical stripping reduces pain and discomfort	Probably beneficial

How substantial are the undesirable anticipated effects?	No reduction in VTE	Low
Do the desirable effects outweigh the undesirable effects?	Probably in select circumstances	Probably yes
What is the overall certainty of the evidence of effects?	Low with no RCTs	Low
How large are the resource requirements associated with the intervention?	Moderate	Low
How large is the incremental cost relative to the net benefit?	Moderate	Unknown
What would be the effect on health inequalities?	None	None
Is the opinion acceptable to key stakeholders?	Yes	Unknown
Is the opinion feasible to implement?	Yes	Yes

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