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GUIDELINES

Japanese Dermatological Association Guidelines

Wound, Pressure Ulcer, and Burn Guidelines-5: Guidelines for the management of lower leg ulcers and varicose veins, second edition

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Abstract

"Wound, Pressure Ulcer, and Burn Guidelines-5: Guidelines for the management of lower leg ulcers and varicose veins, second edition" is revised from the first edition, which was published in the *Japanese Journal of Dermatology* in 2011. The guidelines were drafted by the Wound, Pressure Ulcer, and Burn Guidelines Drafting Committee delegated by the Japanese Dermatological Association and intend to facilitate physicians' clinical decisions in preventing, diagnosing and management of lower leg ulcers and varicose veins. We updated all sections by collecting documents published since the publication of the first edition. In particular, we added clinical question 8 (CQ8), which addresses endovenous laser ablation for varicose veins, a procedure that became covered by the Japanese national health insurance after the writing of the first edition, and endovenous radiofrequency ablation, which became covered by national health insurance in 2014. We also rearranged the subsequent clinical question (CQs) for easier reading. While the addition of these new techniques has increased the number of options available within the treatment algorithm, differences have arisen in the indication for surgery depending on the facility performing the treatment. Therefore, these have been abbreviated.

†Deceased 2020.

For affiliations, see Table 1.

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1 | BACKGROUND TO THE DRAFTING OF THE GUIDELINES FOR THE MANAGEMENT OF LOWER LEG ULCERS AND VARICOSE VEINS

Guidelines are "documents systematically prepared to help medical specialists and patients to make appropriate judgments in specific clinical situations." There are guidelines for lower leg ulcers and varicose veins—which are frequent causes of lower leg ulcers—overseas, but not in Japan. Moreover, only a few books have provided detailed explanations of the differential diagnosis of leg vein disorders, which account for approximately 80% of all causes of lower leg ulcers, or of compression therapy/surgical therapy, which play important roles in their treatment.

Varicose veins are treated in multiple clinical departments. However, as patients often visit the dermatology department first for leg ulcers, the present Guidelines for the Management of Lower Leg Ulcers and Varicose Veins were prepared in consideration of the importance of the dermatologist's role. Also, the disease concepts of chronic venous insufficiency (CVI) and chronic venous disorders (CVDs) and the CEAP (based on clinical, etiologic, anatomic, and pathophysiologic data) classification of these disorders are presented. The objective of the present guidelines is to properly guide the diagnosis and treatment of lower leg ulcers and varicose veins by systematically presenting evidence-based recommendations to support clinical decisions.

2 | STATUS OF THE GUIDELINES FOR THE MANAGEMENT OF LOWER LEG ULCERS AND VARICOSE VEINS

The Wound, Pressure Ulcer, and Burn Guidelines Committee (Table 1) is composed of members delegated by the Board of Directors of the Japanese Dermatological Association (JDA). It has met and produced written deliberations several times since October 2008, and has drafted a commentary on wounds in general and five treatment guidelines, including the Guidelines for the Management of Lower Leg Ulcers and Varicose Veins, by taking into consideration the opinions of the Scientific Committee and the Board of Directors of the JDA. The present Guidelines for the Management of Lower Leg Ulcers and Varicose Veins reflect the current standards of diagnosis and treatment in Japan. However, patients have varied backgrounds, including different underlying diseases, degrees of symptom severity, and complications. Therefore, physicians who perform diagnoses and treatments should determine an approach to diagnosis and treatment together with their patients, and the contents of their decisions need not always be in complete agreement with the present guidelines. Moreover, these guidelines cannot be cited as references in lawsuits or other disputes.

3 | MAIN CHANGES TO THE SECOND EDITION

We updated all sections by collecting documents published since the publication of the first edition. In particular, we added clinical question 8 (CQ8), which addresses endovenous laser ablation for varicose veins, a procedure that became covered by the Japanese national health insurance after the writing of the first edition, and endovenous radiofrequency ablation, which became covered by national health insurance in 2014. We also rearranged the subsequent clinical question (CQs) for easier reading. While the addition of these new techniques has increased the options available within the treatment algorithm, differences have arisen in the indication for surgery depending on the facility performing the treatment. Therefore, these have been abbreviated.

4 | SPONSORS AND CONFLICTS OF INTEREST

All expenses involved in the drafting of the Guidelines for the Management of Lower Leg Ulcers and Varicose Veins were borne by the JDA. No aid was provided by specific organizations, enterprises,

TABLE 1 Wound/Burn Guideline Drafting Committee (the head of each section is underlined).

Chairperson: Hironobu IHN (Professor, Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University)	
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or pharmaceutical companies. In the event that a committee member (Table 1) participating in the drafting of these guidelines was involved in the development of a specific, relevant drug, that member abstained from determining to what degree the item in question was recommended. Aside from that, no committee member has any conflict of interest relevant to the drafting of these guidelines to disclose.

5 | COLLECTION OF EVIDENCE

Databases used: Medline, PubMed, Japana Centra Revuo Medicina Web, and Cochrane Database of Systematic Reviews (including all Evidence-Based Medicine Reviews). References obtained through manual search by each member were also added.

Search period: Searchable work published between January 1980 and December 2013 was reviewed. Recent published work of importance was added when considered appropriate.

Adoption criteria: Priority was placed on systematic reviews of randomized controlled trials (RCTs) and papers on individual RCTs. When these were not available, cohort studies and case-control studies were included. Although some reports of case-series studies were also used as references, published work on basic experiments was excluded.

6 | CRITERIA FOR DETERMINATION OF THE EVIDENCE AND RECOMMENDATION LEVELS

The following criteria adopted in the Guidelines for the Diagnosis and Treatment of Malignant Tumors edited by the JDA were used as a reference to determine the evidence levels.

Evidence levels:

I. Systematic reviews/meta-analyses.
II. One or more RCT.
III. Non-RCT (including before/after comparative studies with statistical analyses).
IVa. Analytical epidemiological studies (cohort studies).
IVb. Analytical epidemiological studies (case-control studies/cross-sectional studies).
V. Descriptive studies (case reports and case-series studies).
VI. Opinions of special committees and individual experts.

In addition, the *Minds Handbook for Clinical Practice Guideline Development 2014* was used as a reference for the recommendation levels.

Recommendation levels:

There are two levels of recommendation:

1: Recommended.
2: Proposed as one option.

If the level of recommendation cannot be determined, it is set as "none." This includes cases in which a clear recommendation cannot be made.

The recommendations state the strength of evidence (described as A, B, C, and D) together with the level of recommendation, as in the following examples:

1. Treatment I is recommended for patient P (1A) (i.e., strongly recommended based on strong evidence).
2. Treatment I is proposed as an option for patient P (2C) (i.e., weak recommendation based on weak evidence).
3. We propose that treatment I not be performed for patient P (2D) (i.e., weak recommendation based on very weak evidence).
4. We recommend that treatment I not be performed for patient P (1B) (i.e., strong recommendation based on moderate evidence).

7 | REVIEW BEFORE PUBLICATION

Prior to the publication of these guidelines, the annual meetings of the JDA from 2012 to 2015 were used to present the committee's annual drafting progress, to solicit opinions from association members, and to make necessary revisions.

8 | PLANS FOR UPDATES

The present guidelines are scheduled to be updated in 3 to 5 years. However, if a partial update becomes necessary, it will be presented on the website of the JDA, as appropriate.

9 | DEFINITIONS AND EXPLANATIONS OF TERMINOLOGY

Lower leg ulcers: This term includes all ulcers that occur in the lower leg. They may be induced by various causes but are most often caused by venous disorders. In Western populations, approximately 70% to 80% of lower leg ulcers are reported to be venous ulcers. Approximately 10% of lower leg ulcers have arterial causes, and both venous and arterial causes are involved in some cases. Therefore, lower leg ulcers are mostly due to circulatory disturbances. Other causes include collagen disease, vasculitis, pressure ulcer, malignant tumor, infection, and contact dermatitis.

Venous ulcers of the lower leg: Venous ulcers of the lower leg are also called venous stasis ulcers, stasis ulcers, or simply venous ulcers. They are ulcers caused by disturbances of the venous return (venous stasis). Venous hypertension induces dermatitis, and the further addition of minor traumas such as contusions frequently triggers ulcer formation. These ulcers are frequently caused by primary varicose veins, although they may also be caused by secondary varicose veins. They often occur in the lower third of the lower leg to the dorsum of the foot.

Stasis dermatitis: Also called stasis eczema. Eczema/dermatitis caused by venous stasis or venous hypertension. It often occurs in the lower leg and is frequently caused by primary varicose veins, although it may also be caused by secondary varicose veins (Figure 1).

Venous hypertension of the leg: High venous pressure in the peripheral areas of the lower leg, even during leg exercise in a standing position (e.g., heel raises, stepping exercise). During rest in a standing position, venous pressure to the height of the central vein ranging from approximately 80 to 100 mm Hg is exerted on the ankle region even in a normal limb. However, when exercising the ankle, the pressure rapidly decreases to approximately 30 mm Hg due to the action of the skeletal muscle pump. In primary varices, due to venous valve insufficiency, the pressure only decreases to approximately 60 mm Hg even during exercise, and this pressure shows little decrease or even an increase when exercising the leg in cases of deep vein occlusion such as deep vein thrombosis (DVT). This condition in which the peripheral venous pressure of the leg does not decrease is called venous hypertension of the leg.

Varicose veins: A disease in which the superficial veins of the leg become dilated and tortuous. Despite the name, some lesions are not varicose. Varicose veins are divided into primary and secondary ones.

Primary varicose veins: These may be concisely called primary varices. This name refers to the condition in which the superficial veins of the leg become dilated and tortuous when the cause is in the dilated/tortuous veins themselves. Most varicose veins are primary.

Secondary varicose veins: These may be called secondary varices for concision. They are varices that occur secondarily, as the causes are not in the dilated/tortuous superficial veins themselves. Causes of secondary varices include not only DVT and thrombosis sequelae (post-DVT varices) but also pregnancy, intrapelvic tumor, arteriovenous fistula, and vascular tumor. Although post-DVT varices are common, caution is necessary in their diagnosis, as they may be totally indistinguishable from primary varices in examinations performed to check the patency of deep veins when reperfused after DVT. In these cases, the skeletal muscle pump of the lower leg does not function sufficiently because of deep venous valve incompetence (valvular reflux), and venous hypertension of the leg (venous stasis) persists. If the saphenous vein functions as a bypass for deep veins in the standing position as well, misdiagnosis of the condition as primary varices and surgical treatment for varices may result in postoperative exacerbation of the venous stasis and progression of the condition. In addition, there may be no clear valve reflux or deep vein occlusion despite a history of DVT.

Leg veins: Leg veins can be classified into superficial veins, deep veins, and communicating branches.

Superficial veins of the leg: Veins running in areas near the skin surface—including the great and small saphenous veins and their branches—are collectively called superficial veins of the leg. Approximately 10% to 20% of the leg's venous blood is normally returned via these superficial veins. Both superficial and deep veins have many valves, and the leg's venous return is accomplished by the action of the skeletal muscle pump and of these valves. If deep veins, which are the primary channels of venous return, are impaired by DVT, the superficial veins serve as a bypass, and secondary varices may develop if left untreated.

Great saphenous vein: One of the superficial veins of the leg. It originates anteriorly to the medial condyle, ascends on the medial side of the lower leg, runs on the medial side of the knee and thigh, and joins the femoral vein in the inguinal region. Many superficial veins that form its branches join it before it drains into the femoral vein. It also communicates with deep veins through communicating (perforating) branches. The great saphenous vein frequently consists of a single trunk, although it may be divided into two or three parallel vessels.

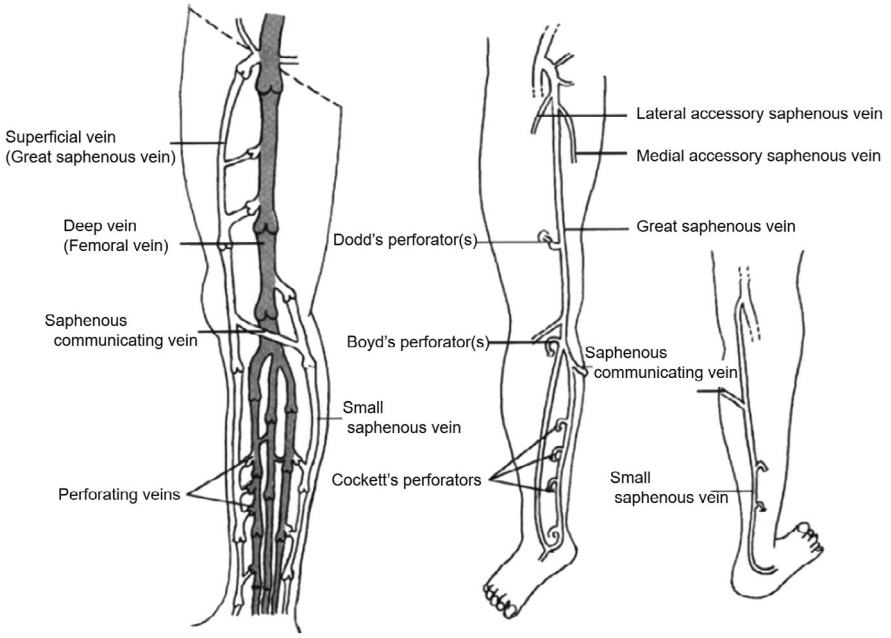


FIGURE 1 Varicose veins. Adapted from Ito.[1]

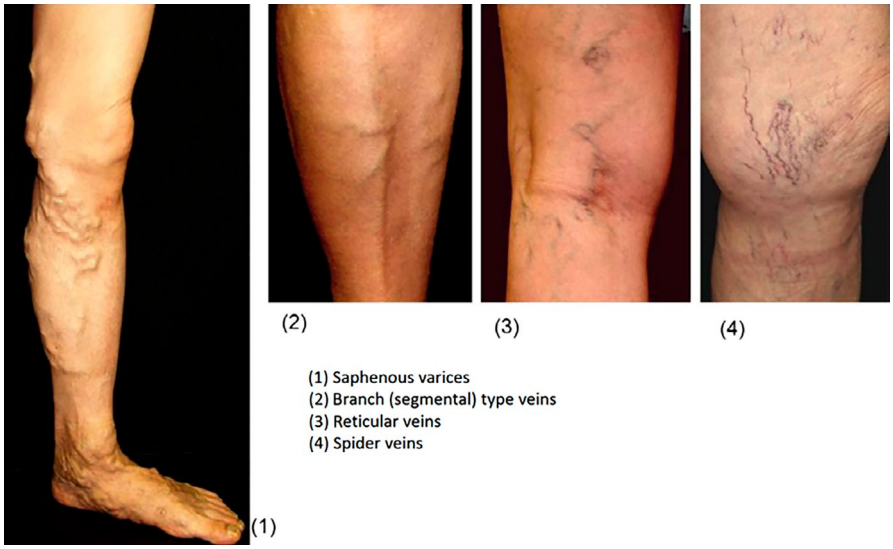


FIGURE 2 Morphological classification of primary varicose veins. From Ito.[1]

Small saphenous vein: The small saphenous vein is usually a single superficial vein that runs on the posterior side of the leg. It originates posteriorly to the lateral condyle, ascends to the popliteal region nearly in the center of the posterior aspect of the lower leg, and drains into the popliteal vein. Its cephalic portion, extending from one-third to one-half, is located under the fascia. It has branches connecting it to deep veins, and superficial veins connecting it to the great saphenous vein. The course of the small saphenous vein shows wide individual variation. While it drains into the popliteal vein in approximately 60% to 70% of individuals, it does not join the popliteal in some, or it joins the popliteal but ascends on the posterior side of the thigh until it joins the great saphenous vein in the inguinal region in others (Figure 2).

Deep veins of the leg: Veins that run in parallel with arteries in deep areas of the leg. The veins that share the names of arteries of the lower leg fuse below the knee to form the popliteal vein, which then becomes the superficial femoral vein, joins the great saphenous vein in the inguinal region, and drains into the external iliac vein. These veins normally return approximately 80% to 90% of the leg's venous blood.

Communicating branches: Also called perforating branches. These are veins with a diameter of ≤3 mm that connect superficial and deep veins. They have venous valves, and blood normally flows in one direction, from superficial to deep veins.

Insufficient communicating branches: Also called insufficient perforating branches. These are communicating branches that show reflux from deep to superficial veins due to valve insufficiency from venous stasis caused by leg varices.

Morphological classification of primary varices:

Primary varices can be classified from (1) to (4) as described below. Note that different types may be observed simultaneously.

(2) to (4) may collectively be called small varices.

1. Saphenous varices: Also called truncal varices. These are the most frequent type of primary varices requiring treatment.

   Great saphenous varices are dilated and meandering veins on the medial side of the thigh to the lower leg. They are caused by reflux of the great saphenous vein immediately below its junction with the femoral vein due to valve insufficiency. They may be accompanied by stasis dermatitis or by ulcers above the medial condyle or on the anterior side of the lower leg. Small saphenous varices refer to a dilated small saphenous vein or its branches on the posterior side of the lower leg due to valve insufficiency of the small saphenous vein immediately below its junction with the popliteal vein. They may be accompanied by stasis dermatitis or by ulcers above the lateral condyle. In advanced cases, the reflux extends to the great saphenous vein of the lower leg through intersaphenous veins, and a rash may also be observed immediately above the medial condyle, together with varices in the medial side of the lower leg. In addition, when great and small saphenous varices are present simultaneously, venous stasis may occur in the entire circumference of the lower half of the lower leg.
2. Side branch varices: Also called branch varices. They are dilated and meandering superficial veins other than the saphenous vein that are not accompanied by varices or reflux in the truncal saphenous vein. As their solitary occurrence is relatively rare, careful examination is necessary to avoid overlooking saphenous varices.
3. Reticular veins: Blue and retiform dilated veins with a diameter of 2 to 3 mm.
4. Spider veins: Thin, reddish purple veins with a diameter of ≤1 mm.

Chronic venous insufficiency (CVI): Also called CVDs. CVI is defined as a "disease in which tiredness, edema, swelling, pain, secondary varices, eczema, skin sclerosis, and ulcers of the leg appear as a result of disturbances of the venous return to the heart due to some cause." It is caused by persistent venous hypertension of the leg from untreated DVT sequelae or varicose veins. It is recommended to determine the definitive CEAP classification to decide on a treatment plan.

Varicose syndrome: Also called stasis syndrome. This collectively refers to symptoms induced by venous stasis of the leg (from the foot to the lower leg: edema, malaise/tiredness, stasis eczema, purpura, pigmentation, hemosiderin deposition, white atrophy, and lower leg

ulcers). The syndrome is primarily caused by untreated primary varicose veins and DVT sequelae, and the treatment differs with the cause. The former should be treated with surgery of the varicose veins causing the symptoms, while the latter requires conservative treatments such as strict compression therapy. This syndrome is also called CVI or CVD.

CEAP classification: The CEAP classification adopted by the American Venous Forum in 1994 (revised in 2004) is widely applied to varicose diseases of the leg. In this classification, the clinical signs (C) are classified into 0 to 6, the etiology (E) into c, p, s, and n, the anatomic classification (A) are classified into s, p, d, and n, and the pathophysiological dysfunction (P) into r, o, and n (Table 2).

Deep vein thrombosis: DVT is primarily a condition in which thrombi are formed in the deep veins of the leg. Pulmonary embolism (PE) and DVT, which often concur, may be collectively called venous thromboembolism (VTE), or venous thrombosis. Virchow triad—(i) impairment of the endothelial cells, (ii) disturbance of the blood flow, and (iii) hypercoagulability—has been proposed as the cause of thrombosis. Recently, the view that DVT develops from thrombus formation in the soleal vein has also been presented. While its causes are diverse, DVT has been reported to occur in approximately half of patients after total knee replacement. While DVT and PE are occasionally called "economy class syndrome," this is not an appropriate name, as the condition also appears in situations other than air travel.

TABLE 2 CEAP classification.

Clinical classification
C0: No visible or palpable signs of venous disease
C1: Spider veins (telangiectasias; diameter ≤1 mm) or reticular veins (diameter ≤3 mm)
C2: Varicose veins (varicose veins with a diameter ≥3 mm when standing)
C3: Edema
C4: Skin lesions (C4a: pigmentation or eczema; C4b: lipodermatosclerosis or white atrophy)
C5: Healed venous ulcer
C6: Active venous ulcer
Etiological classification
Ec: Congenital
Ep: Primary
Es: Secondary
En: No venous cause identified
Anatomic classification
As: Superficial veins
Ap: Perforating veins (communicating veins)
Ad: Deep veins
An: No venous location identified
Pathophysiologic classification
Pr: Reflux
Po: Obstruction
Pr,o: Reflux and obstruction
Pn: No pathophysiology identifiable

Source: Eklöf et al.[2]

Guidelines for the prevention of DVT: Guidelines for the prevention of pulmonary thromboembolism and DVT (VTE). DVT is a cause of PE that occurs frequently (particularly after surgery and childbirth) and often leads to unfortunate outcomes. In Japan, therefore, preventative measures and medications began to be covered by national health insurance in 2004.

Post-thrombotic syndrome: The symptoms induced primarily by venous hypertension of the leg in the chronic period after DVT. In that period, symptoms are alleviated by the development of collateral blood flows and the reperfusion of deep veins. However, if the poor development of collaterals or deep vein valve insufficiency (valvular reflux) persist, the skeletal muscle pump of the leg does not function adequately, and sustained stasis of the venous blood results in leg tiredness, edema, swelling, pain, secondary varices, eczema, pigmentation, dermal sclerosis, and ulcers.

Thrombophlebitis: Phlebitis primarily caused by thrombosis of the superficial veins (distinct from DVT occurring in deep veins). It complicates conditions such as Buerger disease, Behçet disease coagulation/fibrinolytic abnormalities, thrombocytosis, and malignant tumor. However, in the leg, it often occurs with venous stasis. In the arm, it is often iatrogenic, being caused by intravenous injection.

Congenital varices: Inconspicuous congenital varices often cause venous dilation starting in children from school age. While their symptoms are similar to those of adult varices, stripping surgery is often indicated if the deep veins are patent. A characteristic congenital varices condition is Klippel-Trenaunay syndrome, which is accompanied by varicose veins, angioma (including venous anomalies), and elongation of the affected limb.

9.1 | Explanations of diagnoses/tests

Doppler auscultation: Examination of the blood flow state with an ultrasound Doppler auscultator (Figure 3). This examination is indispensable to the diagnosis of peripheral arterial occlusive disease and leg vein diseases. Doppler auscultators are the most useful diagnostic tool to use in initial examinations to screen for varicose veins of the leg and lower leg ulcers, as they are compact, lightweight, and easy to operate. Doppler auscultation must be performed with the patient in a standing position, using a probe coated with a sufficient amount of jelly to avoid compression of the skin. This allows for the confirmation of the presence of blood flow in the deep veins and of reflux in superficial veins (i.e., in the great and small saphenous veins and their branches). If a reflux murmur is heard when inducing reflux through the Valsalva maneuver or the lower leg milking maneuver, the condition is abnormal. Typically, no reflux murmur is heard in the superficial veins.

Trendelenburg test: A conservative test used to examine the valve function of the great and small saphenous veins and the

FIGURE 3 Doppler auscultators. Available types include those with an auscultator function only (left), and those that also allow the detection of the blood flow direction (right).

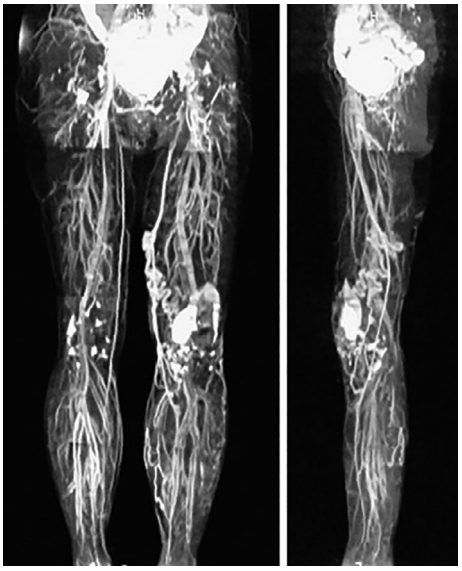


FIGURE 4 Magnetic resonance venography (left great saphenous vein varicosity). The image on the right is a lateral image of the left leg.

perforating branches. A patient with varicose veins is placed supine with the legs elevated to empty the superficial veins and varices (if varices are not emptied in this position, the deep veins are occluded or the varices themselves are filled with thrombi). While maintaining the elevation of the legs, a tourniquet (rubber band) is applied to the femoral region. The patient is asked to stand up, and the examiners verify whether the varices become filled with blood. If they fill immediately, there may be incompetent communicating branches at the foot side of the tourniquet or reflux of the small saphenous vein. If the varices show no marked swelling, there is only reflux of the great saphenous vein, which is prevented by the tourniquet. If swelling of the varices is confirmed after removing the tourniquet, valvular incompetence of the great saphenous vein is considered likely.

Perthes test: A conservative test to examine the patency of deep veins and the valve function of perforating branches. A tourniquet is applied to the femoral region of a patient with varicose veins after confirming the presence of varices in a standing position. The patient is then asked to perform a stepping movement or heel raises in this position. If the swelling of the varices is reduced by the action of the skeletal muscle pump, the deep veins are inferred to be patent. If no marked change is observed, incompetence of the communicating branches at the foot side of the tourniquet is inferred. On the other hand, if the varices are exacerbated, obstruction of the deep veins is suspected.

Leg venography: This test is primarily performed to confirm patency of the deep veins, and is conducted in a semi-standing or standing position using a fluoroscopic table. After tourniquets have been applied to the thigh, lower leg, and ankle, the dorsalis pedis vein is punctured, a contrast agent is injected, and the influx of the contrast agent into the deep veins is imaged at the same time as it is confirmed fluoroscopically. Once the deep veins are visualized, the tourniquets are released, and the branches and varicose veins are observed. Although this is an invasive test, its range of visualization is limited.

Contrast-enhanced computed tomography (CT) of the leg: A contrast agent is generally injected through an arm vein, and CT images are obtained in the venous phase of the leg by adjusting the timing of the scanning to enhance the imaging ability of the leg veins. The preparation of three-dimensional images is useful as a preoperative examination. In addition, if there are thrombi, they can be observed as filling defects.

Color Doppler ultrasonography of the leg: Although the courses of the veins and varices and the locations of the branches and perforating branches can be examined with ultrasound tomography, the simultaneous use of duplex scanning enables a close examination not only of the superficial veins, but also of the presence of perforating branch incompetence and of the state of the deep veins.

Magnetic resonance venography of the leg: A noninvasive examination of the leg veins using magnetic resonance imaging (MRI). By emphasizing liquid signals based on T2-weighted imaging and by specifying the direction of the blood flow, veins can be visualized selectively by eliminating the effects of the arteries. This examination provides detailed information about the deep and superficial veins and their communicating branches. When three-dimensional images are prepared, it is the most useful preoperative evaluation procedure. However, clear images may not be obtained if lower leg edemas or similar conditions are present. In addition, it is contraindicated in patients who have a heart pacemaker or metallic foreign material in their body (Figure 4).

Venous plethysmography of the lower leg: A noninvasive examination of the lower leg veins. The venous return function is evaluated by measuring the changes in the lower leg volume associated with changes in the body position, exercise loading, and avascularization. Variations of this test include air plethysmography, photoplethysmography, and strain gauge plethysmography, although air plethysmography has recently become the most commonly used.

The venous return function of the lower leg skeletal muscle pump can be evaluated/quantified through muscle pump plethysmography, and the compression method can be used to check for circulatory disturbance of the deep veins.

Ankle brachial pressure index (ABI or ABPI): The blood pressure is measured in the arm and leg (usually in the posterial tibial and dorsalis pedis arteries), and their ratio (leg blood pressure/arm blood pressure) is calculated. The normal range is 1.0 to 1.4, while values of ≤0.9 are generally considered abnormal. However, the ABI may be normal in arteriosclerosis of the leg. Currently, this examination can be performed rapidly with a blood pressure/pulse wave measurement device (ABI/PWV). These devices simultaneously measure the arterial pressure and the pulse wave velocity in the four limbs, allowing the differentiation between a normal state and arteriosclerosis.

9.2 | Explanation of treatments

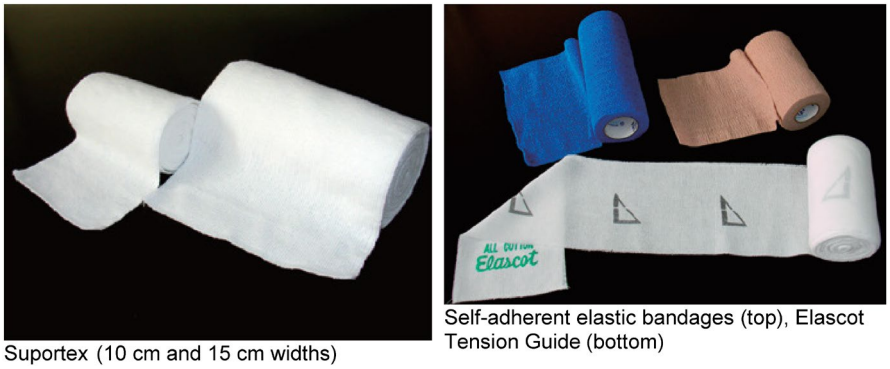
Compression therapy: The most important conservative treatment for varicose veins, DVT, and lymphedema. Elastic bandages or elastic stockings are used. If there are ulcers, it is easy to use an elastic bandage that can be wound around the limb while adjusting the compression pressure. If there are no ulcers, stockings are convenient. However, caution must be taken in patients with peripheral arterial stenosis of the leg. It has been reported that compression therapy should particularly be avoided in patients with ABI values <0.8. When there are ulcers and stronger compression pressure is needed, an elastic bandage with a lower elasticity is sometimes effective when concomitantly used as a second layer of wrapping to provide pressure. Elastic bandages or stockings are applied immediately after rising in the morning, and are worn until bedtime. The legs are elevated by approximately 10 cm during sleep (by placing two cushions under the lower legs). Compression therapy should be continued in limbs with varices not treated surgically, and for 2 to 3 months after surgical treatment.

Elastic bandages: Stretchable bandages used for compression therapy. Elastic bandages are relatively inexpensive and allow for adjustment of the compression force and area. However, they are prone to being displaced or loosened, and they can apply force unevenly depending on how they are applied. Nevertheless, if there are ulcers, they are easier to use than stockings as they cause less pain from the compression and are less likely to allow displacement of the gauze covering the ulcers. They should be applied starting from the foot, and a 10-cm-wide bandage should be used to compress the lower leg, while a 15-cm-wide product should be selected to compress the entire leg. Some practice is required to be able to wrap the bandage around the leg in a way that provides uniform compression. Therefore, there are self-adherent elastic bandages that stick to themselves just by wrapping, and others that come with guides to make them easy to apply for uniform pressure (Figure 5).

Elastic stockings/socks: Stockings used to treat leg vein disorders and lymphedema. Elastic stockings are also used to prevent intraoperative or postoperative DVT. They exist as pantyhose, thigh-high stockings, and knee-high socks, with or without a toe section. They are sold by multiple manufacturers, and are labeled by size (SS, S, M, L, LL) and compression force (strong, medium, mild) to allow for selection according to the length and thickness of the leg. They also have various material thicknesses, and thicker fabric is preferable for lymphedema treatment. Sufficient explanations must be provided to patients receiving compression therapy with stockings. They must be told that stockings of an appropriate size are difficult to put on at first, that those easy to put on are not a good fit for their leg (they lack compression force), and that rubber kitchen gloves make them relatively easy to put on (Figure 6). Devices providing assistance to put on elastic stockings are also sold (Figure 7).

Support stockings/socks: These elastic stockings are articles of clothing marketed as “tightening stockings” or “compression stockings.” As sufficient grip strength is needed to put on medical stockings, elderly patients and those with reduced grip strength may be recommended to wear multiple layers of support stockings.

Surgery for varicose veins: Comprehensive term for surgical treatments of primary varicose veins. Procedures such as stripping, high ligation, sclerotherapy, endovenous ablation, and subfascial endoscopic perforator vein surgery are insured treatments. Regardless of the procedure selected, the surgery must be performed after checking the patency of the deep veins, marking the locations of the veins by Doppler auscultation and ultrasound examination with patients in the standing and recumbent positions, and determining the site of the surgery. The different surgical methods are described below.



Suportex (10 cm and 15 cm widths)

Self-adherent elastic bandages (top), Elascot Tension Guide (bottom)

FIGURE 5 Elastic bandages.

FIGURE 6 Elastic stockings. Pantyhose (upper left), thigh-high stockings (upper right), knee-high socks (lower left), rubber gloves used for weak grips (lower right).

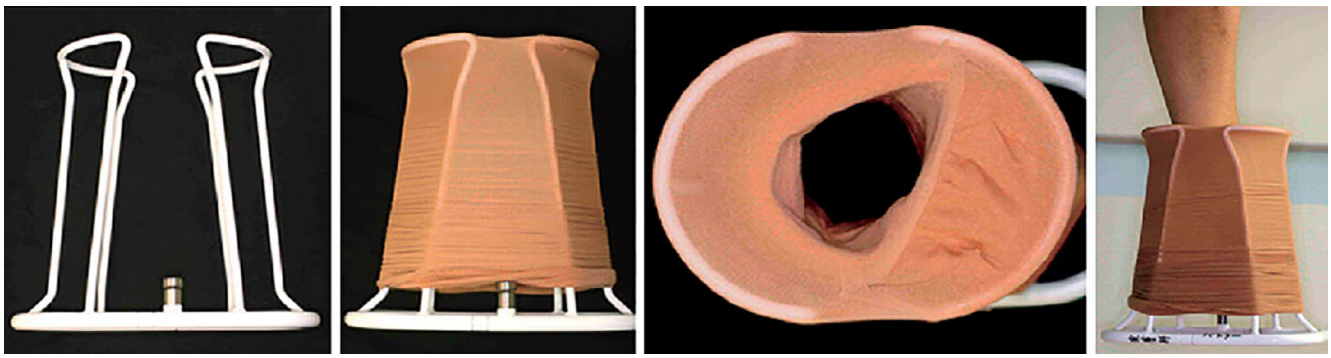


FIGURE 7 Assistance device for application of elastic stockings (Butler). Other application assistance devices include Easy Slide, Doff N′ Donner, and Stocking Donner.

Stripping: This is the procedure of choice when the dilation of the saphenous vein is pronounced (criterion for thick varices: the diameter of the great saphenous vein in the inguinal region is ≥8 mm when standing, although this criterion differs between facilities) or when there is a marked venous tortuosity. It is a radical treatment that involves extraction of the saphenous vein that has developed valvular incompetence. It provides consistent results as it also blocks incompetent communicating branches. Recently, an increasing number of facilities have been using tumescent local anesthesia, which allows the patient to move their ankle joint or to walk immediately after the operation, as it prevents the postoperative development of venous thrombi.

After high ligation and separation of the great saphenous vein in the inguinal region, a stripping wire is inserted from the great saphenous vein in the lower leg toward the inguinal region, an olive head is affixed, and the vein is stripped (Babcock stripping); or the vein is tied to the stripping wire so that it can be invaginated and stripped (invagination stripping). While the latter causes less nerve damage, caution is needed, as the vein can rupture during the stripping procedure. Although the procedure is occasionally called radical varicectomy, recurrence (i.e., reflux via another superficial vein) is reportedly observed in 30% to 40% of patients 5 years after surgery.

High ligation: This procedure is selected when the dilation of the saphenous vein is moderate. It is performed under local anesthesia. A skin incision is made slightly inferiorly to the inguinal crease for great saphenous varices, and in the popliteal region for small saphenous varices. The subcutis is detached to expose the saphenous vein, the site of its drainage into a deep vein is identified, and the saphenous vein is removed after double ligation to prevent stenosis. The branches that drain into deep veins are simultaneously ligated and separated. Recurrence has been observed when high ligation is performed alone. Therefore, many facilities will perform ligation and separation at three sites (namely, in a high position and above and below the knee), and will follow it up with sclerotherapy at a later date.

Sclerotherapy: A treatment for small varices that involves the injection of a sclerosing agent into the varices. Polidocanol is covered by national insurance. After using a fine needle (e.g., 27 G and 30 G) to inject 0.5% to 3% polidocanol into the varices, the site is compressed with an elastic bandage (compression sclerotherapy). Recently, a method by which polidocanol is mixed with air, foamed, and injected (foam sclerotherapy) has also been used. However, this procedure is not indicated for varicose veins and saphenous varices exceeding 8 mm in diameter in a standing position. Therefore, it is usually not performed alone for varicose veins that may cause leg ulcers.

Endovenous ablation for varicose veins of the leg: The efficacy of this procedure is equal to that of stripping for saphenous vein varicosities. It involves ablating the varicosities using a catheter. Both endovenous laser ablation (980 nm and 1470 nm) and radiofrequency ablation are covered by national health insurance. The procedure is performed by puncturing the saphenous vein under ultrasonic guidance, anesthetizing the area of the vein to ablate with tumescent local anesthesia, and inserting the tip of laser fibers or a radiofrequency ablation device into the saphenous vein

inferiorly to its junction with a deep vein under ultrasonic guidance. The vein is then ablated under ultrasonic confirmation, and the process is repeated while withdrawing the ablation device in order to ablate/occlude the saphenous vein. As such, this procedure is not indicated in the presence of marked tortuosity or when the diameter of the varicosity is large. Since this surgery carries the risk of formation of an endovenous heat-induced thrombus near the junction of the saphenous vein and the deep vein that can result in DVT, repeated postoperative ultrasonic screening is required. In addition, national health insurance can only be applied to endovenous ablation when it is performed by a physician who has undergone specific training.

Indications and exclusion criteria described in the "Guidelines for Endovenous Treatment of Varicose Veins of the Leg"
1. Indications
(i) Deep veins are patent.
(ii) The average diameter of the saphenous vein 5–10 cm distal to the saphenous-femoral junction (SFJ) or the saphenopopliteal junction is at least 4 mm. Moreover, an average diameter no greater than 10 mm is recommended.
(iii) There are symptoms of varicose veins (e.g., tiredness, pain, edema, and leg cramps) or there is stasis dermatitis.
(iv) Endovenous treatment is not indicated when the terminal valve is competent and no valvular incompetence is found at the SFJ, even if it is found in the saphenous vein. However, this excludes cases in which the Dodd perforator is a cause of reflux.
2. Exclusion criteria: The exclusion criteria for endovenous treatment are as follows.
(i) CEAP clinical class C1 (spider/reticular varicose veins)
(ii) The patient has DVT or a history of DVT.
(iii) The patient has an arterial blood flow disorder.
(iv) The patient has difficulty walking.
(v) The patient has multiple organ failure or disseminated intravascular coagulation.
(vi) The patient is taking oral contraceptives or hormones.
(vii) The patient has severe heart disease.
(viii) The patient is in shock or pre-shock.
(ix) The patient is pregnant or may be pregnant.
(x) The patient is undergoing steroid therapy.
(xi) The patient has Behçet disease.
(xii) The patient is taking osteoporosis medicine (raloxifene) or multiple myeloma medication (thalidomide).
(xiii) The patient has predisposing factors to thrombosis (e.g., protein C deficiency, protein S deficiency, antithrombin III deficiency, and antiphospholipid syndrome).

Drawn from *Jpn J Phleb*. 2010;21(4):289–309.

Subfascial endoscopic perforator vein surgery: This procedure is indicated when pigmentation, sclerosis, atrophy, or ulcers are present across a large area of the leg skin. It is also indicated if incompetent perforating branches are identified via ultrasound, reflux is observed in these veins, or if previous surgery for varicose veins is expected to be insufficient. This procedure replaces open perforator ligation (Linton procedure). An endoscope is inserted from the cephalic side of the location of the incompetent perforating branch, and the latter is ablated/removed subfascially, or is ligated using clips.

External medications: These are drugs applied through the skin or directly to skin lesions for local treatment. They are prepared by compounding various active ingredients with a base.

Wound-dressing materials: Wound-dressing materials can be classified into dressing materials (modern dressing materials) and medical materials such as gauze (classic dressing materials). The former are medical materials designed to provide an optimal environment for wound healing by maintaining a moist environment. They must be used selectively according to the state of the wound and the amount of exudate. The latter types allow the wound to dry and cannot maintain a moist environment if the amount of exudate is low. Other medical materials, aside from conventional gauze, that provide an optimal environment for wound healing by covering the wound and maintaining a moist environment, may also be called wound-dressing materials or dressing materials.

Dressing materials: Modern wound-dressing materials used to create a moist environment for wounds. Conventional sterilized gauze is excluded.

10 | BASIC PRINCIPLES BEHIND THE GUIDELINES AND THE DIAGNOSTIC AND THERAPEUTIC ALGORITHMS

The basic principle informing the design of the present guidelines is to assist the differential diagnosis of disturbances of the venous return, which are the predominant cause of lower leg ulcers, and the selection of appropriate treatment. In venous ulcers of the lower leg, it is important to treat the cause, venous stasis (venous hypertension). Therefore, while our algorithm includes compression therapy as the most important element, it also shows the selection of surgery and sclerotherapy for primary varices, and the necessity of strict compression therapy for secondary varices.

Figure 8 shows a diagnostic and therapeutic algorithm based on the above basic principle.

11 | SUMMARY OF CLINICAL QUESTIONS

Table 3 shows the clinical questions (CQs), the level of recommendation, and a description of the recommendation for each.

CQ1: If leg ulcers are present, is it useful to evaluate leg veins as a potential cause?

Description of the recommendation: As a majority of leg ulcers are caused by venous circulatory disorders, we recommend evaluating the possibility of leg ulcers caused by primary or secondary varicose veins.

Level of recommendation: 1C.

Commentary:

- As there is only one analytical epidemiological study[3] and few expert opinions[4–6] on the causes of lower leg ulcers, the evidence level is IVb. However, because it is widely known that disturbances of the venous return frequently cause leg ulcers, the level of recommendation is 1C.
- In the United States, there are 600 000 new cases of lower leg ulcers annually, and approximately 80% of them are reported

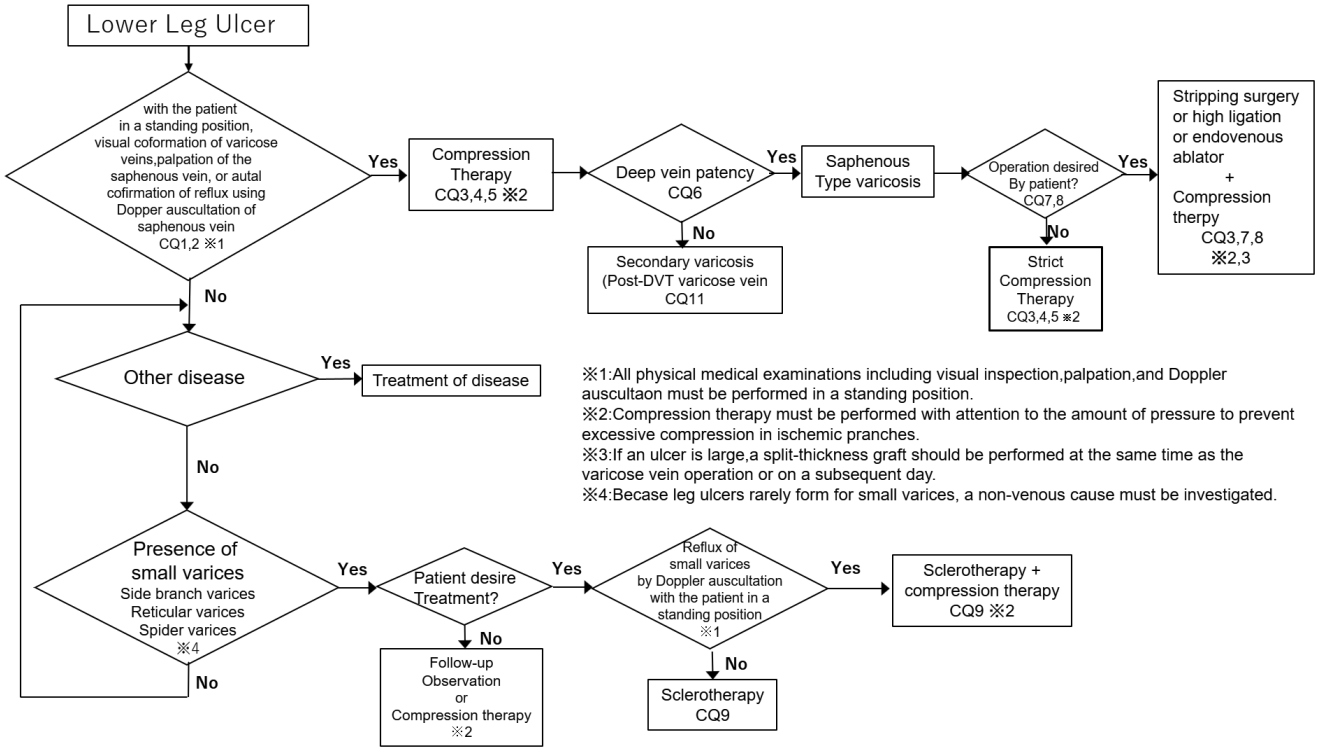


FIGURE 8 Diagnostic and therapeutic algorithm for lower leg ulcers and varicose veins (excluding congenital varicose veins and similar conditions).

to be caused by disturbances of the venous return.[3,4] A report from Germany indicated that approximately 80% to 90% of lower leg ulcers were caused by vasculopathy.[5] In Japan, their precise incidence is unclear, because there has been no large-scale epidemiological investigation of lower leg ulcers. However, it is crucial to evaluate venous ulcers (caused by primary and secondary varicose veins) as possible causes of lower leg ulcers.[6–8]

- When there are lower leg ulcers, an evaluation of suspected venous ulcers (due to primary or secondary varicose veins) should be performed. However, as vascular disorders are uninvolved in approximately 10% of lower leg disorders, efforts must be made to identify the cause.[3–5]
- Certain medical history features and venous ulcer symptoms often allow for a differential diagnosis of lower leg ulcers from other causes during a medical interview. Prior to the development of ulcers, it is common to observe swelling, tiredness, and itching of the lower leg more commonly in the evening than in the morning. These are symptoms of primary leg varices and DVT. Patients also often complain of cramping while sleeping at night. Primary varicose veins are often observed in patients who work standing up and in those with a history of sports involving the application of force onto the legs. DVT presents with blood coagulation disorders, protracted bed rest, a history of malignant tumor, trauma, immobilization of the legs, or prior surgeries (particularly a history of treatment with knee or hip replacement surgery). Therefore, the medical interview is important.[6,8]

CQ2: When evaluating leg ulcers, is it useful to perform Doppler auscultation of the leg veins?

Description of the recommendation: We recommend Doppler auscultation of the leg veins with the patient in a standing position for leg ulcer evaluation.

Level of recommendation: 1C.

Commentary:

- As they are compact, lightweight, and easily operated, Doppler auscultators can be used to diagnose incompetence of the leg veins—the most common cause of leg ulcers—simply and reliably. A case-control study[9] reported that in typical cases, the performance of Doppler auscultation ahead of time enabled an accurate diagnosis of venous incompetence even if no ultrasound was performed. Another report[10] indicated that Doppler auscultation provided nearly the same sensitivity and specificity as ultrasound for the confirmation of reflux in superficial veins. Doppler auscultation remains a useful diagnostic screening method to date,[1,11–13] and it can be performed easily in an outpatient setting. Therefore, it was given a recommendation level of 1C. Moreover, there are no papers with a high evidence level, as it is a widespread method.
- The usefulness of Doppler auscultation has been confirmed ever since Sigel et al. compared a diagnosis obtained using the Doppler method with venography findings in 1967.[14] Koyano et al. reported that the rate of agreement between Doppler findings and the venography gold standard was 72% to 96%. Doppler auscultation is

TABLE 3 Summary of clinical questions.

Clinical question	Level of recommendation	Description of the recommendation
CQ1: If leg ulcers are present, is it useful to evaluate leg veins as a potential cause?	1C	As a majority of leg ulcers are caused by venous circulatory disorders, we recommend evaluating the possibility of leg ulcers caused by primary or secondary varicose veins.
CQ2: When evaluating leg ulcers, is it useful to perform Doppler auscultation of the leg veins?	1C	We recommend Doppler auscultation of the leg veins in a standing position for leg ulcer evaluation.
CQ3: Is compression therapy useful for leg ulcers caused by primary or secondary varicose veins?	1A	Compression therapy for venous leg ulcers leads to faster ulcer improvement and a higher healing rate. Therefore, we strongly recommend compression therapy for leg ulcers caused by primary or secondary ulcers.
CQ4: Is debridement useful for leg ulcers (caused by primary or secondary varicose veins) that have necrotic material?	1C	The removal of necrotic material from leg ulcers speeds up their reduction. Therefore, we recommend debridement, particularly active surgical debridement.
CQ5: Are topical medications or dressing materials useful for leg ulcers caused by primary or secondary varicose veins?	2A	We propose the use of topical medications and dressing materials as one option. However, the fundamental treatment for venous leg ulcers is compression therapy.
CQ6: Is the use of imaging to confirm the patency of deep veins useful for varicose veins of the leg?	1A	For varicose leg veins, we recommend confirming the patency of deep veins with vascular ultrasound (color Doppler ultrasound), contrast-enhanced CT of the venous phase, magnetic resonance venography, leg venography, or similar methods as part of the preoperative examination.
CQ7: Are stripping and high ligation useful for leg ulcers caused by primary varicose veins?	1A	We recommend varicose vein surgery (stripping, high ligation) on the saphenous vein for leg ulcers caused by primary varicose veins.
CQ8: Is endovenous ablation (laser, radiofrequency) useful for leg ulcers caused by primary varicose veins?	1A	Endovenous ablation surgery of the legs with laser or radiofrequency has the same effectiveness as the conventional treatments of stripping and high ligation. Therefore, we recommend endovenous ablation surgery for leg ulcers caused by primary varicose veins.
CQ9: Is sclerotherapy useful for leg ulcers caused by varicose veins?	1A 2A	For leg ulcers caused by small varices (excluding the saphenous vein—i.e., side branch varices, reticular varices, spider varices), we recommend the use of sclerotherapy together with compression therapy (1A). However, as the use of polidocanol (Polidocasklerol) in the main trunk of the saphenous vein is not covered by insurance in Japan, we propose it as one option for saphenous varicose veins (2A).
CQ10: Are skin grafts useful for leg ulcers caused by primary varicose veins?	2A	We propose skin grafts as one option for the treatment of leg ulcers caused by primary varicose veins. However, the basic treatments for leg ulcers caused by primary varicose veins are surgery for varicose veins (stripping, high ligation, endovenous ablation) and compression therapy.
CQ11: Is surgery for varicose veins (stripping, high ligation, and endovenous ablation) *contraindicated* for secondary varicose veins?	1A	If the deep veins of a patient with secondary varicose veins caused by DVT are not patent, there is an extremely high risk that surgery for varicose veins will worsen the venous circulation. Therefore, *we recommend not performing* surgery for varicose veins.

becoming more widely used as an easy-to-perform, noninvasive diagnostic method.[15]

- The test is performed with the patient in a standing position, with lower leg milking or the Valsalva method used to induce reflux. If the sound of reflux can be heard in the surface veins, it is possible to diagnose varicose veins or superficial venous incompetence. When placing the probe immediately over the great or small saphenous vein and listening, secondary varices can be suspected if a continuously rising sound is heard.[1] In addition, in some cases, blood flow sounds in superficial veins are not confirmed with a Doppler auscultator when there are old secondary varices.[13] In these cases, it is necessary to use an imaging test or similar method to check for DVT (Figure 9).

CQ3: Is compression therapy useful for leg ulcers caused by primary or secondary varicose veins?

Description of the recommendation: Compression therapy for venous leg ulcers leads to faster ulcer improvement and a higher

FIGURE 9 Method for examination of superficial veins of the leg with Doppler auscultation. First, while the patient is standing, the probe is placed against the skin directly above the great saphenous vein or a varicose vein at the medial side of the knee, and the presence of venous reflux is examined while compressing and releasing the calf (left figure). Next, the probe is placed at the base of the great saphenous vein, and the presence of reflux is again examined in a similar manner (right figure). If reflux is heard, valvular incompetence in the superficial veins can be diagnosed. Auscultation of the small saphenous vein is performed in the same manner, below the popliteal region of the posterior lower leg. If continuous arterial sounds (rising sounds) are heard at the saphenous vein while the patient is in a standing position, a circulation disturbance in a deep vein (such as deep vein thrombosis) is suspected.

healing rate. Therefore, we strongly recommend compression therapy for leg ulcers caused by primary or secondary ulcers.

Level of recommendation: 1A.

Commentary:

- There are four systematic reviews of compression therapy for venous ulcers of the leg.[16–19] The evidence level is I, and the level of recommendation is 1A.
- When performing compression therapy for venous ulcers of the lower leg, the superficial veins become compressed, and the venous reflux is physically restrained. As a result, lower leg ulcers improve faster than when left untreated, and the cure rate increases.[16] Moreover, the continuation of compression therapy after venous ulcers of the lower leg are cured reduces the recurrence rate.[17] In addition, lower patient compliance with compression therapy increases the recurrence rate of lower leg ulcers.[20] Therefore, we recommend explaining the importance of compression therapy to patients even after lower leg ulcers have healed and continuing the treatment.
- While lower leg ulcers caused by DVT sequelae are intractable, improvement can be expected from strict compression therapy for mild to moderate lesions.[18] Moreover, the incidence of DVT sequelae can be significantly reduced by the continuation of compression therapy after the onset of the condition.[19,21]
- Regarding the mechanism of the therapeutic effect, compression therapy is considered to physically prevent the reflux of venous blood and to mitigate venous hypertension of the leg by compressing the superficial veins, which leads to cure of the lower leg ulcers.
- Compression therapy is a basic treatment that should be performed as often as possible for venous ulcers of the lower leg. However, if the ulcers are complicated by peripheral arterial disease, compression therapy may induce ischemia in the leg. When peripheral arterial disease is present, compression therapy can lead to arterial blood flow disturbances. Therefore, if the ABI suggests arterial blood flow disturbance, compression therapy must be performed with caution to avoid excessive or uneven compression. It has also been proposed that the arterial blood flow should be evaluated by performing Doppler auscultation of the posterior tibial artery and the interdigital arteries before and after compression therapy.[8,13]
- When performing compression therapy with elastic bandages (Figure 5) or elastic stockings (Figure 6), it is important to ensure appropriate pressure by using the correct materials, as shown below. Elastic bandages are more effective than ordinary nonelastic bandages. Figure 10 shows an example of compression therapy using an elastic bandage.
- As the therapeutic effect varies with the degree of compression at the ankle, the pressures shown in the table should be adapted according to the patient's condition (Table 4). The degree of compression at the ankle can be measured with an instrument designed to measure the body pressure at the sites of pressure ulcers. Just like elastic bandages, elastic stockings should be selected by seeking the appropriate pressure at the ankle for the disorder in question. However, elastic stockings may be difficult to put on because of their low stretching range. The use of Butler, a device to assist with putting on elastic stockings, or rubber gloves may facilitate their application (Figure 7).

CQ4: Is debridement useful for leg ulcers (caused by primary or secondary varicose veins) that have necrotic material?

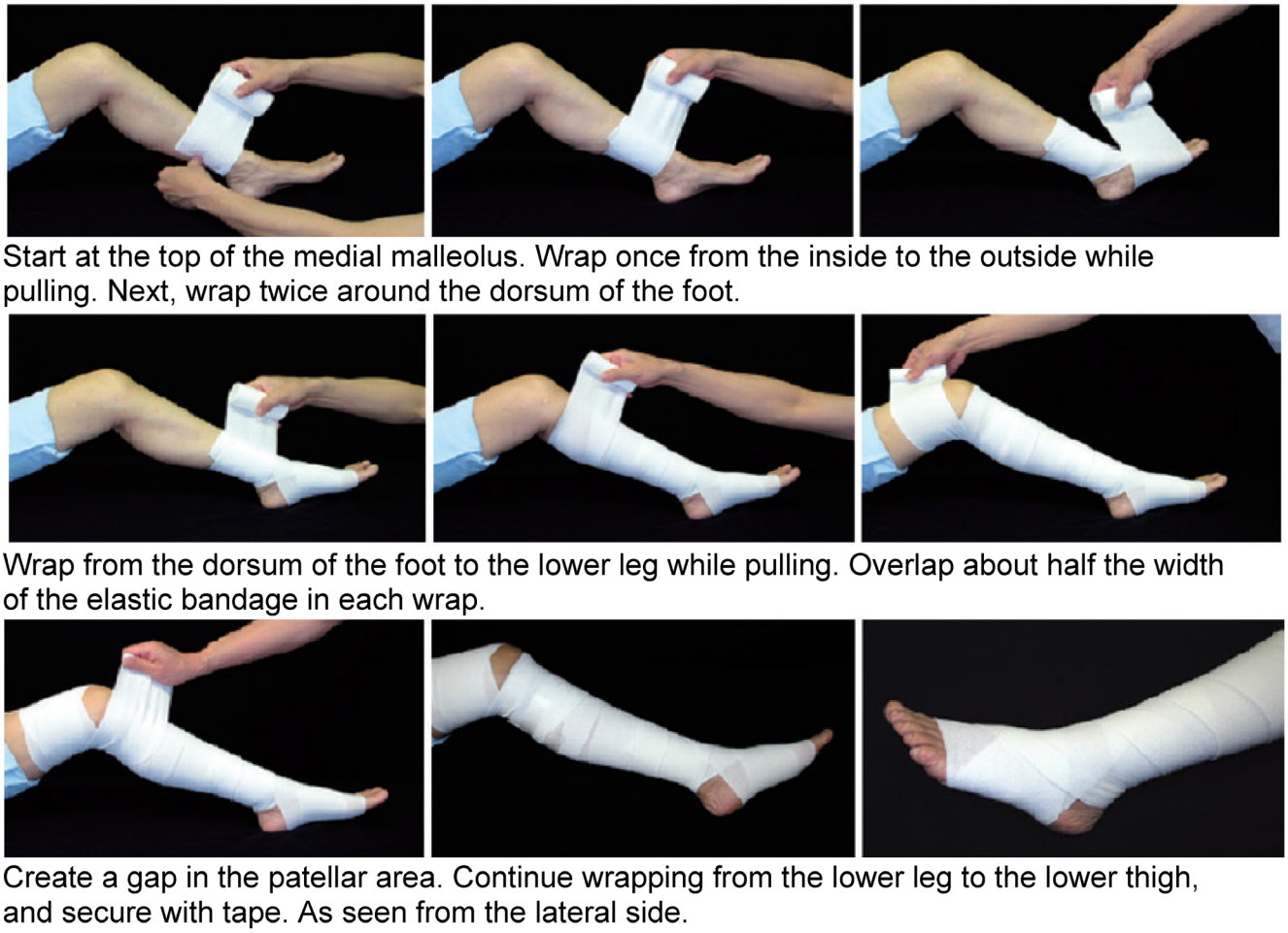


FIGURE 10 Example of how to wrap an elastic bandage (10 cm width).

TABLE 4 Ankle pressures (in mm Hg units).

<20	Prevention of thrombosis, prevention of varicose leg veins, following varicose vein stripping surgery, edema due to various other conditions
20–30	Mild varicose veins, varicose veins in the elderly
30–40	Ordinary varicose veins, following sclerotherapy, sequelae of venous thrombosis (mild)
40–50	Leg ulcer with varicose veins, varicose veins with severe edema, sequelae of deep vein thrombosis, lymphedema
>50	Severe lymphedema

Quoted and adapted from Sakaguchi S, ed. Clinical Phlebology. Nakayama Shoten, 1993.

Description of the recommendation: The removal of necrotic material from leg ulcers speeds up their reduction. Therefore, we recommend debridement, particularly active surgical debridement.

Level of recommendation: 1C.

Commentary:

- Regarding the usefulness of debridement for venous ulcers of the lower leg, a cohort study about surgical debridement[22] reported that the removal of necrotic material promoted satisfactory granulation. Therefore, the evidence level is IVa and the level of recommendation is 1C. Moreover, according to expert opinions,[23–25] the regression of ulcers was significantly faster in a group that received surgical debridement than in a group that did not.
- Inactive tissues such as necrotic materials generally have reduced resistance to infection, which allows the proliferation of bacteria, and delays wound healing. Debridement is performed to remove such necrotic tissue and excessive bacteria, and to eliminate factors that impede healing.[26]
- The removal of necrotic material has also been reported to promote satisfactory granulation in ulcers caused by secondary varices.[22] Therefore, debridement should actively be performed for venous ulcers that have necrotic material attached to their

surface. For debridement other than surgical, refer to the guidelines on wounds in general and on pressure ulcers.

CQ5: Are topical agents or dressing materials useful for leg ulcers caused by primary or secondary varicose veins?

Description of the recommendation: We propose the use of topical agents and dressing materials as one option. However, the fundamental treatment for venous leg ulcers is compression therapy.

Level of recommendation: 2A.

Commentary:

- There are a few systematic reviews that have investigated the utility of topical agents and dressing materials for venous ulcers of the lower leg. Therefore, the evidence level is I.[27–31] However, as the fundamental treatment for venous ulcers of the lower leg is compression therapy, the use of topical agents and dressings is supplementary. Therefore, the level of recommendation is 2A.
- For lower leg ulcers caused by primary varices of the saphenous vein, varicose vein surgery (stripping, high ligation, endovenous ablation) is the first choice to correct the causative state of the venous hypertension.[1]
- However, if consent for surgery cannot be obtained, if surgery cannot be performed because of complications, or if it is contraindicated because the deep veins are not patent due to post-DVT secondary varices, topical agents and dressing materials may be used in conjunction with compression therapy to create a moist environment to promote ulcer healing. However, no clear difference in the healing of ulcers according to the type of topical agent or dressing material has yet been presented.[27–36]
- Specifically, if there is necrotic tissue in the ulcer, topical agents and dressing materials are applied after debridement (CQ4). For more details, refer to the guidelines on wounds in general and on pressure ulcers.
- If compression therapy causes intense pain at the ulcer site, ethyl aminobenzoate ointment 10%, a topical local anesthetic, can be prescribed in Japan as an effective external anesthetic for skin ulcers.[1,37] In addition, xylocaine jelly 2% (lidocaine hydrochloride jelly 2%), a lubricant and surface anesthetic, can also be used. However, as both drugs can cause contact dermatitis—or in rare cases, shock or poisoning symptoms—it is necessary to perform a thorough medical interview with the patient and to evaluate his or her condition before using them.

CQ6: Is the use of imaging to confirm the patency of deep veins useful for varicose veins of the leg?

Description of the recommendation: For varicose leg veins, we recommend confirming the patency of deep veins with vascular ultrasound (color Doppler ultrasound), contrast-enhanced CT of the venous phase, magnetic resonance venography, leg venography, or similar methods as part of the preoperative examination.

Level of recommendation: 1A.

Commentary:

- As varicose veins may be secondary varices, it is necessary to confirm the patency of deep veins to determine the therapeutic strategy. There are four meta-analyses of imaging examinations for the diagnosis of the presence or absence of DVT.[38–41] Therefore, the evidence level is I and the level of recommendation is 1A. However, the diagnosis of chronic DVT has been reported to be difficult even when using imaging tests.[42,43]
- In meta-analyses on the diagnosis of DVT, vascular ultrasound (color Doppler ultrasonography) and magnetic resonance venography were nearly the same as leg venography.[38,39] In another meta-analysis,[40] the results of venous phase contrast-enhanced CT and of vascular ultrasonography were comparable.
- While leg venography was once regarded as the gold standard of imaging techniques for the diagnosis of DVT,[44] it has recently been used less frequently because of its invasiveness and complexity. The usefulness of vascular ultrasonography, venous phase contrast-enhanced CT, and magnetic resonance venography as alternatives has been reported in one meta-analysis of each modality.[38–40] Regarding vascular ultrasonography (a minimally invasive examination), the diagnostic sensitivity for central DVT was reported to be 94.2%, while the diagnostic sensitivity and specificity for peripheral DVT were 63.5% and 93.8%, respectively.[38] Regarding magnetic resonance venography (which includes multiple different imaging methods), the diagnostic sensitivity and specificity were reported to be 91.5% and 94.8%, respectively, in comparison with venography.[39] The sensitivity and specificity of contrast-enhanced CT for the diagnosis of DVT were reported to be 95.9% and 95.2%—i.e., similar to those of vascular ultrasonography.[40] Based on these reports, all of these imaging modalities are considered useful for diagnosing DVT and confirming deep vein patency.
- Post-thrombotic syndrome after DVT is a frequent cause of secondary varices. However, the DVT may go undiagnosed, as it often shows no clinical symptoms.[45] In particular, there is no indication for varicose vein surgery if the deep veins are occluded (CQ9), and the patency of the deep veins must therefore be confirmed. The risk factors of DVT include predisposition to thrombosis, prolonged immobility, prolonged surgery, old age, obesity, malignant neoplasms, hormone therapy, fracture or plaster cast immobilization of the leg or foot, and leg paralysis.[46,47] These must be confirmed in a medical interview. Moreover, if there is swelling in the leg, no reflux is heard during Doppler auscultation despite dilation of the superficial veins, and venous murmurs ascending the superficial veins can be heard when the patient is standing still, a thorough examination should be actively performed with secondary varices in mind.[42]

CQ7: Are stripping and high ligation useful for leg ulcers caused by primary varicose veins?

Description of the evaluation: We recommend surgery for varicose veins (stripping, high ligation) on the saphenous vein for leg

ulcers caused by primary varicose veins. Regarding endovenous ablation, which yields equivalent results to surgery for varicose veins, see CQ8.

Level of recommendation: 1A.

Commentary:

- As there is a systematic review[48] that combines large-scale RCTs, the evidence level is I and the level of recommendation is 1A. When performing surgery (stripping, high ligation) on the saphenous vein in addition to compression therapy for lower leg ulcers caused by primary varices, the recurrence rate after cure of the lower leg ulcers was found to be significantly lower than after compression therapy alone, although there was no difference in the initial cure rate.[49,50] However, it is not clear whether surgical therapy is superior to compression therapy.
- We recommend surgery (stripping, high ligation) for the treatment of venous ulcers of the lower leg caused by primary varices that do not respond to compression therapy, for lower leg ulcers in which compression therapy cannot be performed, or to reduce the risk of recurrence after the ulcers have been cured. However, the benefits and risks of each procedure must be explained, and the patient's consent must be obtained before performing varicose vein surgery.

CQ8: Is endovenous ablation (laser, radiofrequency) useful for leg ulcers caused by primary varicose veins?

Description of the recommendation: Endovenous ablation surgery of the legs with laser or radiofrequency has the same effectiveness as the conventional treatments of stripping and high ligation. Therefore, we recommend endovenous ablation for leg ulcers caused by primary varicose veins.

Level of recommendation: 1A.

Commentary:

- Endovenous ablation for primary varices has been the subject of systematic reviews and meta-analyses[51–54] that have analyzed multiple RCTs. Therefore, its evidence level is I. In addition, it shows equivalent or superior utility to conventional surgical therapies, and US[55] and UK[56] guidelines recommend it over stripping or high ligation. Therefore, its level of recommendation is 1A.
- The guidelines for venous leg ulcers in the United States recommend endovenous ablation and surgery equally.[57] However, there is no direct evidence that the endovenous ablation of venous leg ulcers helps to improve the healing rate or to shorten the healing time.[48,58]
- In Japan, two modalities—endovenous laser treatment (980 and 1470 nm) and radiofrequency treatment—and four device models are currently covered by national health insurance. An RCT compared the efficacy and complications from each device model and reported that the 1470-nm laser[59] and the radiofrequency device[60] resulted in fewer complications than the 980-nm lasers, while showing equivalent efficacy.
- Endovenous ablation is only eligible for national health insurance coverage when performed by a physician who has completed specific training. In addition, the procedure should be performed according to the Guidelines for Endovenous Treatment of Varicose Veins of the Leg[61] prepared by a committee of the Japanese Society of Phlebology.

CQ9: Is sclerotherapy useful for leg ulcers caused by varicose veins?

Description of the recommendation: For leg ulcers caused by small varices (excluding the saphenous vein—i.e., side branch varices, reticular varices, spider varices), we recommend the use of sclerotherapy together with compression therapy (1A). However, because the use of polidocanol (Polidocasklerol) in the main trunk of the saphenous vein is not covered by insurance in Japan, we propose it as one option for saphenous varicose veins (2A).

Level of recommendation:

1A for sclerotherapy for small varices.
2A for sclerotherapy for saphenous vein varicosity.

Commentary:

- There are two systematic reviews of sclerotherapy for varicose leg veins. Therefore, the evidence level is I. In terms of clinical symptoms and aesthetic outcome, sclerotherapy was more effective than compression therapy alone.[62] However, there was a higher recurrence rate after sclerotherapy than after surgery.[63] We determined a recommendation level of 1A for sclerotherapy performed on leg ulcers caused by small varices. However, as the application of polidocanol (Polidocasklerol) to the main trunk of the saphenous vein is not covered by insurance in Japan, the recommendation level for its application to saphenous vein varicosities is 2A.
- There is a document that compares surgery and sclerotherapy for varicose veins (both with and without lower leg ulcers). It reports that sclerotherapy was superior within 1 year of treatment, but that the recurrence rate increased over 3 to 5 years of long-term follow-up, and that surgery therefore ultimately yielded more favorable results.[63] In fact, many of the varicose veins that cause lower leg ulcers are saphenous varices.
- In recent years, foam sclerotherapy has started to be performed on saphenous varices, and this technique has been reported to be more effective than liquid sclerotherapy for saphenous varices.[64] The results of a phase III clinical trial of the application of a polidocanol foam preparation to varices of the great saphenous vein have been reported overseas.[65] According to this report, foam sclerotherapy was effective in resolving venous obstruction and reflux in 83.4% of patients after 12 months. These results were superior to those from liquid sclerotherapy, but inferior to those from surgery. Moreover, DVT was observed in 2.5% of the patients. The recurrence rate over a longer timeframe in this study is unknown, and lower leg ulcers were not studied.

- In an RCT that compared compression therapy alone with compression therapy performed with foam sclerotherapy on leg varices with lower leg ulcers, the latter was reported to have a higher rate of healing, although the difference was not statistically significant.[66]
- However, sclerotherapy may be performed for lower leg ulcers caused by small varices excluding saphenous varices, as well as for residual varices after surgery (high ligation, stripping of the saphenous vein).[1]

CQ10: Are skin grafts useful for leg ulcers caused by primary varicose veins?

Description of the recommendation: We propose skin grafts as one option for the treatment of leg ulcers caused by primary varicose veins. However, the basic treatments for leg ulcers caused by primary varicose veins are surgery for varicose veins (stripping, high ligation, endovenous ablation) and compression therapy.

Level of recommendation: 2A.

Commentary:

- There is a systematic review[67] of the usefulness of skin grafts for lower leg ulcers caused by primary varices. Because it did not conclude that skin grafts are useful, our level of recommendation is 2A.
- When performing skin grafting for lower leg ulcers caused by primary varices, there is an expert opinion that it should be performed after controlling the venous hypertension in the leg.[68] A cohort study also reported that compression therapy before and after skin grafting promoted healing.[69] Therefore, the basic treatments are surgery for varicose veins (stripping, high ligation, endovenous ablation) and compression therapy. There is also a case-series study indicating that if the ulcer is large, the addition of skin grafting shortens the treatment period and prevents ulcer recurrence.[70] In addition, a joint, prospective, nonrandomized, multicenter trial showed that skin grafts ease ulcer pain.[71] Therefore, assuming that surgery for varicose veins and compression therapy are already being implemented, skin grafts can also be considered.
- Lower leg ulcers from primary varices are caused by a lack of oxygen supply to the skin due to venous hypertension and disturbance of the venous return of the leg.[72] It is well known that the survival of skin grafts in ulcerated areas deficient in blood supply is poor. Therefore, before performing grafting, the state of granulation of the ulcer floor must be evaluated. If the granulation is satisfactory, skin grafting may be performed simultaneously with varicose vein surgery. However, if the ulcer floor is covered with inadequate granulation tissue or if the ulcer is infected, the skin graft is unlikely to survive.[73] Therefore, the venous return of the affected limb should be improved with varicose vein surgery, and skin grafting should be performed secondarily once satisfactory granulation tissue has formed on the ulcer floor. Compression therapy of the leg is also important after skin grafting.

CQ11: Is surgery for varicose veins (stripping, high ligation, endovenous ablation) contraindicated for secondary varicose veins?

Description of the recommendation: If the deep veins of a patient with secondary varicose veins caused by DVT are not patent, there is an extremely high risk that surgery for varicose veins will worsen the venous circulation. Therefore, we recommend not performing surgery for varicose veins.

Level of recommendation: 1A (we recommend not performing the procedure).

Commentary:

- Many expert opinions state that varicose vein surgery should not be performed if the deep veins are completely occluded.[1,74] There is also only one RCT on varicose vein surgery after reperfusion of the deep veins.[75] Therefore, the evidence level is II. Since there is an extremely high risk of exacerbating the venous stasis in the leg, we recommend not performing surgery in this context (1A). With regard to endovascular ablation, according to the Guidelines for Endovenous Treatment of Varicose Veins of the Leg published by the Japanese Society of Phlebology, one of the exclusion criteria for endovascular therapy is the presence of DVT or a history of it.[61] Therefore, similar to stripping and high ligation, this procedure should be avoided.
- Many secondary varices present as dilated and tortuous superficial veins that act as collaterals due to a circulatory disturbance of the deep veins occurring as a DVT sequela. Therefore, if the deep veins are completely occluded by thrombi, or if stripping or high ligation has been performed in superficial veins that function as collaterals, there is also an extremely high risk of exacerbating the venous stasis of the leg from an anatomical perspective.[1,74]
- Regarding patients after reperfusion of the deep veins and with reflux in superficial veins, Barwell et al. performed an RCT of patients with chronic superficial/deep venous insufficiency accompanied by lower leg ulcers to compare treatment by compression therapy alone with treatment by compression therapy plus surgery. While there was no significant difference in the rate of cure of existing lower leg ulcers, the recurrence control rate was significantly higher in the compression therapy plus surgery group.[75] However, patients in whom reperfusion of deep veins was performed after DVT only accounted for about 10% of the two groups, and the results specific to these reperfusion cases were not mentioned. Therefore, the effectiveness of the treatment in these patients is unclear.

CONFLICT OF INTEREST STATEMENT

Tamihiro Kawakami, Minoru Hasegawa, and Hideki Fujita are editorial board members of the *Journal of Dermatology* and co-authors of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication. Takafumi Kadono is the Editor-in-Chief of the *Journal of Dermatology* and a co-author of this article. He was excluded from editorial decision-making related to the acceptance and publication of this article. Editorial decision-making was handled independently by deputy editors to minimize bias.

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