Chapter

Perspective Chapter: Diagnosis and Treatment of Venous Leg Ulcer

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Abstract

Venous leg ulcer (VLU) represent a pathological tissue change in the form of a defect in the lower leg which occurs as a complication of chronic venous insufficiency. The prevalence of VLUs varies between 1.5–3% in the total population and 4–5% in persons over the age of 80. Venous ulcer is usually localized on the inner side of the lower third of the leg, oval, circular or irregular in shape. It is usually fibrous or covered with fresh granules that bleed heavily to the touch. It is very important to have a comprehensive clinical examination at the very beginning. Subsequent non-invasive and sometimes invasive tests may be indicated for diagnosis and treatment planning. Inadequate diagnosis results in inadequate therapy. The goal of therapy is complete restitution of the tissue defect and prevention of recurrence. The three basic elements of VLUs therapy are: local therapy, compression therapy and surgical treatment. If VLUs do not heal despite the application of standard therapeutic modalities, there are opportunities to apply new treatment technologies. The modern approach to the treatment of VLUs is based on the application of various biophysical interventions and medical devices.

Keywords: venous disease, venous leg ulcers, wound healing, diagnosis, venous leg ulcers treatment

1. Introduction

Venous leg ulcer (VLU) represent a pathological tissue change in the form of a defect in the lower leg which occurs as a complication of chronic venous insufficiency (CVI) [1]. Chronic ulceration is defined as ulceration on the lower leg that lasts (does not heal) within 6 weeks, and is caused by various etiopathogenetic factors [2].

Venous leg ulcers often heal slowly and result in long-term suffering and intensive use of health care resources [3, 4]. A VLUs represent a growing health problem, and they are a condition that is very expensive to treat for both the health system and patients.

A VLUs endangers the patient's normal life. Treatment of VLUs requires dedication and cooperation between the patient and the doctor. The health-related impact of VLUs is increasingly recognized as a valuable outcome measure for assessing interventions, especially when complete cure is unlikely [5]. Adults with VLUs often have multiple disabling symptoms, including pain, sleep disturbance, depression, swelling of the lower extremities, fatigue and symptoms associated with inflammation of lower leg (redness, localized heat, discomfort due to high exudate levels and itching) [6].

The prevalence of VLU varies between 1.5–3% in the total population and 4–5% in persons over the age of 80 [1]. Studies have shown that 1–2% of the adult population either has or has had venous ulceration [7]. The prevalence of VLU in Western European countries in the population over the age of 18 is 0.1–0.3% [1].

It is very important to point out that a certain number of VLUs heal very slowly or not at all. In a period of about 4 months with the application of adequate therapy, about 50% of VLUs heals [8, 9]. However, about 20% of VLUs do not heal even after 2 years from the beginning of treatment, and about 8% even after 5 years from the beginning of treatment [1]. At the annual level, the recurrence rate of VLUs ranges from 6–15% [1]. The risk of recurrence over a period of 1 year ranged from 30–57% [1].

Risk factors for VLUs are numerous, and most patients have more than one. Most of these factors are immutable and this group includes being female, elderly, having previous venous thrombosis of the legs, pulmonary embolism, multiparity, musculoskeletal and joint diseases [7, 10]. Obesity and sedentarianism are risk factors that can be influenced on [11]. The genetic traits of an individual can also be emphasized as a predisposing factor [7, 12], but the specific gene or set of genes responsible for the occurrence of this disease has not been determined so far. In people with varicose veins, Forkhead box C2, located on chromosome 16q24 [13], was isolated.

Despite the application of different standard treatment modalities for VLUs, a certain percentage of venous ulcers do not heal. Studies have shown that prolonged healing time or refractoriness to applied therapy may be due to an increase of T lymphocytes and granulocytes, lack of oxygen, growth factor and cytokine imbalance [10]. For this reason, we are working on the development of modern therapeutic modalities, while the number of new techniques for the VLUs care has increased in recent years and is constantly improving [14].

2. Symptomatology

Venous ulcer is usually localized on the inner side of the lower third of the leg, oval, circular or irregular in shape. The surface of the ulcer depends more on the degree of development than on the etiology. It is usually fibrous or covered with fresh granules that bleed heavily to the touch (**Figure 1**).

The ulcer area is thickened, pigmented and induced, together with subcutaneous adipose tissue. These changes correspond to lipodermatosclerosis, which is in fact a pre-ulcerative condition [15].

The absence of lipodermatosclerosis in the vicinity of the ulcer surface suggests that the ulcer may not be of venous origin. The presence of dilated venules, most often around the maleolus, below the ulcer surface, is also significant as a consequence of the transmission of increased venous tension through insufficient communicating veins. The presence of larger, dilated incompetent communicating veins is very significant for venous ulcers. An ulcer localized on the lateral side of the lower leg is often associated with an incompetent saphenous vein [16]. The presence of edema, lipodermatosclerosis and varicose superficial veins also supports the venous ulcer genesis. When examining ulcers, it is necessary to always examine the condition of the arterial circulation [17].

Figure 1.
Typical venous ulceration.

3. Diagnosis

Although simple at first glance, the diagnosis of venous disorders is essentially difficult due to specific hemodynamic conditions in the venous bloodstream.

A well-taken anamnesis can greatly help us in making an adequate diagnosis, and just the taking of anamnesis is considered to be a special skill, but for now there are no adequately conducted studies on the value of specific items for anamnesis. It is necessary to take data related to [18]: major symptoms exhibited and experienced, previous medical history, varicosity and treatment of varices, superficial and deep venous thrombosis, leg ulcer, peripheral arterial vascular disorder, diabetes mellitus, rheumatoid arthritis, extensive leg trauma, nutritional status, patient mobility, family anamnesis and specific leg ulcer aspects (duration, pain, previous treatment, symptoms of ulcer infection, the ankle joint mobility).

Today, the following diagnostic procedures are used to examine the venous system: Color-flow duplex ultrasound in the diagnosis of vascular diseases is widespread today, both because of its high sensitivity and accuracy, and the fact that it is a simple and safe diagnostic procedure. This method measures the diameter of the blood vessel, the duration of reflux, the presence of flow and the compressibility of the vein. The examination is performed in a standing position [19]. When examining the deep venous system up to the inferior vena cave, the patient is placed in a supine position [20]. The duration of reflux in normal proximal veins of the legs is <1 s while in distal veins <0.5 s.

Direct venous pressure measurement is an invasive diagnostic method where venous pressure is directly measured using a cannula in the superficial vein of the

foot [21]. It was found that there is a direct correlation between the height of the pressure in the vein of the foot and the height of the pressure in the deep veins at the height of the ankle. Direct measurement of venous pressure is rarely used today because it is an invasive diagnostic technique and is not recommended as a routine diagnostic method in patients with venous ulcers.

Ankle-brachial pressure index (ABPI) is used to evaluate adequate arterial blood flow. A large number of studies have shown that about 30% of patients with VLUs also have a disease of the peripheral arterial system. Ulcers that occur in these patients may be due to diseases of the peripheral arterial system or occur in combination with venous insufficiency. Normal ABPI values range from 0.91–1.20. If ABPI is >0.8 arterial abnormality on the arteriogram is generally ruled out (chance >95%) [22].

Plethysmography, phlebodynamometry and phlebography, are less used methods due to inferior accuracy and associated risks [23, 24].

Application of bacteriological examination or biopsy of ulceration and pathohistological examination will be applied in case of suspicion of infection or malignant etiology of ulceration.

4. Differential diagnosis of VLU

The success of the treatment of venous ulcers of the lower extremities depends on the accuracy of the diagnosis. Infectious ulcers are mostly found in the tropics, while neoplastic ones are relatively rare. Ulcers associated with rheumatic disease or diabetes are also common in everyday clinical practice [7]. There is a whole range of etiological causes of ulcers on the lower extremities (**Table 1**).

Differential diagnosis of leg ulcers	
Vascular	venous, ischemic, mixed arterovenous, arteriovenous fistulas, venous malformations, vasculitis, diabetic ulcers, etc.
Traumatic	after sclerotherapy, after surgical interventions, accidental
Edema	lymphedema, renal, cardiac
Infection	tropical ulcers, cutaneous tuberculosis, syphilis, leprosy, parasitic and fungal infections
Malignant disease	Marjolin ulcer, primary squamous cell carcinoma, lymphoma, basal cell carcinoma, malignant melanoma
Other	immunodeficiency, contact dermatitis, nutrition disorder

Table 1.
Differential diagnosis of leg ulcers.

5. Principles of VLUs treatment

The therapy of VLUs is complex and is determined on the basis of: etiology, clinical picture, echosonographic findings, thrombotic status, laboratory findings, comorbidities, nutritional deficiencies, risk factors, economic and medical possibilities for diagnosis and therapy. The goal of therapy is complete restitution (reconstruction) of the tissue defect and prevention of recurrence [25]. Improvement of hemodynamic status (reduction of venous hypertension and venous stasis) is the primary therapeutic goal. The three basic elements of VLUs therapy are [26]:

1. local therapy

2. compression therapy

3. surgical treatment

Adequate VLUs therapy should reduce venous hypertension in the micro and macro circulation [26].

5.1 Local VLUs therapy

Local VLUs therapy is based on the application of the TIME treatment principle [27]:

- Tissue management
- Inflammation and infection control
- Moisture balance
- Epithelial (edge) advancement

Chronic wounds can traditionally be bandaged with gauze, antiseptics, topical antibiotics and adsorbents. This type of therapy requires daily bandaging, making the treatment expensive and ineffective [28].

By wound cleaning, we mean the removal of necrosis, fibrin or other deposits. Necrotic tissue can be removed surgically or treated with an enzymatic wound cleanser. The wound cleans itself by autolysis, if none of these methods is chosen. When performing surgical debridement of ulceration, debridement should be performed to avoid damage to healthy tissue [29]. Antiseptics such as povidone-iodine, chlorhexidine, acetic acid etc. are often used today in the VLUs treatment.

The use of dressings in the treatment of VLUs is efficient and pharmacoeconomically justified. The use of dressings in the treatment of VLUs has shown a significant advantage over the classic gauze bandage in a large number of studies. The advantages of dressing applying in the treatment of VLUs are reflected in [30]:

- faster wound healing (allow constant temperature and humidity, which allows faster cell migration).
- reducing the risk of infection (achieved by releasing silver ions or creating an impermeable barrier to bacteria and viruses).
- greater comfort and cost-effectiveness (do not require daily dressing, reduce painful sensitivity of the wound, and provide significantly better quality of life).

Dressings are divided into primary and secondary. Primary dressings are in direct contact with the wound surface, while secondary dressings have the role of fixing and holding the primary dressing, which also protects the wound surface from the external environment. Today, dressings have the role of both primary and secondary [31, 32].

Type of dressings	Mode of operation
Gels, alginate dressings with additives (Ringer, 0,9%Nacl)	Activation of autolysis
Hydrocolloids, foam, hydrocapillary or silicone coatings	Granulation, creating a moist environment and absorbing secretions
Membranes, acrylates, therapeutic dressings (non-resorbable / resorbable) collagen coatings, cellulose hydrobalanced dressings, nets, films	Reepithelialization
Dressings with the addition of silver, iodine, medical honey, polyhexanide	Anti-inflammatory action

Table 2.
Type and mode of dressings action.

The division of dressings according to the mode of action on wound healing is shown in **Table 2**.

5.2 Compression therapy in the treatment of VLUs

Compression therapy is the most effective form of VLUs conservative treatment. The advantage of this therapy is that it is used on an outpatient basis, patients are able to work during treatment and it is also cheaper compared to surgical treatment [33]. This method of treatment can be applied continuously or intermittently. Before applying the compression bandage, it is necessary to perform local treatment of the ulcer surface, cover the ulcer surface with sterile gauze, after which a compressive bandage is placed. The application of external compression reduces transmural pressure and improves skin changes. Compression bandage compresses the extremities, thus reducing the effect of venous hypertension. Depending on the stage of the vein disease, different degrees of compression therapy are applied.

Compression therapy can be achieved with short-elastic and long-elastic bandages, as well as various compression systems (compression gloves, socks and clothing) [34]. The materials used to make compressive agents have different extensibility, and create different pressures under the applied compressive agents both at rest and while walking.

In relation to the degree of compression, compression means are divided into four classes (**Table 3**) [35].

These compression values refer to in vivo measurements in the medial B_1 area (end of the Achilles tendon / calf muscle insertion) measured while lying down [36].

Compression systems may contain elastic and inelastic materials. Multilayer systems (two-layer and four-layer) function as inelastic systems even if they contain mainly elastic components. An inelastic bandage is known to have high stiffness compared to an elastic bandage. The stiffness of the compression therapy system can be determined by determining the static stiffness index (SSI). This index is determined by measuring the values of the pressure between the compression system and the patient's skin (subband pressure). Pressure is measured first when the patient is lying down and then in a standing position. The difference between these two measurements is SSI. If SSI is >10, the compression system is characterized as inelastic, while if SSI is <10, the compression system is marked as elastic [37].

Compression therapy systems in which SSI is high (inelastic or multilayer compression system) give higher pressure during standing and lower pressures when the patient is lying down compared to a system with lower SSI (elastic compression system).

Class	Levels of compression	Indications
Class 1	<25 mmHg	Prevention of DVT, Mild oedema, Tired-aching legs
Class 2	25–35 mmHg	Mild VV, Mild to moderate oedema, VV during and after pregnancy
Class 3	35–45 mmHg	Venous ulcers (including healed ulcers) DVT, Superficial thrombophlebitis, Following venous surgery and sclerotherapy, VV with severe oedema, Post-thrombotic syndrome, Mild lymphoedema
Class 4	45–60 mmHg	Severe lymphoedema, Severe CVI

Table 3.
Levels of compression and indications.

Contraindications	
Absolute	**Relative**
Advanced peripheral artery disease (critical ischemia)	Mild to moderate peripheral artery disease
Decompensated heart failure	Advanced peripheral polyneuropathy
Septic phlebitis	Chronic compensated heart failure
Phlegmasia cerulea dolens	Intolerance or allergy to the materials used
Advanced peripheral artery disease (critical ischemia)	Treatment-related pain
	Florid infectious diseases (initial phase of erysipelas/cellulitis)

Table 4.
Absolute and relative contraindications for the application of compressive therapy.

Contraindications to the use of compression therapy are shown in **Table 4** [38]:

The use of compression therapy may be associated with the appearance of certain signs and symptoms that indicate the appearance of complications. The most common complications of compression therapy are necrosis, skin trauma, discoloration, pain, paresthesia, burning sensation, etc. [39].

5.3 Surgical treatment

Surgical treatment of VLUs is one of the types of treatment. Today, surgical procedures are performed on the superficial venous system, deep venous system and venous perforators. It should also be noted that surgical procedures on these three venous systems can be combined [40]. One of the ways of VLUs surgical treatment is the Vigoni-Schmeller procedure. This method involves excision of ulcers and surrounding altered tissue with removal of compartment syndrome of the lower leg by the Hach method [41].

6. New technologies applied in VLUs treatment

The modern approach to the treatment of VLUs today is based on the application of various biophysical interventions such as electromagnetic therapy, phototherapy,

electrical stimulation and ultrasound therapy. The modern method of treatment today includes the use of stem cell therapies, biological skin equivalents (such as bilayered living cellular construct (BLCC), or 3D-printed hydrogel dressing [42, 43].

In addition to the application of standard methods of treating VLUs, the following are also used: oxygen therapies, negative pressure wound therapy and platelet-rich plasma therapy. The use of a muscle pump activator or device with occasional pneumatic compression in a number of patients with VLUs has been shown to be very successful [44, 45].

Electromagnetic therapy (EMT) also has a significant place in VLUs therapy. EMT devices generate a pulsed electromagnetic field (PEMF). PEMF increases the number of fibroblasts and macrophages in the wound, which results in rapid wound healing. Studies have shown that PEMF increases the deposition of fibrin and collagen and reduces the inflammatory process [46].

Low-level light therapy (LLLT) as a variant of phototherapy has a prominent place in the treatment of VLUs [47, 48]. The use of LLLT devices activates cells through a photochemical effect. There is an increase in cellular activity [43] resulting in accelerated tissue healing, granulation tissue formation, increased protein synthesis, increased cell proliferation, anti-inflammatory modulation and pain reduction [43, 49]. This method is a non-contact method of treating VLUs, and LLLT devices usually direct a beam of light around the entire surface of the wound [48].

Electrical stimulation (ES) stimulates angiogenesis by activating mitogen-activated protein kinase (MAPK) and increasing vascular endothelial growth factor (VEGF). The application of ES leads to increased fibroblast proliferation by stimulating the production of fibroblast growth factors (FGF). The application of ES has been shown to be effective in reducing the inflammatory process and regulating bacterial growth [50].

Ultrasound therapy (UT) has found a significant place in the treatment of VLUs as one of the auxiliary therapeutic modalities [51, 52]. The effect of ultrasound on tissues is reflected in the increase of blood flow in the tissue and the induction of physical changes in the structure of collagen. This type of therapy promotes cell proliferation, angiogenesis and protein synthesis. UT also accelerates the formation of granulation tissue, has anti-inflammatory and anti-edematous effects [51, 52]. However, previous research on the application of UT has not given a clear answer on the in vivo healing process [51].

Clinical studies have shown that stem cell therapy (SCT) promotes wound healing in each wound repair phase. The application of SCT accelerates the healing process of VLUs, with a significant reduction in wound area and quality tissue regeneration [53, 54].

Oxygen therapy has a prominent place in the treatment of VLUs. Chronic wound tissues have a very small amount of oxygen, and due to hypoxia, the wound healing process is slowed down. This is particularly pronounced if a transcutaneous oxygen partial pressure (pO_2) is lower than 40 mmHg [55]. Oxygen therapy accelerates wound healing and does not reveal relevant cell damage risk [55, 56]. Today, the following methods of oxygen therapy are used: hyperbaric oxygen therapy and topical oxygen therapy.

Negative pressure wound therapy (NPWT) accelerates the healing process of VLUs. This is achieved through several mechanisms: reduction of local edema as well as reduction of the number of bacteria, inflammatory mediators and wound exudates. NPWT promotes angiogenesis, promotes tissue perfusion, stimulates tissue granulation, causes wound shrinking, and contraction of its edges [47, 57].

Platelet-rich plasma (PRP) or autologous platelet-rich plasma is a suspension of platelets obtained from whole blood [58]. The concentration of platelets in PRP is two to six times higher than that in the blood [59]. To form a liquid or gel that contains multiple growth factors, PRP is most commonly mixed with thrombin. PRP supplies not only a number of growth factors but also signaling cytokines that also play a key role in new tissue synthesis, angiogenesis, or inflammation regulation [58].

The role of growth factors in wound healing is very complex. Certain growth factors (e.g. TGF-beta) play different roles in different phases of healing. To date, in spite of many years of research, only one growth factor (Becaplermin, PDGF) is registered for the treatment of diabetic foot ulcers and not for venous ulcers [60].

7. Discussion

Venous leg ulcers occur as a complication of CVI. With the aging of the world's population, an increase in the number of obese people with various chronic diseases, the number of patients with VLUs will increase. These patients' performance will be a significant burden on the health care system [61].

Venous leg ulcers are significantly more common in the elderly. In 13% of people, VLUs first appears before the age of 30, and 22% before the age of 40. For this reason, patients with VLUs have a reduced quality of life and varying degrees of physical disabilities. These patients suffer varying degrees of acute and chronic pain [62].

The application of modern diagnostic and therapeutic modalities in the treatment of VLUs in combination with available evidence-based data will reduce the number of patients who will not heal VLUs and who will relapse. Therefore, the use of standard methods of treatment and the use of expensive advanced therapeutic agents is of particular importance.

It is very important to have a comprehensive clinical examination at the very beginning. Subsequent non-invasive and sometimes invasive tests may be indicated for diagnosis and treatment planning. Inadequate diagnosis results in inadequate therapy.

The application of objective tests aims to confirm the diagnosis, determine the etiology of the disease, locate the anatomical site of the venous disease (superficial, deep, and perforating venous system) and the severity of the disease, or identify coexisting peripheral arterial disease [63].

Taking a good medical history is imperative of a good clinical examination. Patients with VLUs have a rich medical history and a number of concomitant comorbidities. Unfortunately, there are not enough studies that have shown the value of specific items for the anamnesis [25]. In practice, it has been shown to be very important to take all data related to the previous medical history as well as the family history and the specific aspects of the ulcer [18].

In order to monitor the healing rate of ulcers, it is very important to perform an accurate and consistent wound measurement. Wound location, area, and characteristics should be documented. Traditionally, length and width are measured in perpendicular distances of wound borders (the longest length with the greatest width at right angles). This measurement can be done manually or via digital photography. These wound measurement methods are inconsistent and sometimes inaccurate. The use of digital software is recommended. The study of Cardinal et al. showed that oval or circular ulcers initially heal better than wounds with large indentations,

multiple segments and skin swellings at the edges. VLUs documentation is important for estimating the healing rates. If in the period from 4 weeks there is no reduction in wound area by 30%, it is unlikely that VLUs will heal by week 12 [64]. Patients with VLUs that heal slowly are ideal candidates for advanced therapy.

In order to make a diagnosis, the following diagnostic procedures are recommended: ABPI and duplex venous mapping. If duplex venous mapping cannot be used to make a valid diagnosis, phlebography, venous angiotomography, and venous angioresonance are recommended [64].

The success and sensitivity of the color-flow duplex ultrasound depend on the researchers and the coefficient of variation of reflux measurements ranges from 30–45% [65]. Studies have shown that duplex diagnostics has high sensitivity and specificity in the diagnosis of superficial and deep venous leg systems [65, 66]. Today, this method represents the gold standard in the diagnosis of venous diseases, enables further classification of chronic venous insufficiency and selection of the optimal treatment of venous diseases.

ABPI test is widely applied in the diagnosis of peripheral occlusive artery disease, because of its accessibility, affordable price, lack of risk, a sensitivity of 95% and a specificity of 99% [64]. Determination of ABPI is not the most reliable in patients with diabetes mellitus because compression of the arteries may not be possible due to medial sclerosis.

Taking an ulcer biopsy is a quick, easy, and effective way to identify less common etiologies in ulcers that are unusual in appearance and where there is a reasonable suspicion of a malignant etiology. Sometimes it is necessary to take multiple biopsy specimens to get an accurate diagnosis [67].

Standard sampling for bacterial colonization has no therapeutic consequence and thus is meaningless. Wound swabs should only be taken if there are signs of infection, prior to initiating therapy, and for MSRA detection. Cultivation and eventual use of antibiotics is only indicated if there are signs of VLUs infection [68].

Successful treatment of VLUs requires a multidisciplinary team to make an adequate diagnosis, assess the condition of the vascular system and determine other factors that affect the healing of ulceration.

The basis of VLUs treatment is to reduce or eliminate the effect of venous hypertension. This is achieved through the use of compression therapy, surgical treatment of venous abnormalities, local ulcer treatment, systemic medications that aid healing and complementary measures [64].

There is relatively little data in the medical literature regarding the cleansing of venous ulcers. The results of a number of prospective and retrospective studies related to surgical debridement of VLUs have shown that this method has a certain place in treatment. The results of a prospective study showed that the presence of dense fibrosis and high levels of mature collagen in ulcer tissue samples directly positively correlates with the speed and success of VLUs healing [26].

Extensive and deep debridement of VLUs that were refractory to therapy until the absence of dense fibrosis and mature collagen in the ulceration is recommended.

The results of a number of studies have shown that there are no justifiable reasons for the use of antiseptics, in principle, cytotoxic agents. Cleaning with ordinary clean water has the same result as cleaning with isotonic sodium solution [26].

The use of dressings in the treatment of VLUs has shown a significant advantage over the classic gauze bandage in a large number of studies. Proper use of dressings is based on clinical protocols containing the etiology of ulceration, clinical assessment

of ulceration (depth, size, degree of purity, contamination, surrounding skin condition, amount of exudate), presence of infection, and general patient condition [30].

Modern dressings today provide optimal physio-chemical conditions necessary for normal wound healing, preventing the development of infection, controlling exudates, reducing the number of debridements and reducing the need for more painful dressings [69, 70].

Effective compression is achieved by precise application of the bend system, which should provide mild compression at rest, but also effective compression during all types of activities. All compression therapy systems achieve this to some extent, and the choice of a bandage or socks requires selection on an individual basis.

The two main principles on which compression therapy is based are [71]:

- creating a closed system that allows internal pressures to be evenly distributed in the leg.

- variation of subbandage pressure according to limb shape and bend tension.

Understanding the principles of compression therapy allows us to define the ideal compression system. The characteristics of an ideal compression system are: includes inelastic component, provides good anatomical grip, enables smooth operation and mobility, provides comfort at rest, easy to apply and adapts to the size and shape of the limbs and does not cause an allergic reaction and shows endurance.

Compression therapy systems must be compatible so that they can be effectively applied in different limb sizes and shapes, while providing therapeutic levels of compression without the risk of damage. The use of multicomponent compression systems has shown significantly better efficiency in the healing of venous ulcers compared to the use of one-component compression systems. Multicomponent compression greater than 30 mm/Hg showed, in addition to high efficiency in wound healing, a reduction in the recurrence of venous ulcerations [72, 73].

After the ulcer has healed, elastic stockings with graduated compression of the appropriate size are used, with a pressure of 30–40 mmHg. In most patients, knee pads are sufficient. In fact, socks above the knee or other compression devices that exceed the height of the knee are uncomfortable to wear and occlude the popliteal vein during knee flexion. Ankle compression >40 mmHg is rarely required. If the patient is associated with arterial insufficiency, socks that produce less pressure around the ankle joint are needed, so as not to lead to skin necrosis [71].

It should be noted that it is very important to apply surgical therapy in order to treat the underlying venous disease whenever possible. The use of surgery can improve and accelerate healing, as well as reduce the risk of recurrence [64].

Unfortunately, up to this date, no randomized studies have been performed on the use of this treatment for VLUs. The problem with the application of surgical therapy in the treatment of VLUs is the lack of valid randomized, controlled studies. Previous studies have had an uneven number of patients and different surgical techniques have been applied. None of the previous studies has shown the advantage of surgical therapy over VLUs conservative treatment.

Based on the recommendations of the Scottish guidelines, surgical therapy should not be the method of choice in the VLUs treatment (an active ulcer). Surgical therapy is also not recommended as a secondary prevention after VLUs healing [74]. The data obtained from the ESHAR study showed that there is no advantage of surgery over compression therapy in the treatment of patients with varicose veins of the lower

extremities. However, this study showed that in relation to the occurrence of disease recurrence, surgical therapy proved to be more successful [75].

The number of new technologies and use of grafting techniques used in the treatment of VLUs has increased in recent years. The future may hold micro- and pixel-grafts, spray on cells and the use of 3D printing to prefabricate vascularized grafts to assist in wound coverage.

Some of the new technologies used in the treatment of VLUs require broader evidence of clinical efficacy and can be considered as experimental therapies [76].

8. Conclusion

Venous leg ulcers occur as a complication of CVI. Venous leg ulcers are significantly more common in the elderly. A VLUs represent a growing health problem, and they are a condition that is very expensive to treat for both the health system and patients. The application of modern diagnostic and therapeutic modalities in the treatment of VLUs in combination with available evidence-based data will reduce the number of patients who will not heal and who will relapse. Therefore, the use of standard treatment methods and the use of expensive advanced therapeutic agents is of particular importance.

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