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## Manual Lymphatic Drainage in the Treatment of Chronic Venous Disease

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Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/67901>

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### Abstract

Chronic venous disease (CVD) is a chronic condition that is associated with venous hypertension, vein's valves damage, venous obstruction, and calf muscle pump impairment. This blood circulatory condition is also characterized by important inflammatory changes affecting the skin, the subcutaneous tissue and the muscles, which are probably triggered by blood stasis and venous edema. With disease progression, severe ulcerative skin damage might occur, which when present represent the more severe stage of this condition. CVD has a significant economic, social and health impact, mostly due to raised morbidity and chronicity.

The treatment of patients with CVD might focus on both the symptoms and secondary changes of the disease, such as edema, skin and subcutaneous changes or ulcers. Usually, initial treatment of CVD patients involves a non-invasive, conservative treatment to reduce symptoms, treat secondary changes, and help prevent the development of secondary complications and the progression of the disease. Complementary, some interventional or surgical treatments can be undertaken.

There are several conservative treatments to treat and prevent complications associated with CVD that have been described in the literature, like manual lymphatic drainage (MLD) and compression, physical exercise, intermittent pneumatic pressure, kinesio taping, electrical muscle stimulation, transcutaneous electrical nerve stimulation, hydrotherapy, and health education. Most of these techniques are complementary to compression therapy or pharmacological treatment.

This chapter will address the role of physical therapists in the management of CVD. The chapter will begin by reviewing the basic physiopathology of CVD, including the role of calf muscle pump. The CEAP classification system and the chronic venous severity score will be presented, as these are main tools for clinical assessment of CVD severity. In the remainder of the chapter will address the physiological effects and recommendations for treating CVD of MLD, based on our clinical experience and own research.

**Keywords:** chronic venous disease, edema, calf muscle pump, manual lymphatic drainage

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## 1. Introduction

The term chronic venous disease (CVD) has been used to describe morphological and functional abnormalities of the venous system of extended duration that are manifested themselves by symptoms and/or signs that indicate the need for evaluation and care by health professionals [1].

Usually, symptoms of leg heaviness, fatigue, and pain are the first complaints referred by patients, which together with varicose veins are present both in mild and severe cases of CVD. These complaints combined with structural changes in superficial, visible veins strongly contribute to a negative self-esteem that also characterizes this disease [2–8]. The diminished health-related quality of life (HRQL) seen in CVD is well studied [2, 8–10]. This negative impact is so important that the previous view of this condition as an aesthetic problem has been abandoned for years.

The socioeconomic burden of CVD is very high. The indirect costs are substantial and are associated with the symptoms, functional impairment, emotional disturbances and negative impact in HRQL [11]. The direct costs of CVD treatment are almost entirely related to its high prevalence, morbidity, and chronicity [11, 12]. In developed countries, around 1–3% of the health costs are due to CVD [13]. However, when patients with less severe stages of the disease are diagnosed and treated early, the physiopathology course of the disease can be prevented or even receded [14].

The severity of CVD is nowadays evaluated based on a multifactorial concept of the disease and using the standardized CEAP (Clinical Etiological, Anatomical and Pathological) classification system. Having a good knowledge of this system is very important to all physical therapist and it is important that health professionals use the same nomenclature so that CVD severity can be accurately assessed and the best treatment delivered [15].

The treatment of patients with CVD might focus on both the symptoms and secondary changes of the disease, such as edema, skin and subcutaneous changes or ulcers. Usually, initial treatment of CVD patients involves a non-invasive, conservative treatment to reduce symptoms, treat secondary changes, and help prevent the development of secondary complications and the progression of the disease. Complementary, some interventional or surgical treatments can be undertaken [15].

Manual lymphatic drainage (MLD) is a low-pressure form of skin-stretching massage, described as a conservative treatment for CVD [16] and as a coadjutant of other treatments, like stockings and surgery [17, 18]. This technique has been proposed for the treatment of venous lymphedema associated to CVD [19, 20], before CVD surgery, or to relief symptoms [17, 18, 21]. It is suggested by the literature that this physical therapy technique should be applied taking into account venous anatomy and that it should increase deep and venous flow [22, 23]. Despite controversial evidence regarding the ability of MLD to reduce edema or lymphedema, this technique when associated with other treatments, the so-called “lymphatic decongestive therapy”, that also includes compression, exercise, and education, may have an important role for improving health and functional status in patients with edema associated to sport injury or related to breast cancer surgery, just to mention two common situations [21, 24–26].

This chapter will address the role of physical therapists in the management of CVD. The chapter will begin by reviewing the basic physiopathology of CVD, including the role of calf muscle pump. The CEAP classification system and the chronic venous severity score will be presented, as these are main tools for clinical assessment of CVD severity. In the remainder of the chapter, we will address the physiological effects of MLD on venous circulation and the recommendations for its use in treating CVD.

## 2. Health and social impact of CVD

### 2.1. Epidemiology

Chronic venous insufficiency, represents the most severe cases of CVD, and its physiopathology is associated with venous hypertension, vein valve damage, venous obstruction, calf muscle pump impairment, inflammation of tissues (skin, subcutaneous tissue, and muscle) and veins, alteration of veins morphology and function. This disease is characterized by abnormal venous reflux, venous edema, and changes of the skin and subcutaneous tissue, with ulcer representing the most severe stage of this condition, and is classified between  $C_0$  (no signs) and  $C_6$  (active ulcer) CEAP classes [13, 27–32]. Despite some controversies, CVD might exist without the presence of signs [3, 13, 33].

The estimated prevalence of CVD varies according to its severity, being around 10, 9, 1.5, and 0.5% for CEAP clinical levels  $C_3$  (venous edema),  $C_4$  (hyperpigmentation or eczema, lipodermatosclerosis, or atrophie blanche),  $C_5$  (healed venous ulcer), and  $C_6$  (active venous ulcer), respectively [33]. The more advanced stages of venous disease, ( $C_3$ – $C_6$ ), appear to affect about 5% of the population [1]. Milder CVD conditions, like telangiectasiae and reticular veins ( $C1$  class), have been reported to affect up to 80% of the population, while the incidence of varicose veins ( $C2$  class) has been reported as ranging from 20% to 64% [1].

Despite its frequency in the population, the prevalence of CVD is still underestimated. Epidemiological data estimate a wide range of CVD prevalence, varying between 1-17% in men and 1-40% in women [34]. In the USA alone, approximately 2.5 million people suffer

from CVD [2]. Variation in estimations of CVD prevalence are likely explained by differences in gender, age, ethnic group, risk factors and variations in diagnostic criteria and methods [1, 34]. A study where 91545 participants were evaluated, found a CVD prevalence of 83.6%, with 63.9% of the subjects classified as C1-C6, and 19.7% as C0. Regarding CVD prevalence according to gender, this study showed higher number of men in C0 class, higher number of women in C1-C3 classes and equal number of men and women in the more severe groups (C4-C6 class) [35]. Considering only the cases of varicose veins (C2), prevalence has been shown to vary in the range 7-40% in men and 25-32% in women [34].

## 2.2. Functional and HRQL implications of CVD

Patients with CVD display impaired functional capacity [2, 36] and diminished HRQL [9, 10, 37, 38]. The severity of CVD, HRQL scores, the clinical signs, and venous ultrasound findings of the disease are usually correlated [39].

The impact of CVD on HRQL is primarily seen in the physical items and in the emotional domain, but in its severest stages (presence of venous ulcers) the mental dimension might also become involved [9]. The impact of severe CVD in HRQL is similar to that of other chronic diseases, such as diabetes, cancer, chronic pulmonary disease, and heart failure [9].

Most of chronic leg ulcers are venous in origin [40]. Patients with venous ulcer present severe pain, which is in relationship with impaired tissue healing ability, diminished HRQL, lowered self-esteem, and poor social interactions [2]. The psychological effects of CVD may be not strictly related with ulceration itself but can else be associated with the symptoms caused by this type of wound (80.5-69.4%), altered appearance and esthetical concerns (66.7%), lack of sleep (66.6%), functional impairment (58.3%), and disappointment with treatment outcomes (50%) [2]. Also, patients with uncomplicated varicose veins often have severe symptoms that adversely affect their HRQL, irrespectively of the severity of the disease, refuting the view that this disease is mostly an aesthetic problem [8]. Estimates indicate that near 30% of patients with symptomatic varicose veins, who may not have had their clinical venous condition diagnosed or treated, display symptoms suggestive of a depressive illness [41].

In this disease, 49% of men and 62% of women have symptoms related to CVD [33], like pain, itching, tingling, cramps, restless legs, swelling, heaviness, and fatigue [3, 8]. A recent survey reveals that 14.9% of the general Greek population refers symptoms and/or present signs related to CVD [42].

The number of symptoms reported by patients with CVD varies but are usually several [4, 5, 8]. Importantly, the number and severity of symptoms are not strictly related to CVD severity and, sometimes, strong symptoms, and those that have the largest impact on HRQL, are present in less severe cases [8]. Nevertheless, despite possible indication for surgery, some studies suggest that the majority of the symptoms in patients with varicose veins are nonvenous related [5]. Indeed, it seems very difficult to separate venous from nonvenous causes of symptoms in CVD [6].

Several studies show the presence of both neuropathic and nociceptive pain in patients with CVD [4, 43]. Nevertheless, patients with CVD may present other comorbidities that make it difficult to isolate the CVD-related pain [43, 44].

Approximately one-third of people with CVD report to be a burden going out of home and participating in social events, and that they avoid wearing clothes exposing their legs or going on vacations to very warm places [42]. According to self-reports, functional status is diminished in these patients [36, 39] also because of some physical dysfunctions, like abnormalities in gait [45], impaired balance, peripheral neuropathy [43, 46] weak leg muscles (plantar flexion and dorsiflexion muscles) [29, 30, 45], or diminished ankle range of motion [10, 30, 47]. These dysfunctions are also associated with impaired muscle pump function in the lower extremity [43], an important risk factor for venous ulceration [48].

### **2.3. Socioeconomic impact of CVD**

Severe CVD has a significant economic impact, mostly due to raised morbidity. Over the last decade, neither CVD-associated and inflation-adjusted mean hospital charge, nor length of hospital stay decreased, possibly as a result of poor advancements in prevention and treatment of this disease [49]. It is estimated that 4.6 million of working days per year are lost as a result of CVD [40]. Painful leg ulcers, the odor, the dressing, the frequent need for treatment, with their associated restrictions and social isolation result in a heavy psychosocial burden [50]. In severe CVD, venous ulcers require wound care, compression, chemical and mechanical debridement, and, in frequent cases, antibiotic therapy [49]. While ulcer treatment is usually done in outpatient settings, in some particularly critical situations it may require hospitalization [40]. Western European countries spend 1.5-2% of their annual health budget in the treatment of this disease [51]. The economic burden is not just associated with clinical visits and outpatient treatments, but also with travel time, loss of work hours for patients and family, and physiological impairment related to analgesic and antibiotic use [49]. Limb amputation is a radical outcome of this disease, although in many of cases these are also related to comorbidities, for instance diabetes and arterial vascular disease [49]. Other important complications, such as hemorrhage, thrombosis and pulmonary embolism, also compound the unhealthy profile of these patients [42]. Deep venous thrombosis may cause chronic conditions like post-thrombotic syndrome and CVD, increasing the costs of the treatment [49]. Preventing deep venous thrombosis and complications is one of the most important aims for reducing socio-economic burden associated to CVD [49].

The chronic nature of the problem results in long-term costs and the frequent recurrences, together with the poor effectiveness of current treatments, further expand the cost of this disease [40].

Despite its cost, the efficacy of the pharmacological treatment of CVD is usually poor, and should be combined with other strategies, such as the use of elastic garment compression [33]. Similar procedures are recommended following surgery and sclerotherapy, in which cases post-operative compression therapy and health education are crucial for treatment success

[42, 52]. There are several risk factors associated with CVD that patients should be informed of by the health professionals, like the use of hormonal contraceptives by women, daily routines (sitting or standing), pregnancy, age, obesity and heredity factors (i.e., family history) [1, 37, 42, 49, 53]. Also important, advice regarding behavioral changes, engaging in so-called venous exercises and the proper use of the health care services, should be offered to CVD patients [42]. Getting the right advice from health care professionals is an important measure for preventing and managing CVD [42].

Because of the wide spectrum of factors that cause functional impairment in these patients and the high costs of treatment [2, 3, 8], the prevention of CVD by educational and prophylactic interventions has been shown to be clinically cost-effective, by avoiding disease progression to the last stages [49, 54].

### 3. Pathophysiology of CDV

Near 60% of blood volume flows in the venous system, the majority of it in the lower limbs and in the cutaneous circulation, and near 20-25% occupies the splanchnic circulation [55]. The venous system returns the blood to the heart and is a low-pressure, slow-velocity, large-volume and low-resistance vascular system [1]. Venous return results from the interaction of diverse mechanisms, like a central pump (respiratory cycle and heart), a pressure gradient, a peripheral venous pump, and veins valvular system [43]. The venous volume in the lower limb is the result of the interaction between these mechanisms and reflects the balance between blood inflow and outflow [1].

CVD is caused by venous hypertension, valvular insufficiency, and/or blood reflux [56–58]. Venous hypertension might be accompanied by outflow obstruction [57] and can affect the superficial, perforator, and deep veins [3, 58]. Insufficient lymphatic drainage or a dysfunction of calf muscle pump are very often associated with this disease [59]. Venous hypertension is related to structural (veins and valves), hemodynamic (obstruction, reflux, stasis), biomechanical (calf muscle pump strength and ankle range of motion) and biochemical factors (leucocyte-endothelial process inflammation) [57, 58].

The exact mechanisms behind the development of CVD are not clear yet [57, 60]. The major hypothetical sequence of events places venous hypertension as the trigger, causing inflammation of the veins' wall and of vein valves, with inflammation, as the condition aggravates, spreading to the skin and the muscles, causing dermal changes, like hyperpigmentation, subcutaneous tissue fibrosis (lipodermatosclerosis), and tissue necrosis and ulceration [20, 51, 57, 59] in the most severe cases [60].

Venous obstruction occurs because of the triad: blood stasis, changes in the vessel wall, and hypercoagulability [61]. This may occur as a phlebitis (obstructions of superficial venous system) or as deep venous thrombosis (obstructions of deep venous system), and can be diagnosed as acute or chronic [12]. The acute deep venous thrombosis may cause nociceptive pain, swelling and tenderness, and both phlebitis and deep venous thrombosis must be confirmed by

venous ultrasonography [57]. The ensuing venous hypertension then opposes venous return, leading to luminal hypoxemia and vein wall distension, which impairs perfusion and causes endothelial hypoxia and leukocyte invasion of the vein's media [61]. A progressive remodeling process is then triggered consisting of hypoxemia-related venous/capillary wall injury, leukocytes accumulation and adhesion, progressive blockage of capillary blood flow, and ongoing damage of subcutaneous tissues and skin (lipodermosclerosis and skin ulceration) [62].

Usually, venous reflux and obstruction occur together [57]. Following obstruction, venous recanalization occurs and blood flow through the vein is restored [61]. However, lysis of the clot or thrombus is usually only partial and the residual thrombus might undergo fibrosis that may completely obstruct the lumen of the vein, for example involving leaflets [61]. Collateral blood circulation may develop in these cases and obstruction may be overcome [57]. Sometimes, calf perforating veins may be an important collateral venous path when the popliteal vein is involved, causing CVD of a secondary etiology [57].

The initial hypertension in CVD may also be caused by valvular incompetence alone [60]. Varicose veins may result from endothelial changes (reduced elastin and smooth muscle content, together with increased collagen) associated with hypoxia, causing weakened venous tone [60]. Other changes include downregulated apoptosis [63], decrease energy for cell metabolism and increased lysosomal activity [64].

### **3.1. Etiology and anatomical location of CVD**

The etiology of CVD can be described as primary, secondary (post-thrombosis) or congenital [13]. Although reflux is the major hemodynamic alteration in CVD, in secondary venous disease most of the cases present a mix of reflux and obstruction [58]. It seems that 80% of cases of CVD have a secondary etiology of post-thrombotic pathology, and 20% are of primary cause, as a result of valvular incompetence [57].

In the superficial system, the insufficiency is most often the result of a primary preexisting weakness in the vessel wall or valve, as a consequence of a direct injury, excessive venous distention caused by hormonal effects or high hydrostatic pressure, or secondary to venous obstruction (i.e., phlebitis) [33, 59, 65, 66]. Failure in valve functioning (superficial veins) may increase superficial venous pressure, resulting in venous dilatation and varicose veins [59]. Although the primary mechanism of valvular incompetence in superficial veins is not fully known [57], it appears that first changes in the mechanical properties of the vein wall caused by increased collagen content and decreased amount of elastin and smooth muscle, leading to vessel enlargement occur and next, valvular insufficiency develops [57].

The perforating veins can also become insufficient by primary incompetence of vein valves or secondary to venous obstruction [67]. In these cases, there is reflux from deep to superficial venous system: with valve incompetence the reflux to saphenous veins may allow the re-entry of venous blood to the deep venous system [67]. In the case of secondary incompetence, the high intravascular pressures are transmitted to superficial veins, causing the enlargement of dermal capillaries and increasing filtration to the interstitial space [57, 67].

Deep veins insufficiency has been suggested to be the consequence of deep veins thrombosis in the majority of cases, i.e., from secondary etiology [59]. However, primary deep venous incompetence is also common (8-22% of the cases [12]) but is usually compensated by a strong muscle [12, 57]. It seems that outflow obstruction and reflux caused by valve damage may cause deep vein thrombosis and these two alterations together increase the probability of the development of post-thrombotic syndrome [12, 61].

Deep venous thrombosis may also occur because of an intrinsic venous process, such as a previous deep venous thrombosis episode with inadequate recanalization or venous stenosis, or because of extrinsic compression, as in May-Thurner syndrome [66]. Also, it can be caused by venous agenesis, such as in the Klippel-Trenaunay syndrome, trauma, surgical mishap, and tumors [57].

Congenital CVD, in which case the condition is already present at birth, also exist. However, this might be recognized only later in life, such as in the cases of the Klippel-Trenaunay (varicosities and venous malformations, capillary malformation, and limb hypertrophy) [33] and Parkes-Weber (venous and lymphatic malformations, capillary malformations, and arteriovenous fistulas) syndromes [66].

#### **4. Venous edema and Lymphedema**

CVD is the most common cause of edema with age 50 and over [68]. The venous edema is a very common clinical manifestation of CVD, particularly in C3 to C6 classes [68-72]. The chronic venous edema may blunt the metabolic and immunological capacity of tissues, thus contributing to the risk of venous ulcer [72]. Venous edema occurs when there is an imbalance between vascular filtration and reabsorption and lymphatic reabsorption [19]. About 90% of capillary filtration (proteins, plasma, and other components) is reabsorbed back to the blood, and the remaining 10% is reabsorbed by the lymphatic circulation [20, 73]. In CVD, blood filtration is increased due to the higher intravascular hydrostatic pressure and raised endothelial permeability due to inflammation [19, 73]. In these conditions, venous edema may occur [19, 20]. This is a pitting edema that gets worse through the day and improves during sleeping because of the lying position and leg elevation. Usually, this edema is accompanied by venous symptoms and signs [19, 20]. Clinically, venous edema is perceived as an increase in fluid volume of the skin and subcutaneous tissue, characteristically diminished by pressure [13]. Venous edema usually occurs around the ankle region, but may extend to the leg and foot [13].

The principal physiological function of the lymphatic circulation is to guarantee homeostasis between the vascular and interstitial fluid compartments [74] and this requires that the lymphatic system compensates the excessive blood filtration at the blood capillary level [19]. Any failure in this process will result in accumulation of a protein rich fluid in the interstitial space, which is associated with an inflammatory reaction, fibrosis, overgrowth of adipose and connective tissue, and other symptoms that characterize the lymphedema [74]. There is

some evidence of lymphatic failure in venous disease. For example, studies with lymphoscintigraphy, reveal that in post thrombotic syndrome the subfascial lymphatic drainage is reduced that may explain edema and lipodermatoesclerosis seen in this situations. Also, patients with ulcer have reduced lymphatic drainage, suggesting that lymphedema is a contributing factor to ulceration [19]. Approximately 20- 30% of individuals with CDV have mix edema (with venous and lymphatic component), because of fluid overload or recurrent cellulitis [70].

Based on the cause, the lymphedema may be classified as primary (congenital or hereditary) and secondary (acquire) forms [74]. Over one third of patients with CVD will have secondary lymphatic dysfunction but when edema is present in these patients, there is the tendency to misdiagnosis it as primary lymphedema [20].

When edema is at the dorsum of the foot, it is associated to squaring of the toes, thick skin, and is of non-pitting edema type [33]. In these cases, it is assumed that a lymphatic compromise exists [33]. The lymphatic circulation may compensate for the excessive filtration, but lymph vessels also suffer damaged with time (microlymphoangiopathy), because of chronic inflammation and accompanying subcutaneous and skin lesions [20, 66]. Therefore, venous edema becomes compound with signs of lymphedema, with non-pitting edema and with hyperkeratosis, papillomatosis, most in retro and post malleolar regions an in the lateral border of the foot [19]. Clinically, this secondary lymphedema may decrease with limb elevation initially, but with time patients will refer aggravation of swelling in the morning and after the night sleep because an increased osmotic pressure in the interstitial space caused by protein blood extravasation [19].

## 5. Muscle Pump Function and dysfunction

The venous return from the periphery to the heart via the venous system is linked to the action of a central pump (heart and respiratory cycle), periphery venous pump, a pressure gradient, and competent veins and/or venous valves [43, 75].

The muscle pump refers to the hemodynamics effect of limb muscles contractions and ambulation on venous circulation, which is twofold: (I) to enhance venous return from the lower extremity, and (II) to stimulate local blood flow and raise muscle perfusion during muscle contractile activity [43, 57]. The calf muscle pump has an important role for the effective venous return and relies on dynamic interaction between the ankle joint, muscle fascia, muscles of the calf and venous valves [43, 57].

During muscle contractions, the venous blood is forced in direction to the heart and the valves prevent reflux during relaxation [27, 48, 76]. As deep veins are tethered to surrounding tissues, muscle relaxation causes the veins to open, lead to a sudden drop in pressure within these vessels [58, 77, 78]. The large pressure gradient caused by the drop in deep veins hydrostatic pressure enhances blood flow from superficial to deep veins trough perforator veins, decreasing superficial venous pressure and enhances arterial inflow [43, 57].

The basic concept of muscle pump operation is that the steep increase in intramuscular pressure that accompanies contraction compresses the deep inner muscle veins and veins in the nearby inter-compartmental spaces, expressing the blood across the unidirectional vein valves. During muscle relaxation, intravascular pressure drops but venous blood backflow is prevented by the rapid closure of vein valves. Vein walls are tethered to the surrounding muscles and, therefore, veins are forced to open during muscle relaxation, resulting in large dropping of hydrostatic pressure inside the deep veins, causing aspiration of the blood flowing the superficial system through the perforator veins. The decreased venous pressure due to the muscle pump action also raises perfusion pressure, thus leading to an increase in blood flow across the limb. Despite the simplicity of this model, the efficacy of the muscle pump relies on multiple factors and shows wide variation even among people free from venous dysfunction [79].

Ambulatory venous pressure (AVP) and air plethysmography are gold standard methods for evaluating muscle pump function (usually the foot and calf pumps together) [80, 81]. For ambulatory venous pressure, the conventional procedure measures the intravascular hydrostatic pressure inside a dorsal foot vein, which is then taken as proxy of the pressure in the veins of the lower extremity. The percentage decrease in AVP shows large variability even in healthy control subjects. In a group of CVI participants, AVP decreased by approximately 75% at the end of ten tiptoe exercise compared to basal values, with no differences in the magnitude of AVP decrease between people with different CVI severities [80]. However, compared to healthy groups (CEAP C0 class), CVI groups show a percentage AVP decrease that on average is only approximately 35% in CEAP classes C4...C5, a value that is half of that for participants in C0 class [79]. Surely, the percentage AVP decrease plus the basal venous hydrostatic pressure at foot level determine the ambulatory drop in hydrostatic pressure in dorsal foot veins. In healthy people, the large percentage fall in AVP combines with normal basal hydrostatic venous pressure, so that in such cases mean AVP lowers to around 30 mmHg, contrasting with mean AVP values >55 mmHg in C4-C6 clinical groups [79]. The AVP pressure has a fairly good relationship with venous incompetence, with the risk of ulceration increasing linearly with ambulatory venous hypertension. According to Nicolaides et al. [82], in a cohort of 220 CVI patients the incidence of venous-related ulcers was 0% when AVP levels were <30 mmHg and attained 100% with AVP >90 mmHg.

The magnitude of decrease in AVP is determined by the amount of blood expressed by the muscular contractions but also by the rate of refilling. The time taken to elevate the pressure back to 90% of basal standing levels, a standard measure of recovery time (RT90), is negatively correlated with venous insufficiency severity, being on average >20 s in healthy people and in those with mild venous disease, lowering to approximately 2 s in severe clinical cases [79, 80]. Like for AVP, RT90 values are also predictive of the risk of ulceration [79]. Data obtained with air plethysmography also confirms the presence of muscle pump deficiency in CVI. Standard measures of air plethysmography include the ejection fraction, the venous filling index to 90% of the basal volume, the residual volume fraction, and the venous volume [80, 83][9,12].

These muscle pump function effects have the potential to alleviate symptoms and counteract disability associated with chronic venous disease. The action of the muscle pump in moving

venous blood centrally is well described and relies on an imbricate relationship between anatomical and biophysical/physiological factors of at least three separate muscle pumps: the foot, the calf, and the thigh muscle pumps thigh [57, 84]. The calf pump is the most important of the three, as a result of its larger capacitance and highest pressure-generating ability. Together, the foot, calf, and thigh muscle pumps assure near 90% of the venous return in the deep venous system of the leg [85].

### 5.1. Thigh muscle pump

The calf muscles, and possibly the thigh muscles, act as a pump, also called as “peripheral heart”, which can generate pressures of up to 300 mm Hg during exercise [86]. Nevertheless, it has been suggested that thigh muscle pump has a minor effect in venous return, compared to calf muscle pump [43, 57, 84].

The thigh muscle pump may be separated in a posterior division that includes mostly the semimembranous muscle, and an anterior division made up by veins from the quadriceps femoris muscle [32]. The veins inside the semimembranous muscle form longitudinal plexus that are connected in the lower part of the muscle with the popliteal vein and with the deep femoral vein upwards. The quadriceps femoris’ veins drain into a large trunk that often join the deep femoral vein to end into the common femoral vein near the root of the thigh. The venous valves of thigh veins may not be entirely competent thus allowing variations in the volume of the thigh venous reservoir to occur with posture changes [84].

### 5.2. Calf muscle pump

The calf muscle pump is in sequence with the foot pump is the most important muscle pump in the human circulatory system [27, 87]. The calf muscle pump is associated with the strong triceps surae muscle and can be separated in two units: a first unit that includes the soleus muscle (leg pump) and its veins, and a second unit situated in the upper leg region and composed by the gastrocnemius muscle and respective veins (popliteal pump) [88]. The veins in the soleus are organized in a lateral larger group and in a medial one. The lateral veins are larger, run vertically and drain into the fibular veins near the superior border of the soleus muscle. The majority of the medial veins drain horizontally into the posterior tibial veins at different heights of the leg but few course vertically and laterally to join the fibular veins. The gastrocnemius veins take their origin from the calf perforators at the lower part of the muscle then giving origin to a number of pedicles that run upwards through the calf to terminate in a single collector draining into the popliteal vein. Through this collector the gastrocnemius pump powerfully ejects the blood into the popliteal vein, and anatomical variations in this collector are linked to differences in calf pump efficacy [88]. Calf muscles contraction can elevate the pressure to approximately 140 mm Hg and increase venous blood flow through the popliteal and the femoral veins [32]. In competent veins, the centrifugal component during muscle relaxation lasts approximately 200 to 300 milliseconds and represents the physiological reflux, in incompetent veins the duration exceeds 500 milliseconds [32].

Less efficient calf muscle pump function (CMPF) (involving especially the gastrocnemius and soleus muscles) has also been related with muscle inflammation, reduced muscle oxygen supply, muscle necrosis, myofibril atrophy (muscle fibers type I and II) and muscle denervation [28, 29]. A study by Araki et al. [89] concluded that venous insufficiency cannot fully explain venous ulceration, pointing to deficient calf muscle pump as a primary factor in CVD-related skin and tissue damage. Several studies show that early treatment, by exercising the muscle pump, can prevent the most severe forms of CVD [14, 90]. The important role of CMPF on the progression of CVD is well established, but in many individual cases impaired calf pump function may go undetected until most severe changes become evident [91]. Therefore, assessable, accurate and non-invasive methods to evaluate CMPF are needed [30, 59, 90–92].

### 5.3. Foot muscle pump

The deep venous system of the foot forms a venous plexus that is composed by a lateral vein, a medial vein, and a deep plantar arch. The lateral and medial plantar veins are usually doubled and course either intramuscularly or in between the plantar muscles from a lateral position distally to a medial position near the ankle, where they drain into the paired posterior tibial veins [93]. The deep plantar arch and the lateral and medial plantar veins receive blood from superficial veins located in the sole of the foot and from the metatarsal veins [85, 93]. The plantar deep venous system is connected with the superficial veins on the dorsum of the foot via several perforator veins. The link between these two venous systems is specially well developed between the medial plantar vein and the medial marginal vein, forming what has been named the “medial functional unit”, which possesses the unique feature of blood flow being directed from deep to superficial vessels [85, 94].

The physiology of the foot pump is still not totally clear. The anatomical design of the deep plantar system, characterized by the presence of paired veins flanking an artery and joined together by connective tissue, and by the close relation between these veins, the plantar muscles and the metatarsophalangeal joints, is well suited to enhance venous blood flow during weight bearing and ambulation. These imply that the foot pump expels the blood through a double mechanism: contact of the foot with the ground, resulting in extension of the tarsal arch and metatarsophalangeal joints associated with compression of the deep veins and the calcaneus plexus, and by contraction of the plantar muscles surrounding the blood reservoir of the deep venous system [88, 93–95]. The foot pump empties during the stance phase of the gait, as a result of weight-bearing, and pushing off action, and refills during the swing phase, when the foot is cleared from ground contact. Through its mechanisms, this pump moves 25–30 mL of blood, equal to the capacity of the deep medial and lateral plantar veins [94]. Individual differences in plantar support and in the pattern of the foot muscles contraction during the stance phase of the gait cycle have the potential to modify the efficacy of the foot pump [96].

These two mechanisms (weight bearing and muscle contraction), however, do not work synchronously, with plantar compression acting first then followed by the action of the muscle contractions at the foot [93]. These two different foot pump mechanisms may both be present

during the stance phase of the gait cycle, but would be active at [93]. Also, certain clinical conditions of CVD could be explained by a conflict between the mechanisms of the foot pump and the leg pumps [97]. The knowledge about the interaction of the lower limb muscle pumps during contraction/relaxation as a mechanism for venous return is still quite poor [57].

#### **5.4. Impairment of calf muscle pump and functional capacity**

Calf muscle pump dysfunction might be caused by weakness of calf muscles but may also be related to decreased range of motion around the ankle joint during walking and other movements [30, 75, 78, 98], neuropathy, muscle denervation or muscle atrophy, or gait abnormalities [29, 36, 43].

Ankle function plays an important role in mobility [36]. Distal leg muscles may exhibit reductions in strength and power with aging, and these affects walking, balance, and increases the risk of falling [99]. Impaired ankle muscles strength has been associated with falls [100]. The power output by dorsiflexion muscles has been found to be closely associated with function in community-dwelling older women in terms of their ability to get up from and sit down on a chair and climb stairs [100]. Plantarflexion strength has been shown to be positively related to both preferred gait speed and fast gait speed [100].

Patients with CVD present limited ankle range of motion [36, 45, 47, 78, 98]. Diminished ankle mobility tends to aggravate as CVD progresses and in parallel with increasing severity of symptoms, thus further contributing to a poor CMPF [78, 98]. Together with decreased ankle range of motion, there is also decreased muscle strength of dorsi and plantarflexors [30, 75], with decreased peak torque, power ability [36], muscle resistance (number of heel rises) [45], and total work performed by the ankle plantarflexors [75]. Other functional alterations associated with CVD include decreased gait speed [36, 45], decreased number of steps per week (in venous ulcer patients) [101], and generally impaired functional capacity and mobility [36]. Also, changes in ankle function alters foot pressure distribution during gait that becomes higher at the midfoot and lower at the toes [43].

These functional alterations, specially the decreased strength of the calf muscles and reduced ambulation, contribute to venous hypertension [30, 43, 46, 47, 57, 98]. Dysfunction of the muscle pumps leads to venous blood not being effectively emptied out of the distal extremity [30]. This rarely occurs as a "primary" disorder in neuromuscular conditions or muscle wasting syndromes; however, clinically significant muscle pump dysfunction often occurs in severe reflux or obstruction [92]. Muscle pump dysfunction appears to be a major mechanism for the development of superficial venous incompetence and its complications, such as venous ulcers, and around 70% of patients with venous ulcer present calf muscle pump dysfunction [48, 66, 89, 91, 102].

Venous blood flow increases during calf muscle contractions in individuals with or without CVD. Popliteal peak flow volume is maximal during the first contraction of the tip-toe set of ten repetitions when the venous reservoir is full [103]. In the CVD patients, but not in the healthy subjects, venous flow augmentation was seen to diminish during the ten tip-toe

exercise [104]. Such apparent calf pump dysfunction might be related to weak calf muscles in CVD patients [29, 30] and is compatible with a lower ejection volume, such as has been measured before in this population with air-plethysmography [92]. In addition, abnormal venous blood reflux from deep to superficial venous system through incompetent perforator veins may blunt blood flow through the popliteal vein [104].

Nonetheless, it seems that calf muscle size is not a strong indicator of the efficacy of muscles to pump venous blood during contractions in patients with venous ulcer [105]. Also, gastrocnemius thickness and some other muscle architectural features, like pennation angle, are similar in patients with low to moderate CVD severity and healthy participants, and seem unrelated with the severity of CVD [104]. Despite this fact, for the medial gastrocnemius, a few morphological parameters (like higher muscle fascicle length, and pennation angle) are associated with the degree of increase in peak flow velocity in the popliteal vein during tip-toe movement [104].

## 6. Clinical and functional assessment of CVD (CEAP classification, VCSS)

### 6.1. CEAP Classification

Health professionals-reported outcomes, such as VCSS and CEAP classification, are convenient, easily evaluated, and relevant [15].

The CEAP classification was created to facilitate communication about CVD severity and for scientific research [13]. The CEAP classification was based on 1) clinical manifestations (C), 2) etiologic factors (E), described as congenital, primary, secondary (post-thrombotic), 3) anatomical distribution of disease (A), that can be located at superficial, perforator or deep veins, and 4) underlying pathophysiological findings (P), such as reflux, obstruction or both reflux and obstruction [13]. Subscripts are applied to designate S (symptomatic) from A (asymptomatic) limbs [65]. According to CEAP, there are six CVD categories that range from C<sub>0</sub> to C<sub>6</sub> [13, 65]. Also, the N subscript indicates no evidence of disease and is applicable to E, A, and/or P of CEAP [13, 65].

The C<sub>0</sub> represents those individuals with objective evidence of venous disease (i.e., E, A, and/or P), but with no clinical manifestations. The C<sub>1</sub> is characterized by the presence of telangiectasia or reticular veins (< 3 mm in diameter). In the C<sub>2</sub> class varicose veins (> 3 mm in diameter) are present. The C<sub>3</sub> distinguishes itself from the preceding categories by the presence of edema of venous etiology. In the C<sub>4</sub> class, there are now skin trophic changes, like C<sub>4a</sub> for pigmentation and/or eczema, and C<sub>4b</sub> for lipodermatosclerosis and/or white atrophy. Classes C<sub>5</sub> and C<sub>6</sub> are associated with the occurrence of venous ulcers: the C<sub>5</sub> corresponds to cases of prior ulceration that healed, and C<sub>6</sub> to cases with active venous ulcers [13, 65].

Reticular veins, also called blue veins, subdermal varices, and venulectasies, are dilated subdermal veins, usually 1 mm to less than 3 mm in diameter and with tortuous paths [13].

Telangiectasias, also called spider veins, hyphen webs, and thread veins, represent the confluence of dilated intradermal venules less than 1 mm in caliber [13].

According to the guidelines, varicose veins (also called varix, varices, and varicosities [13]) should be palpable in an upright position and represent abnormal veins with at least 3 mm in diameter, [3, 13, 33]. Varicose veins can be present as a result of hypertension caused by reflux and/or obstruction, as discussed before [12, 57].

The development of varicose veins most frequently involves the saphenous veins, saphenous tributaries, or nonsaphenous superficial leg veins [13]. Varicose veins are usually tortuous, but tubular saphenous veins with demonstrated reflux may be classified as varicose veins [13]. Corona phlebectatica, also called malleolar flare and ankle flare, is commonly viewed as an early sign of CVD, and designates the accumulation of numerous small intradermal veins packed together on the medial or the lateral aspects of the ankle and foot [13].

The venous edema is a pitting edema that get worse through the day and static positions and improves at night with decrease hydrostatic pressure , accomplished for example in supine position and lower limb elevation, and usually is accompanied with venous symptoms and signs [19, 20].

The presence of pigmentation means that the skin becomes darker and brownish [13]. This results from extravasation of red blood cells into the interstitial space [57]. Blood extravasation and skin pigmentation is most noticed around the ankle, but may also be visible in the leg and foot [13, 106].

Atrophie blanche (white atrophy) is an induration of tissues This skin alteration, that should not be confused with healed venous ulcers, is usually well localized. and has the shape of a circular white and atrophic skin surrounded by dilated capillaries and sometimes by hyperpigmentation [13, 106].

Lipodermatosclerosis is also clinical sign of tissue induration, characterized by local chronic inflammation and fibrosis of skin and subcutaneous tissues at the lower region of the leg (also compromising the Achilles tendon), sometimes preceded by diffuse inflammatory edema of the skin, which may be painful and which often is referred to as hypodermatitis [13, 106]. Clinically, lipodermatosclerosis must be differentiated from lymphangitis, erysipelas, or cellulitis by their characteristically different local signs and systemic nature characteristics [13].

The eczema is an inflammation process, erythematous dermatitis, which may progress to blistering, weeping, or scaling eruption of the leg skin, and may be located anywhere in the leg [13, 106]. Eczema is very frequent in uncontrolled CVD, but may also be associated to sensitization to local therapy [13].

Venous ulcers are the worst clinical sign of CVD and represent the loss of integrity of the skin, with a full-thickness defect and occur most frequently near the ankle region [13], at the site of major perforating veins and the greatest hydrostatic pressure [66]. Venous ulcers are also characterized by failure to heal spontaneously and are sustained by CVD [13].

The CEAP classification is the gold standard for classification of chronic venous disorders today and its use is recommended by the relevant guidelines [33]. Nevertheless, for proper use of CEAP some facts have to be taken into account: the CEAP classification is limited as a severity classification,  $C_2$  summarizes all kinds of varicose veins, in  $C_3$  it may be difficult to separate between venous and other reasons for edema, and corona phlebectatica is not included in the classification [107]. Further revisions of the CEAP classification may help to overcome the still-existing deficits [107]. Complementary to this classification system, some concepts were defined to give consistency to the scientific terms, like the CVD concept that designates any venous disorder associated to every clinical class, and the concept of chronic venous insufficiency, which represents the more severe stages of the disease ( $C_{3-6}$ ) [13, 65].

The CEAP classification is the gold standard for classification of chronic venous disorders today, and its use is recommended by the relevant guidelines [33]. Nevertheless, when using the CEAP system a few issues must be acknowledged: as a classification system the CEAP has limitations. For example in  $C_3$ , it may be difficult to separate between venous edema from edema with other causes [106].

## 6.2. Venous clinical severity score (VCSS)

The Venous clinical severity score (VCSS) was developed to supplement the CEAP classification and to give an additional weight to the more severe consequences of CVD [108]. The VCSS score has shown good intra- and inter-observer reliability and responsiveness to change [108–110]. This is a score that quantifies 10 items using the range: 0 (none), 1 (mild), 2 (moderate), and 3 (severe), with a total range score of 0–30 (best to worst) [106, 108–110]. In CEAP classes  $C_0$  to  $C_6$ , the VCSS score is reported to range between of 3–18 [111]. A worthwhile clinical improvement for patients with CVD can be observed with a relative improvement of 70% in VCSS score [110] or with an absolute improvement of 4 points [7]. Differences between clinical classes are 1–2 points of VCSS below  $C_3$ , and 2–5 points above  $C_3$  [111]. The items of the VCSS are:

- Pain or discomfort; (i.e., aching, heaviness, fatigue, soreness, burning, with presumed venous origin), patients are asked to describe for each leg the category that best describes this item;
- Varicose veins (with diameter  $\leq 3$  mm in standing position);
- Venous edema (presumed venous origin, i.e., pitting edema present every day and with significant changes by standing/limb elevation or evidence of venous etiology, like varicose veins or history of deep vein thrombosis) - clinical staff must exam both legs and should ask patients about the extent of edema experienced;
- Skin pigmentation (presumed of venous origin and not including focal pigmentation over varicose veins or pigmentation due to other chronic diseases) - clinical staff must exam each leg;
- Inflammation (more than just recent pigmentation, like erythema, cellulitis, venous eczema, dermatitis);
- Induration (presumed of venous origin with secondary skin and subcutaneous changes, such as chronic edema with fibrosis, hypodermatitis, white atrophy, and lipodermatoesclerosis);

- Active ulcers number
- Active ulcers duration (patients are referred to describe the duration of the longest unhealed ulcer);
- Active ulcers size (score according the size of the largest active ulcer);
- Use of compression therapy (patients should be asked about their compliance to compression therapy).
- The assessment of the items of VCSS score should be carried out for both legs.

Despite their relevance, VCSS and CEAP evaluation can be biased by observer expectations and because patient-reported outcomes are recognized by medical authorities as the ultimate outcome for health-care interventions, self-reported assessment of symptoms and HRQL is recommended for CVD as well [15, 112]. The most comprehensively validated scales for assessing HRQL in CVD include the chronic venous insufficiency questionnaire (CIVIQ), for population with CVD and without ulcer; the Aberdeen varicose vein questionnaire (AVVQ), for population with varicose veins; and the venous insufficiency epidemiological and economic study on quality of life (VEINES-QOL), for population with CVD of all classes [113].

## 7. Conservative treatment of CVD

The main goals of conservative treatment for CVD, used as an adjunctive treatment or in isolation, focus on both the symptoms and secondary changes of the disease, such as for instance, edema, skin and subcutaneous changes or ulcers [33], and the prevention of secondary complications, like venous thrombosis [114]. Usually, initial treatment of CVD involves a non-invasive conservative treatment to reduce symptoms and help prevent the development of secondary complications and the progression of the disease [66]. Complementary, or posteriorly, some interventional or surgical treatments can be undertaken [33, 66].

Behavioural education, like giving advices to raise the legs to minimize edema and reducing intra-abdominal pressure, about the right exercises, for using compressive stockings and proper care of the skin and wounds, together with pharmacological therapy, is the most common referred conservative treatments [33, 66]. The conservative pharmacological treatment with venoactive drugs may be indicated for patients with pain and edema and should be implemented in association with compression for healing venous ulcers [33]. If conservative treatment is unsuccessful or provides an unsatisfactory response, then further treatment, including surgery, should be considered based on anatomic and pathophysiological features [66].

Interventional treatments, like sclerotherapy, ablative therapy with endovenous radiofrequency and laser, endovascular therapy, are less invasive than surgery for treating CVD [66]. It has been recommended to use these techniques to treat superficial incompetence (endovenous thermal ablation, as laser and radiofrequency) and varicose veins (sclerotherapy) [33].

Surgical treatments are recommended in severe forms of CVD, like venous ulcers that did not heal after 6 months of treatment [66]. There are several surgical procedures described in the

literature, like ligation, stripping and venous phlebectomy, subfascial endoscopic perforator surgery or valve reconstruction [66].

In CVD, compression, like that provided by stockings, is recommended as a primary treatment, except when patients are candidates for vein ablation, in which case compression is also suggested as an adjuvant treatment, particularly to prevent ulcer recurrence [33]. Compression therapy is recommended as a complement to surgery (like stripping), and to venoactive drug treatment, in order to control edema and pain, and to enhance venous ulcer healing [33].

The severity of the disease is related with the difficulty of the peripheral venous system to evacuate the venous blood from the periphery in the direction of the heart [33], resulting in venous stasis [33, 115]. Furthermore, it is assumed that there is a strict relation between blood flow velocity and secondary deep vein thrombosis [114]. The prevention of stasis is a main goal in CVD treatment and decisive in preventing venous complications and is frequently done through conservative approaches. Conservative CVD treatment might include intermittent pneumatic compression [116], compression stockings and bandages [77, 117, 118], and muscle pump activation using electrical muscle stimulation [77, 119], transcutaneous electrical nerve stimulation [119], or active and passive movements [103, 119]. In this regard, MLD maneuvers may be an alternative treatment to enhance venous flow [21–23]. Nevertheless, this intervention needs specialized professionals and could be an expensive health care treatment. Teaching caregivers or patients simple lymphatic drainage, despite the lower efficacy showed in the treatment of lymphedema, when compared with MLD applied by professionals [25], could be an alternative.

The important role played by the ankle range of motion and calf muscle strength in the efficacy of CMPF is now widely recognized [30, 36, 43, 45, 90]. Likewise, altered CMPF seems to play a key role in the physiopathology of CVD [30, 36, 43, 45]. Physical exercise is nowadays widely recommended for CVD management [90, 120]. In previously conducted randomized controlled trials, exercise training in patients with CVD [90] or with post-thrombotic syndrome [120] was shown to improve calf muscles' peak torque at slow (60°/s) and fast (120°/s) speeds [90], maximal heel rise repetitions [120], CMPF [90], and HRQL [120]. However, the role of physical exercise in ameliorating the measures of clinical severity of CVD or in improving few performance features, such as joint range of motion or work and power ability of ankle plantarflexors could not be clearly demonstrated [90, 120].

## 8. Manual lymphatic drainage

There are four recognized techniques of MLD: the Földi [121], Vodder [122], Casley-Smith [123] and Leduc [124].

The four methods of MLD show some differences, but the major basic principles are very similar. In short, the maneuvers should be applied softly (with specific exceptions), should consist of a skin-stretching form of massage (not sliding), should comply with the direction of lymph flow, should be done using the entire hand or exceptionally with fingers, and should begin at the proximal regions of the extremity [122–126].

MLD is used as a conservative treatment of lymphedema, independently of the specific method [127]. In the case of the Leduc method, MLD consists of a skin-stretching [127] form of massage that applies low pressure (<40 mm Hg) to the underlying tissues [124] along the anatomical distribution of the superficial lymphatic vessels and ganglions, stimulating lymph flow [128, 129] and the reabsorption of interstitial fluid and macromolecules through the lymphatic circulation [124, 128, 129]. At the lower extremity, the call-up maneuver, a technique belonging to the Leduc method initiates with inciting (or call-up) maneuvers in the inguinal region (ganglionic stimulation) and then progresses distally along the lower extremity down to the edematous region, again employing call-up maneuvers, in order to stimulate lymph flow by enhancing the contractility of lymphagions of lymph collectors, [128, 129]. The reabsorption maneuver, another Leduc technique, is then applied over the edema to drain the interstitial fluid and soluble macromolecules through the lymphatic circulation [128–130] by stretching the leak filaments (connections between connective tissue to endothelial cell of lymphatic capillaries) when the skin is mobilized [128–130]. The whole procedure ends with a second round of call-up maneuvers, which are then applied in the reverse direction, ending at the groin region, in the case of the lower limb [128, 129]. Technically, the call-up maneuver initiates with the most proximal part of the hand and ends with the hands touching the skin while producing skin-stretching and is applied to promote the increase of lymph flow [128, 129]. The reabsorption maneuver initiates with the most distal part of hand and ends with hands touching the skin while applying skin-stretching [128, 129].

### **8.1. Contraindications/Precautions**

There are several contraindications and precautions for MLD and decongestive lymphatic therapy. It is suggested that cardiac, pulmonary and renal functions should be monitored because of temporary increase in blood flow and circulatory loading [73]. As for the contraindications, the literature describes erysipelas, lymphatic systemic infection and lymphangitis, meaning inflammation of the lymphatic system, as absolute contraindications for MLD and decongestive lymphatic therapy [131]. Severe renal and heart failure are also contraindications for the use of multilayer bandages and intermittent pneumatic compression [132], whereas caution should be enforced when employing MLD in patients with severe cardiac insufficiency [128, 131, 132]. Unstable hypertension, thyroid dysfunction, hepatic cirrhosis with abdominal fluid (ascites), superior vena cava obstruction, untreated tuberculosis or malaria, are also contraindications for physical treatment [131, 132]. If swelling occurs for a long time after initial breast surgery, medical examination should be sought and any physical treatment will be stopped if inflammation occurs [132]. Also, Crohn disease, recent surgery, and diabetes are some additional clinical conditions that may be monitored for precaution [73].

### **8.2. Manual Lymphatic Drainage in Lymph edema**

There are several indications for the use of MLD other than lymphedema, like CVD, post-thrombotic syndrome, chronic wounds, traumatic edema (iatrogenic, postsurgical, and musculoskeletal injury), complex regional pain syndrome, and lymphedema [73].

The evidence of MLD for the treatment of edema (related to cancer or traumatic during sport activity, or other orthopedic injuries) [25, 26, 133] and in improving functional status (related to total knee arthroplasty) [24] is unclear but has been considered somehow effective, but more research is needed. Nevertheless, MLD might have an important role in CVD by improving HRQL, symptoms [134, 135], and range of motion [24] when edema/lymphedema is present. In palliative treatment, MLD improves pain and dyspnea [25].

Based on a systematic review, the importance of MLD for preventing the incidence of lymphedema is unclear [25]. A meta-analysis shows that MLD does not provide further therapeutic benefit in reducing lymphedema related to breast cancer, when compared to the standard treatment or with compression therapy [25], but another study has demonstrated a benefit when employing MLD in these cases [136]. However, the small benefit of MLD must be evaluated together with its cost in terms of time and money spent by patients and health care systems and such cost-benefit evaluation favours the option for compression therapy by using multilayer bandages or compression hosiery and adding MLD only if the response to treatment is unsatisfactory [136].

Lymphatic drainage employing a simpler sequence, but using the same principles as MLD, in a way that can be applied by patients as a self-drainage [137, 138] is less effective than MLD in reducing limb volume or lymphedema related to breast cancer but can be used as a more economical MLD option [25].

It has been also suggested that MLD, despite the augmentation of lymph flow (increasing lymphatic contraction and lymphatic reabsorption), might also be responsible for increasing arteriolar blood flow, redirection of flow toward collateral vessels, anastomoses, and perhaps stimulating angiogenesis, but these hypothetical effects of MLD need scientific evidence [73].

Younger patients, those heavier in weight and higher in body mass index are more likely to show poor lymphedema treatment outcome after intensive decongestive therapy [25]. When an elastic sleeve and multilayer bandaging are associated to MLD, there is a higher chance that the lymphedema treatment is successful [139].

Decongestive lymphatic therapy is the physical treatment for lymphedema by combining MLD with other treatments, like low-stretch bandaging and compression garments, exercise, and skin care, and sometimes also with intermittent pneumatic compression [30, 127, 140]. This method may reveal itself as effective in the treatment of lymphedema of the lower limb as it is for that affecting the upper limb as a result of cancer [135, 141].

Most often, decongestive lymphatic therapy is applied along two phases: the first is the edema reduction and intensive one, and the second one is the maintenance phase [127, 142, 143].

Decongestive lymphatic therapy is often prescribed for patients with venous ulcer and when CVD are associated with mixed edema (lymphatic and venous origin), now combining MLD, compression bandages, and stocking, physical therapy to improve calf muscle performance, and in few cases, intermittent pneumatic compression [16]. In the case of CVD, wearing compression garments is essential for treatment efficacy [16, 143].

### 8.3. Manual lymphatic drainage in CVD

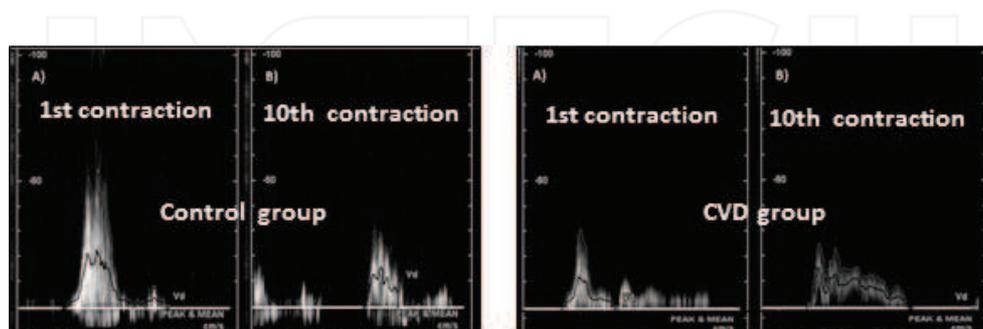
#### 8.3.1. The technique

The manual technique of MLD is not usually described in the literature. Nevertheless, based on research [21–23], the hands of the physical therapist must do the maneuvers producing a low pressures form of skin stretching. The pressure applied by the hands onto the skin and underlying soft tissues should be carefully adjusted to remain soft and just enough to stretch the skin for at least 4 s. When both legs are treated, the whole session take approximately 40–45 min [17, 18, 21]. The duration and the number of sessions at the studies assessing the role MLD in CVD patients [17, 18] are similar, during 2–5 weeks, patients should complete 10–14 sessions of MLD.

The sequence of the maneuvers follows that commonly used for lymphedema, first, moving from proximal to distal and, second, moving from distal to proximal [128, 129]. The maneuvers can be applied in the following sequence: inguinal region (10 MLD maneuvers), progressing downwards through the thigh, (30 MLD maneuvers at medial and 30 at lateral aspect of thigh), the popliteal region (10 MLD maneuvers applied immediately above the popliteal fossa and another 10 times maneuvers performed immediately below the popliteal fossa), downwards to the leg (30 MLD maneuvers at medial and lateral aspect of leg), and finishing in the dorsal aspect of the foot 30 MLD maneuvers). Next, the manoeuvres should be carried out in the reverse order upwards: 15 maneuvers on the dorsal aspect of the foot, 15 maneuvers both on lateral and medial aspect of the leg, 5 maneuvers both below and above popliteal fossa, 15 maneuvers above both the lateral and above the medial aspect of the thigh, 5 MLD maneuvers on the inguinal region (**Figure 1**)[21]

#### 8.3.2. Physiological effects in venous hemodynamic

Some studies suggest that MLD has an effect on blood flow in superficial veins, especially through the call-up maneuver [144]. Also the real impact of MLD in hemodynamics has been suggested to be insignificant [128]. One study concluded that 5 to 15 minutes of MLD does not



**Figure 1.** Venous ultrasound assessment at popliteal vein during 1st and 10th calf contraction. Venous ultrasound assessment at popliteal vein during 1st (A) and 10th (B) calf contraction, during tiptoe movement for both control (no CVD) and CVD ( $C_0$ – $C_4$ ) groups.

change cardiac output in patients with heart failure despite the near 100% increase in venous return after 5 minutes of MLD [128]. Nevertheless, recent studies reveal that in real-time the blood flow in superficial and deep veins increase, despite the presence or absence of venous pathology [22, 145].

Current concepts regarding MLD indicate that each maneuver should take around 4 s from beginning to end [22, 23, 129]. MLD techniques, which are based on manual stretching of the skin and underlying soft tissues, increase venous blood flow along the superficial veins, as has already been suggested [144], but also along the deep venous system, which course beneath the deep fascia. As commonly taught, the call-up maneuver is applied in a proximal to distal direction and enhances venous blood flow. The reabsorption maneuver instead begins distally and then moves proximally, stimulating lymph flow and fluid reabsorption [129]. One study does not substantiate such differential effects between the two maneuvers [22]. In fact, the two maneuvers enhanced venous blood flow to a similar extent and in both deep (femoral vein) and superficial (great saphenous vein) veins.

The amount of strain applied to the skin and deeper tissues by MLD is not known. Although studies using radiolabelled tracers demonstrate the efficacy of MLD in stimulating lymph flow, the exact mechanisms by which these techniques work are not fully elucidated [121, 130]. Skin and deep fasciae are connected by ligamentous structures at the level of the thigh, knee, popliteal fossa, and leg, which give stability to the skin and act like an anchor during lower limb movements [146]. The skin stretching applied during MLD might produce enough increase in pressure upon underlying structures to enhance venous flow in superficial and deep veins, as occurs during the physiological stretching of the skin during limb movement [147].

MLD must take into account venous anatomy and venous blood flow direction just like the lymphatic anatomy and the lymph flow directions, particularly when applied to larger body segments (like the course of GSV), such as the thigh, to be more effective in increasing venous flow [23, 128, 129, 145, 148].

The increased blood flow in the superficial veins would result in higher blood flow across perforating veins and into the deep veins, thereby raising blood flow in the deep venous system as well. In addition, the pressure applied to the skin, as said before, would probably reach the muscles underneath, and pressure would also increase in deep seated structures including veins, further stimulating blood flow. Also, muscle tone might increase during the time MLD techniques are being applied, induced by the manual stimulation, or in response to the movement of the lower extremity, which could have contributed to the observed increase in venous blood flow.

### *8.3.3. Therapeutic efficacy of manual lymphatic drainage for treatment of patients with chronic venous disease*

MLD has also been used as a conservative treatment for CVD, [16], mostly when venous lymphedema is present [19, 20]. MLD applied before surgery in patients with CVD improves the clinical class of CEAP classification, HRQL, depression, anxiety, edema, and symptoms

[17, 18, 21]. Nevertheless, foot volumetry and reflux volume index only improve when MLD is associated to surgery and compression stockings [17, 18].

Previous studies show that MLD (10 sessions in 2 weeks) used in CVD patients who were referred to vascular surgery is effective in diminishing pain and edema and in improving HRQL [17]. When employed for a longer period of time (14 sessions in 5 weeks), MLD also seems to effectively contribute, together with surgery, to improve CVD severity [18]. However, such effect of MLD could be explained by faster recovery during the post-operative time. However, a recent study reveals that MLD (4-weeks period of MLD treatment, comprising ten 40 to 45 min-duration of each of 10 sessions) has a real effect in improving CVD-related symptoms, pain-HRQL and clinical severity (mostly related to venous edema), independently from vascular surgery, with the positive outcomes of MLD persisting after 1 month follow-up [21]. Nonetheless, MLD seems to be ineffective in changing leg volume, ankle muscles strength, ankle active range of motion, and the physical, social or psychological components of HRQL of CIVIQ [21].

There is no evidence that MLD treatment may significant change ankle muscles performance (either during plantarflexion or during dorsiflexion) and ankle range of motion. However, the role of physical exercise in ameliorating the measures of clinical severity of CVD or in improving some performance features, such as joint range of motion or work and power ability of ankle plantarflexors, could not be clearly demonstrated [90, 120].

However, the possibility that MLD might improve ankle function during more natural activities, such as gait, has not been assessed yet.

MLD increases peripheral venous blood flow in superficial and deep veins in normal limbs and in those with CVD and may be an important conservative treatment for prevent blood stasis and its complications [21–23, 125]. The prevention of stasis, by increase venous return, is a main goal in CVD treatment and decisive in preventing venous complications, and there are several conservative approaches [114]. During the application of the MLD maneuver (with pressure <40 mmHg), the volume of venous blood outflow from deep and superficial veins increases substantially without collapsing the veins [22, 23].

Studies suggested that despite the increase of venous flow during MLD being similar in healthy and CVD groups ( $C_{1-3}$ ), in most severe cases of this disease this augmentation might not occur [22, 23]. CVD causes significant damage to the skin and underlying tissues. Persistent inflammation of the skin leads to disease complications such as lipodermatosclerosis, characterized by fibrosis and microcirculatory changes [149], leg edema [27] may interfere with the movement of the skin and underlying soft tissues essential to MLD efficacy.

The adherence to compressive stockings is usually decisive to manage symptoms and complications of CVD and venous stasis [150]. Some studies refer the importance of wearing compression stocking during the application of MLD [17, 18]. In one study, 23 out of the 41 patients did not wear compression stockings and only four participants fully adhere to this treatment, with no influence on MLD efficacy. However two patients in the control group (no MLD treatment) were excluded during the study because they present deep venous

thrombosis and coincidentally these two participants did not comply with the use of compression stocking [21].

#### 8.4. Recommendations for treating CVD with MLD

MLD should be applied as a low pressure, manual skin-stretching form of massage applied from distal to proximal throughout the lower limb, with the two hands of the physical therapist placed side by side and respecting the anatomy and flow of venous vessels, in order to increase venous return from the lower limb in subjects with or without CVD (C<sub>1-5</sub>).

MLD treatment for CVD should be applied during 2–5 weeks; patients should complete 10–14 sessions (45 min duration for both legs) of MLD. The sequence of MLD maneuvers should be applied proximal to distal, followed by a sequence in reverse direction (i.e., from distal to proximal) such as recommended for lymphedema [124, 128]. Because inflammation may be present in these patients, direct manual skin-stretching should be avoided over the edema, as for local inflammation in lymphedema. Although there is no evidence of the efficacy of MLD in treating venous ulcer (C<sub>6</sub>), it can be applied in these patients as long as no contraindications are present [21].

Despite no evidence that MLD prevent secondary complications associated to venous stasis, like venous thrombosis, the use of MLD may be an option to increase superficial and deep venous flow [23, 104]. In particular, MLD is recommended before venous surgery and should be complemented with compression stockings [17, 18].

It is recommended to use MLD to relief edema, symptoms, severity of disease, and ameliorate HRQL. These effects are more consistent when MLD is used as a coadjutant treatment of compression stocking [17, 18, 21]. When adherence to compression treatment is difficult, MLD can be an option to relief symptoms and improve HRQL in patients with CVD [21].

Compromised muscle pump function, low muscle strength, and limited ankle range of motion can be addressed with other conservative approaches, like physical exercise.

## 9. Conclusion

CVD is a very common disease across the world. Despite the cosmetic issues, there are very important dysfunctions associated with this pathology, like muscle pump dysfunction, symptoms like pain, limitation of range of motions and muscle strength, gait alterations, Lymph(edema), higher risk of deep venous thrombosis, among other. Physical therapists may have an important role in assessing (using a uniformed procedure with other health professionals) and treating these dysfunctions using a wide number of strategies, like exercise, Kinesio taping, and others. MLD may be an alternative coadjutant conservative treatment of patients with CVD, previous or not to surgery. Although there is already information about the importance of MLD as a treatment choice for CVD, further research is warrant to determine the best way to combine this approach with the existing CVD treating tools.

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