Posttraumatic Lower Limb Edema

22

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22.1 Background

Traumatic injuries of the musculoskeletal system are categorized as direct or indirect, ranging from simple abrasions, lacerations, tendon ruptures, avulsions to complex tissue crushing and fractures of various types.

Thrombosis and edema often complicate mechanical trauma to the soft tissues and bones of the lower limbs both at the site of the trauma and distally. Edema is a chronic disorder caused by the presence of extra fluid in the extracellular space. This complication affects almost all patients with fractures of the lower limbs, whether they undergo surgery or not. Posttraumatic lower limb edema (PTLLO) has a significant effect on the timing of surgical intervention. The risk of chronic wounds and infections can also increase [1]. PTLLO treatment can be demanding and prolonged and seldom leads to full healing. Neither the pathogenesis of posttraumatic edema has been completely elucidated, nor has the mechanism causing this disease to become chronic [2]. Inflammation and lymphatic obstruction at the trauma site and deep venous thrombosis (DVT) are likely to play a significant role [3]. This chapter discusses the etiopathogenesis of posttraumatic edema in lower limbs and a study of the related literature of the last few years, discussing the results of treatment and future treatment prospects.

22.2 Etiopathogenesis (Table 22.1)

The four cardinal signs of inflammation identified by Celsus, i.e., erythema, pain, raised local temperature and edema, are invariably associated with musculoskeletal injury. Edema (swelling) is mainly caused by extravasated blood, which increases

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Table 22.1 Common causes of PTLLO with underlying mechanism

Cause	Underlying mechanism
Secondary Lymphedema (surgery/trauma)	Lymphatic obstruction
Chronic venous insufficiency	Increased capillary permeability caused by local venous hypertension
Deep venous thrombosis	Increased capillary permeability
Complex regional pain syndrome (reflex sympathetic dystrophy)	Increased capillary permeability (neurogenically mediated)
Infection/cellulitis	Increased capillary permeability

the content of tissue compartments. An inflammatory response to the damaged tissues and extravasated blood is followed by this. The enhanced vascular endothelial permeability increases fluid filtration in extravascular and extracellular spaces. This results in more tissue volume enlargement and impaired perfusion of the affected tissue. The reduced supply of blood compromises circulation in the tissues and induces a deficiency of oxygen in the region. This oxygen deficiency disrupts cellular metabolism. As they do not have adequate energy for active transport across the cell membrane, hypoxic cells lose water. As a result, leakage of intracellular fluid further exacerbates edema. The increased distance between the capillary vessel and the cell reduces the availability of oxygen to cells that already have increased demand for it. The diffusion of oxygen decreases approximately three-fold for each unit of distance between the cell and the capillary vessel. Edema leads not only to cellular hypoxia but also to increased interstitial pressure, capillary constriction and impaired blood flow. Following the extravasation of blood or bone marrow into the surrounding tissues, most of the edema fluid is removed through venous vessels through resorption by the capillaries. However, cellular components and cell fragments as well as large molecular weight proteins are removed through lymphatics. First, they are taken up by capillary vessels that open into extravascular space. Subsequently, the lymph travels through the ascending vessels to the lymph nodes and through the descending vessels to the thoracic duct, which leads to the left venous angle. The lymphatic system has valves that prevent the lymph from moving backward. However, this is not to say that the lymphatic system functions in the same way as the vascular system. The lymphatic system is open, which means that the lymph can travel from distal to proximal locations, from subfascial to superficial vessels, but also in reverse direction [4]. Over the last years, resolution techniques superior to those of the "older" techniques of lymphoscintigraphy and lymphography have been used to depict the structure of lymphatic vessels during the posttraumatic edema of the lower limbs. Lohrmann et al. [5], who used magnetic resonance for lymphangiography in a group of patients with chronic posttraumatic edema, revealed lymphectasis up to 5 mm in diameter, increased lymphatic outflow and development of collateral vessels at calf level. Interestingly, collateral vessels developed for both suprafascial and subfascial (deep) lymph vessels [5]. Immobilization is one of the factors supporting posttraumatic edema. The effect can be explained both by the mechanism of the muscle pump, described by Le Dentu in the nineteenth century and by other independent mechanisms related to the loading of the limb, which most likely leads to the longitudinal stretching of venous vessels and

thus emptying them [6]. On the other hand, recent studies have shown that the lymphatic system is solely responsible for the removal of fluid from extracellular space [7]. The roles of all "players" in the flow of blood, lymph and extracellular fluid in the human body have not been fully determined to date and further study of edema pathogenesis is required. Studies are currently underway on individual susceptibility to the edema of the lower limbs. The results by Sugisawa [8] show reduced pumping pressure in the lymphatic system as an independent risk factor for the development of the lower limb edema [8]. It is possible that idiosyncratically low pumping pressures in the venous system would predispose these individuals to more severe PTLLO. A significant proportion of posttraumatic edema patients have not shown signs of active or past thrombosis. In addition, the classical theory that emphasizes the role of extravasated blood as a factor that promotes lymphatic blockage has been largely negated by the results of newer studies by Szczesny and Olszewski and Lippi et al. [9, 10]. In addition, many patients with posttraumatic edema of the lower limbs have the classic signs of inflammation, which would be difficult to attribute solely to impaired venous or lymphatic outflow. The long-term activation of the inflammatory process involving numerous cells and transmitters is likely to occur in patients with PTLLO [11]. It is caused by the accumulation in tissues of protein-rich filtrate, which indicates an inflammatory reaction. In fact, Maisel et al. [12] have concluded that this contributes to fibrosis, weakened immunity and diminished healing abilities [12]. In some chronic cases, edema of the limb favors erysipelas infections due to insufficient venous and lymphatic circulation, while erysipelas becomes an aggravating factor for lymphedema as a consequence of relapsing outbreaks [13].

22.3 Assessment of PTLLO

22.3.1 History

The history should include the timing and mechanism of the injury, treatment received and progression of swelling and intensity of pain in acute cases. Swelling may be in the soft tissues, the joint or the bone. It is important to establish whether it followed an injury, whether it appeared rapidly (think of a hematoma or a hemarthrosis) or slowly (due to inflammation, a joint effusion or infection. In cases with delayed presentation, a suspicion of cellulitis, DVT (Fig. 22.1) and compartment syndrome should be kept in mind while elucidating history.

22.3.2 Physical Examination

The lower extremity inspection should focus on the medial malleolus, the bony part of the tibia, and the dorsum of the foot. Particular attention should be made to the skin condition, vascular inflow, and innervation. Acute changes in the skin from the injury include wounds (Fig. 22.2), hematomas, degloving injuries, ecchymoses, and blisters (Fig. 22.3) The zone of internal injury is often greatly underestimated by the

Fig. 22.1 Acute DVT with overlying cellulitis

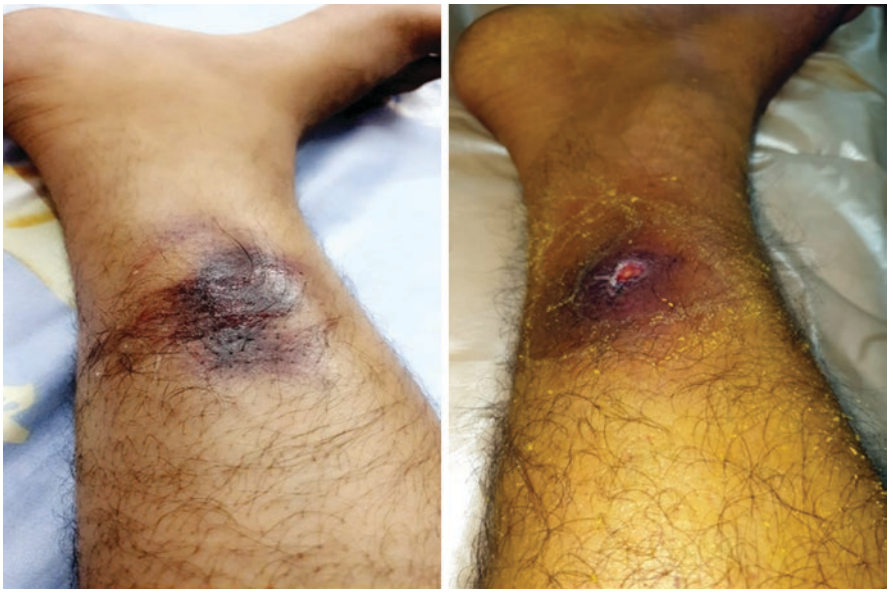

Fig. 22.2 Posttraumatic Cellulitis (right) later changing into abscess (left)

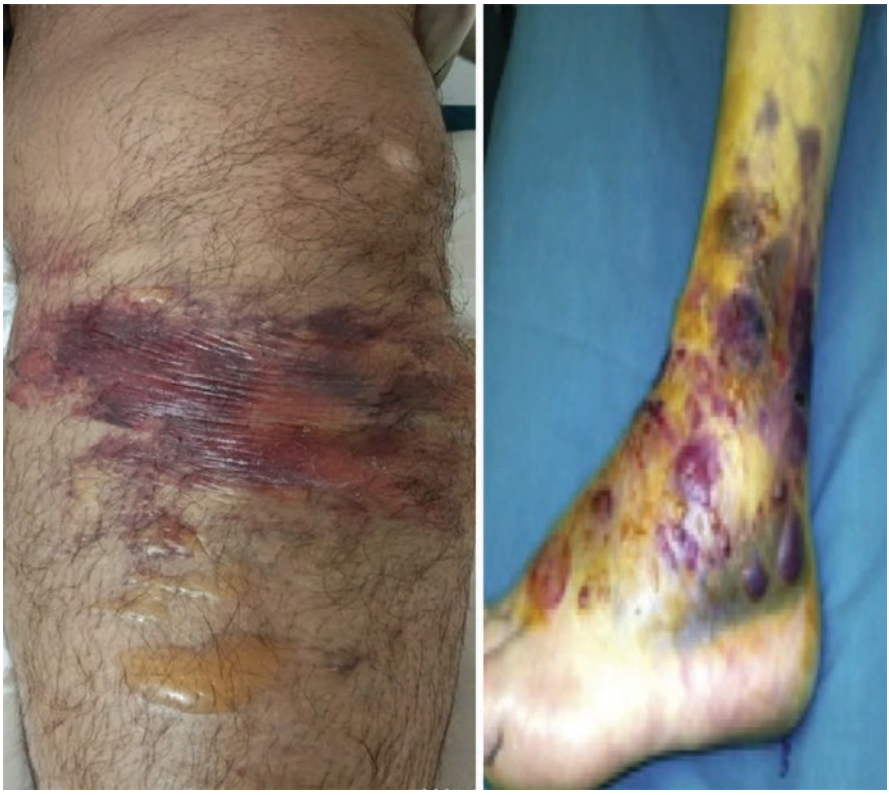

Fig. 22.3 Hemorrhagic blebs

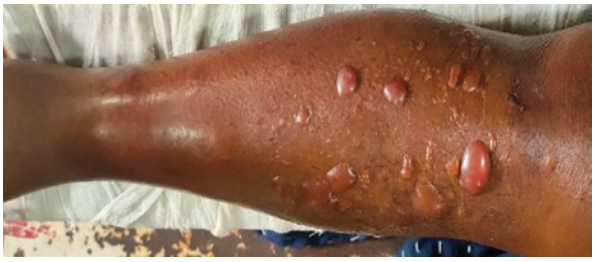

Fig. 22.4 Non-hemorrhagic blebs with impending compartment syndrome

external appearance of the limb and actual extent will be revealed later on. An injury with an associated fracture can cause diffuse vascular damage to the bone, periosteum, and muscle. Acute interstitial swelling can proceed to the point where capillary pressure is overcome and can lead to compartment syndrome (Fig. 22.4). Two distinct blister types are sometimes seen after fractures: clear fluid-filled vesicles and blood-stained ones (Fig. 22.5). Both occur during limb swelling and are due to the elevation of the epidermal layer of skin from the dermis [14]. There is no

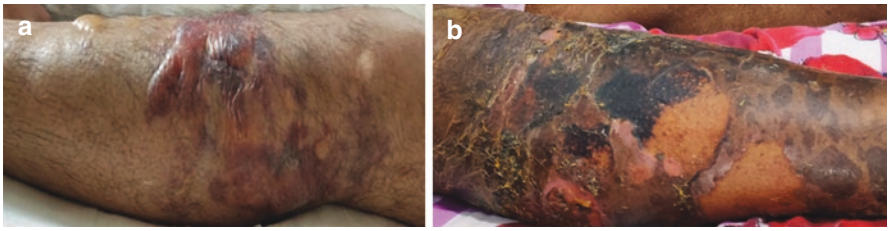

Fig. 22.5 Acute hemorrhagic blebs (**a**). See the true extent of soft tissue involvement which is revealed after 2–3 weeks post injury (**b**)

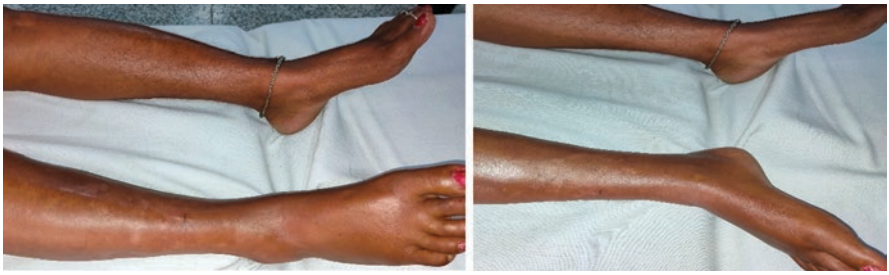

Fig. 22.6 Complex Regional Pain Syndrome (CRPS). (Note the shiny skin and trophic changes as compared to contralateral limb)

advantage to puncturing the blisters (it may even lead to increased local infection) and surgical incisions through blisters, while generally safe, should be undertaken only when limb swelling has decreased.

In cases presenting late, tenderness to palpation over the edematous area is consistent with DVT and complex regional pain syndrome type 1, i.e., reflex sympathetic dystrophy (Fig. 22.6). In comparison, lymphedema normally does not elicit tenderness. For example, acute cellulitis and DVT (Table 22.2) can cause increased local temperature and erythematous discoloration of the skin. The skin can look shiny with atrophic changes in the late stages of complex regional pain syndrome. In the early stages of lymphedema, the skin has a doughy texture, and in later stages, it becomes fibrotic, thickened, and verrucous.

Koban et al. [15] have shown that contralateral leg may be used to assess whether the affected leg is actually swollen by using a relatively simple normal tape measure although it is not a reliable technique [15]. Water displacement volumetry is a more accurate method that measures leg volume but is used mainly in research settings.

Chronic venous stasis disease can complicate both operative and nonoperative treatment methods. An incision through tortuous dilated veins leads to difficulty in hemostasis, bleeding, hematoma formation, and occasionally difficulty with wound healing. Varicosities predispose to venous stasis, especially in an immobilized limb. The risk of venous thrombosis and pulmonary embolism are increased.

Table 22.2 Common causes of PTLLO with their clinical presentation

Cause	Presentation	Examination
Secondary lymphedema (surgery/trauma)	Onset: Chronic; insidious; often following lymphatic obstruction from trauma or surgery	Early: Dough-like skin; pitting Late: Thickened, verrucous, fibrotic, hyperkeratotic skin, painless heaviness in extremity
Chronic venous insufficiency	Onset: Chronic	Soft, pitting edema with reddish-hued skin; predilection for medial ankle/calf, venous ulcerations over medial malleolus
Deep venous thrombosis	Onset: Acute	Pitting edema with tenderness, with or without erythema; positive Homans sign
Complex regional pain syndrome (reflex sympathetic dystrophy)	Onset: Chronic; following trauma	Soft tissue edema distal to traumatized part Associated findings: (early) warm, tender skin with diaphoresis; (late) thin, shiny skin with atrophic changes
Infection/cellulitis	Onset: Acute	Warmth, tender and erythema

Fig. 22.7 Morel-Lavallée lesion of tibia without any fracture

Another entity, although rare is a Morel-Lavallée lesion (Fig. 22.7). This is a posttraumatic, closed degloving injury occurring deep to subcutaneous plane due to disruption of capillaries resulting in an effusion containing hemolymph and necrotic fat. MRI is the investigation of choice in the evaluation of the Morel-Lavallée lesion. Early diagnosis and management is a must as any delay or missed lesion will lead to infection of effusion and/or extensive skin necrosis.

22.3.3 Diagnostic Testing

In patients who present with acute onset of unilateral lower extremity swelling, a d-dimer enzyme-linked immunosorbent assay can rule out DVT in low-risk patients. However, as per the latest ACR guidelines, this test has a low specificity, and d-dimer levels may be increased even in the absence of thrombosis [16].

22.3.4 Ultrasonography

Venous ultrasonography is the imaging modality of choice in the evaluation of suspected DVT [16]. Duplex ultrasonography can also be used to confirm the diagnosis of chronic venous insufficiency.

22.3.5 Lymphoscintigraphy

USG cannot detect lymph flow, therefore, indirect radionuclide lymphoscintigraphy, which shows absent or delayed filling of lymphatic channels, is the diagnostic modality for lymphedema when clinical diagnosis is doubtful. T1-weighted MR lymphangiography can be used to directly visualize the lymphatic channels in suspected lymphedema cases.

22.3.6 Magnetic Resonance Imaging

Patients with unilateral PTLLO, who are negative for DVT on duplex ultrasonography certainly require additional imaging to detect the cause of edema (Table 22.3). MR angiography with venography of the lower limb is used to evaluate for intrinsic or extrinsic pelvic or thigh DVT [16]. Magnetic resonance imaging may aid in the diagnosis of other musculoskeletal pathologies, such as a gastrocnemius muscle tear or ruptured popliteal cyst.

Table 22.3 Common causes of PTLLO along with common diagnostic modalities and management strategies

Cause	Diagnosis	Management
Secondary lymphedema (surgery/trauma)	Mainly clinical diagnosis Lymphoscintigraphy T1-weighted magnetic resonance lymphangiography	Manual decongestive physiotherapy with Compression stockings and adjuvant pneumatic compression
Chronic venous insufficiency	Duplex ultrasonography Ankle-brachial index to evaluate for arterial insufficiency	Compression stockings or Pneumatic compression device
Deep venous thrombosis	D-dimer assay Duplex ultrasonography MR venography to rule out pelvic or thigh DVT	Anticoagulation therapy Compression stockings Thrombolysis in select patients
Complex regional pain syndrome (reflex sympathetic dystrophy)	Clinical mainly Radiography Three-phase bone scintigraphy Magnetic resonance imaging	Physical therapy Tricyclic antidepressants Calcium channel blockers Ganglionic blocks Systemic steroids

22.4 Therapy of PTLLO in View of the Latest Studies

Swelling is almost inevitable after a fracture and may cause skin stretching and blisters. Persistent edema is an important cause of joint stiffness and therefore it should be prevented if possible and treated energetically if it is already present, by a combination of elevation and exercise and stabilization of fractures. An injured limb usually needs to be elevated; after reduction of a leg fracture the foot of the bed is raised and exercises are begun. Active movement helps to pump away edema fluid, stimulates the circulation, prevents soft-tissue adhesion and promotes fracture healing. A limb encased in plaster is still capable of static muscle contraction and the patient should be taught how to do this.

22.4.1 Lifestyle Programs

Patients of PTLLO are recommended to maintain a healthy body mass Index, as obesity itself results in edema [17].

22.4.2 Elevation

Elevation is a simple, effective and popular treatment method, particularly immediately following an injury. However, the need to immobilize the patient is associated with it, which may give rise to more complications.

22.4.3 Cryotherapy Facilities

In continuous cryotherapy, ice water circulates between icebox and cold pad applied to the patient with a daily change of ice water. In standard cryotherapy, the injured limb is treated with ice packs which are usually changed 4 times a day or as tolerated by the patient. The 24-hour circumferential reduction in PTLLO is around 16% after standard cryotherapy and 32% after continuous cryotherapy. The efficacy of cryotherapy has not yet been reliably investigated in posttraumatic edema [18]. At the same time, according to Hohenauer et al. [19] the reduction of edema by cryotherapy is most likely not due to a simple reduction in vascularization due to decreased vessel contraction, but also because of a decrease in leukocyte adhesion [19].

22.4.4 Compression

Compression therapy increases the outflow of venous and lymphatic fluids, prevents fluid retention in extracellular space and allows for virtually unrestricted activity. The use of personalized stockings prepared to accommodate the patient's leg size is

included in the guidelines for the treatment of chronic conditions given by the Executive Committee of the International Society of Lymphology in 2020 [20]. It is recommended that elastic bandages be used alone or alternately with layers of compressed cotton wool in the treatment of acute cases. Rohner-Spengler et al. [1] compared three treatment regimens for posttraumatic edema in the lower limbs immediately before and after surgery in a randomized clinical trial with a strict protocol. Patients of the unilateral ankle or hindfoot fractures were split into three categories treated with (1) ice compresses and limb raising, (2) multilayer compression with elastic bandage or (3) intermittent pneumatic compression. Compression bandaging with elevation was found to be most effective in reducing posttraumatic edema in both pre- and post-surgery cases [1]. Mechanical therapies, including leg elevation and compression stockings, are recommended [21]. Compression therapy is contraindicated in patients with peripheral arterial disease.

22.4.5 Physical Therapy

According to the latest opinion of the International Society of Lymphology, as a stand-alone procedure, lymphatic drainage, used in some centers, is ineffective [20]. As per Cohen [22], combination of manual treatment, *skin care*, and compression bandaging are very effective in complicated decongestive therapy, but it requires high costs and is time-consuming [22]. To date, no definitive findings have been used in trials affecting large numbers of patients; this approach is, therefore, not approved for general use in the literature. If this procedure is taken into consideration, it must be borne in mind that the effectiveness of therapy relies on daily treatment by a trained physiotherapist who massages the proximal and then distal parts of the limb in order to stop an uncontrolled rise of pressure in the soft tissues [23].

The supporters of Kinesio Taping say that it promotes the drainage of interstitial edema into lymph vessels [24]. There is some evidence for the efficacy of Kinesio taping for the treatment of postoperative edema. This evidence is, however, not yet convincing given the limitations of the published trials [24].

22.4.6 Heat Therapy

Heat treatment, which involves warm saline water immersion, laser, and electromagnetic irradiation, is effective in chronic situations. To decrease leg volume and enhance skin tonometry, microwave heat treatment was paired with compression stockings, wet saline water immersion, and benzopyrones [25]. This method of therapy is widely used because it has no side effects before or after treatment and assists in the regaining of joint mobility.

The mechanism of action of thermal treatment is not fully known. One recent review concluded that electromagnetic radiation heat reduces edema by decreasing

inflammation rather than by improving lymphatic flow. However, the biggest weakness of this study was that it was done on normal healthy volunteers rather than patients with lymphedema, and heat may produce different effects in the two groups [26]. Histologically, the skin after heat treatment for lymphedema shows a near resolution of perivascular cellular infiltration, disappearance of the so-called lymph lakes, and dilatation of blood capillaries.

22.4.7 Pharmacotherapy Programs

Currently, diuretic medications, traditionally recommended for acute edema reduction, are not advised for the care of PTLLO patients. Water and electrolyte balance are disrupted, edema returns soon after discontinuation of drug administration and, most importantly, protein content in the extracellular space can increase [17].

22.4.8 Micronized Purified Flavonoid Fraction (MPFF)

Micronized distilled flavonoid fractions are well-known venoactive drugs. They play an important role in the management of edema in the lower limbs caused by chronic venous and lymphatic insufficiency. The medication's numerous beneficial effects, such as enhancing lymphatic pump efficiency, reducing capillary filtration, and suppressing the involvement of enzymes involved in the synthesis of inflammatory mediators, have all been well established in previous studies [27].

However, Fotiadis et al. [28] found that venoactive agents (a combination of diosmin and hesperidin) have been not effective in posttraumatic edema and the agents have not diminished edema or pain [28].

For the prevention of posttraumatic edema, proteolytic enzymes combined with other medications have also been used. PTLLO after ankle sprains was not minimized by phlogenzyme, a mixture of trypsin, bromelain, and rutin [29].

22.4.9 Benzopyrones

Benzopyrenes help to treat lymphedema by eliminating edema fluid, increasing limb softness, and decreasing raised local temperatures. Benzopyrones function by increasing the number of macrophages in the body, which improves proteolysis and, as a result, protein and edema removal. Furthermore, excess protein reduces inflammatory and fibrotic processes, as protein which is a good culture medium for bacterial growth is eliminated, resulting in significantly fewer secondary infections. Low toxicity, oral or topical application, and the lack of need for compression therapy were all listed as benefits of benzopyrones, which is especially advantageous for patients who cannot tolerate high-pressure treatment [30].

22.5 Other Causes

Complex Regional Pain Syndrome (CRPS) is a chronic pain condition that occurs due to posttraumatic tissue injury of the lower extremities. A clear pathophysiological mechanism has not been established yet and different mechanisms are considered to play a role in the etiopathogenesis of CRPS [31]. Complex regional pain syndrome is treated with physical therapy in combination with ganglionic blocks and medications such as systemic steroids and tricyclic antidepressants [32].

22.5.1 Future Prospects

There are results based on animal tests, showing the feasibility of treatment with saturated physiological saline solutions which enforce osmosis across the skin. In these studies, the skin is viewed as a semipermeable membrane through which osmosis can occur. No human trials of this approach have been published.

Sports centers employ different devices to incorporate cryotherapy with intermittent pneumatic compression (e.g., Powerplay). According to the hypothesis, muscle temperature drops more rapidly in the midst of simultaneous compression. More research is needed to evaluate the effect of compression on physical activity, which is calculated as the same as exercise, as well as the efficacy of such therapies [33].

Sulodexide facilitates the healing of venous ulcers and is frequently used in patients to prevent a recurrence. In a metanalysis, it was found that sulodexide was a beneficial venoactive with a positive effect on the major signs and symptoms of chronic venous disease including reduction of edema [34]. It is also likely to exert a systemic effect on the course of chronic venous disease by interfering with inflammatory chemokines. But to date, there have been no studies of sulodexide in PTTLO.

Indocyanine green fluorescence lymphography is a novel, real-time imaging technique for superficial lymphatic mapping [35]. van Zanten et al. [4] used this technique to image the superficial lymphatic vessels of the lower limbs in patients with severe compound tibial fracture and also to evaluate the length of the maximum regeneration of lymphatic function in these patients after reconstructive plastic surgical procedures [4]. None of the free flaps demonstrated any functional lymphatic vessels; the fasciocutaneous flaps and the skin graft demonstrated impaired lymphatic vessel function and dermal backflow pattern similar to that in lymphedema. Local flaps demonstrated lymphatic blockage at the scar edge.

Hu and Pan [36] have discussed in a recent review about the potential of Adipose-derived stem cells (ADSCs) therapy as a promising approach for lymphedema [36]. Lin et al. [37] concluded that prophylactic ciNPT (closed incision negative pressure therapy) use in the trauma area after surgery reduced postoperative swelling and pain resulting in the improved early range of motion [37].

Further clinical trials are also needed to find the early and vigilant treatment of soft tissue and bone fractures that facilitate quicker recovery of natural circulation in the vascular and lymphatic beds.

22.6 Summary

Treatment of posttraumatic edema in the lower limbs can be difficult and lengthy and seldom leads to full healing. Posttraumatic edema pathogenesis has not been fully explained. Most of the work in this field has been done by Szczęsny and Olszewski [9, 38, 39]. They have studied the primary role of immune response and lymphatic obstruction in the development of PTLLO. The extravagated blood had little effect on the skin, subcutaneous tissue, or lymphatics, although it activates lymphocytes in the LN. The BMC and saprophyte bacteria triggered a significant inflammatory reaction in the local area and lymph nodes. All of these factors can contribute to local edema during the early stages of traumatized tissue healing. Although the fracture or wounded tissues are clinically healed, the local inflammatory response at the injury site continues, and cytokine signals are transmitted to the regional lymph nodes (Szczęsny and Olszewski 2000–2012) [9]. Isotope lymphography was used to assess the immune and lymphatic system responses of trauma patients with closed lower limb fractures and soft tissue injuries. All had dilated lymphatics in the limb, and swollen inguinal lymph nodes in 62% of the cases while only 24% of the patients had venous thrombosis [39]. The role of the immune system in the development of CRPS has been documented in several studies.

Hörmann et al. [24] have concluded in a recent systemic review that, there is some evidence for the efficacy of Kinesio taping for the treatment of postoperative edema [19]. Multilayer compression therapy results in a faster reduction of ankle and hindfoot edema and was an effective treatment of PTTLO in patients with ankle and hindfoot fractures [1].

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