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Review

Lymphedema and lower limb edema: what do foot and ankle orthopedists need to know? A narrative review

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Abstract

Objective: To review in the literature updates on lymphedema and differential diagnoses of lower limb edema for foot and ankle orthopedists.

Methods: This is a narrative review, and the search was conducted on the PubMed and SciELO databases, using established keywords. Articles published in the last 15 years were included. The research question was "What do foot and ankle orthopedists need to know about lymphedema and lower limb edema?"

Results: Lymphedema is one of the causes of chronic lower limb edema, characterized by excessive lymphatic fluid in the interstitial medium due to impaired lymphatic drainage. It can be classified as primary or secondary lymphedema, with trauma being one of the most important etiologies of the latter. The diagnosis of this condition is primarily clinical, typically established through a thorough medical history and physical examination. Complementary examinations can evaluate indirect signs of lymphedema or direct signs of lymphatic dysfunction through lymphoscintigraphy. The differential diagnosis of chronic lower limb edema is challenging, and venous, cardiac, and traumatic etiologies, as well as lipedema, should be considered.

Conclusion: A thorough clinical examination, combined with appropriately indicated diagnostic tests such as lymphoscintigraphy, is essential for the differential diagnosis of chronic lower limb edema—a common finding in orthopedic clinical practice.

Level of Evidence V; Narrative review.

Keywords: Lymphedema; Diagnosis; Diagnosis, differential; Foot; Ankle.

Introduction

Chronic edema is defined as swelling that persists for more than three months and involves one or more of limbs, hands or feet, upper body (chest/chest wall, shoulders, and back), lower body (buttocks and abdomen), genitals (scrotum, penis and vulva), head, neck or face[1,2]. The body area most affected is the lower limbs, whose edema is observed in 96.4% of the population studied[1,3].

Lymphedema is an often underdiagnosed and neglected condition. Chronic lower limb edema should be carefully investigated, regarding the duration of the condition (acute or chronic), unilateral or bilateral involvement, and the presence of associated symptoms, such as skin changes and pain—symptoms that foot and ankle specialists encounter in daily practice. In this context, the diagnostic approach relies on an adequate clinical examination and, sometimes, on informative complementary examinations[4].

Given the high prevalence of chronic edema reported by patients in daily foot and ankle orthopedists' practice, the objective of this narrative review is to search the literature for updates on lymphedema and differential diagnoses of lower limb edema.

Methods

This study was based on the fundamental steps for conducting a narrative review. The literature search was performed between October 2024 and March 2025 on the PubMed and Scielo electronic databases, including articles

Study performed at Universidade Federal de Alfenas, Faculdade de Medicina, Alfenas, MG, Brazil.

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published in the last 15 years. The terms used in the DeCS/MeSH in Portuguese and English were: Linfedema (Lymphedema), Pé (Foot), Tornozelo (Ankle), Membros Inferiores (Lower limbs) Diagnóstico (Diagnosis), Diagnóstico Diferencial (Differential Diagnosis), Epidemiologia (Epidemiology) e Patologia (Pathology). The Boolean operators AND and OR were used. The studies were selected in a non-systematic manner based on the critical analysis of the authors, and those articles that contributed meaningfully to addressing the research question were selected: "What do foot and ankle orthopedists need to know about lymphedema and lower limb edema?". The most recent publications with the highest level of evidence were prioritized.

Results and discussion

Twenty-six articles met the established inclusion criteria and were included in the review.

Definition

Lymphedema is the manifestation of edema in one or more segments of the body caused by excessive lymphatic fluid in the interstitial medium due to impaired lymphatic drainage[5]. In addition to lymphatic impairment, notable features include the involvement of inflammatory factors, deposition of fibroadipose tissue, and expansion of adipose tissue[6]. In most cases, lymphedema is a chronic condition that worsens without treatment, predisposes patients to infections, and negatively affects the patient's quality of life[5].

When this condition results from congenital abnormalities in the structural or functional development of the lymphatic system, it is classified as primary lymphedema. In contrast, when it arises secondary to trauma, obstruction, infection, or any other form of injury to the lymphatic system, it is defined as secondary lymphedema[7].

Etiology

Primary lymphedema

Primary lymphedema is due to mutations in several genes involved in the initial formation of lymphatic vessels, their growth, and development. This form of lymphedema may be present from birth or develop later in life[5].

To date, mutations in 28 genes have been identified as causally linked to primary lymphedema. However, these genetic alterations are found in fewer than 30% of cases. Most of the implicated mutations affect genes encoding proteins involved in the lymphatic vascular development pathway, for example, vascular endothelial growth factor C (VEGF-C) or vascular endothelial growth factor receptor 3 (VEGFR-3)[8].

Secondary lymphedema

In developed countries, the main precipitating factors of lymphedema are related to lymphadenectomy and radiotherapy for cancer treatment[9]. In developing countries, lymphatic system infections, such as filariasis, are the most prevalent etiologies of lymphedema[7].

In filariasis, infection by the larvae *Wuchereria bancrofti*, *Brugia malayi,* and *Brugia timori* occurs through the bite of a female mosquito. Once the larvae reach the regional lymphatic vessels, they act both directly and via secreted products, leading to the destruction of lymphatic tissues and unidirectional valves. This results in impaired contractility and dilation of the lymphatic vessels[10].

Trauma is another important cause of secondary lymphedema. The energy involved in orthopedic trauma, which causes bone and soft tissue injuries, is responsible for damaging the lymphatic pathways and promoting chronic lymphedema. The severity of lymphedema is directly related to the extent of lymphatic system damage, which generates activation of the inflammatory cascade, infiltration of immune cells, fibrosis, and accumulation of adipose tissue. On the other hand, the presence of lymphedema in traumatized extremities can delay wound and fracture healing. Thus, the diagnosis of lymphedema, whether coexisting or trauma-induced, should be addressed by orthopedic surgeons aiming to achieve successful surgical outcomes[11,12].

Epidemiology

The LIMPRINT study[1], conducted in 2019, to date, is the largest epidemiological study on the subject and investigated the presence of lymphedema in patients admitted to ward beds of six hospitals in five countries (Denmark, France, the United Kingdom, Australia, and Ireland). A total of 3,401 patients were evaluated, of whom 38% were diagnosed with lymphedema. The main risk factors associated with the condition included advanced age, morbid obesity, heart failure, venous insufficiency, limited lower limb mobility, and neurological deficits. About 96.4% of patients with lymphedema involved the lower limbs, most of them below the knee. As for the cause of hospitalization, the main one is cellulite, responsible for 68.1% of cases[1].

Clinical presentation

Lymphedema can be unilateral or bilateral, with two-thirds of cases being unilateral. In cases of secondary lymphedema, laterality depends on the underlying cause[1]. Patients who have lower limb lymphedema complain of a feeling of heaviness, dull pain, and discomfort in the legs and ankles, especially at the end of the day. Such symptoms are nonspecific and common among several conditions associated with lower limb edema[13].

The main clinical sign on physical examination in cases of lymphedema is edema. Initially, it is soft, becoming hardened and associated with skin changes as the disease progresses. Lymphedema usually begins on the back of the foot or hand and progresses cranially. In addition to the back, the extremities are affected by edema. Hypoplastic and concave nails may be present in cases of primary lymphedema[14].

The International Society of Lymphology (ISL) defined in its consensus, published in 2020, the clinical stages of lymphedema, which summarize the signs found on physical examination as the disease progresses. Stages I, II, and III were defined, and an earlier stage, stage 0, was recognized, in which, despite an impaired lymphatic system, subtle changes in fluid and tissue composition and subjective symptoms, no evident swelling is apparent. Next, there is a description of the clinical findings of each stage. It is important to emphasize that several stages may coexist in the same limb, corresponding to different lymphatic areas[15].

Mild lymphedema

In Stage I, or mild lymphedema, there is an accumulation of interstitial fluid with a higher protein content compared to venous edema. The swelling is typically mild, resolves with limb elevation, and has a soft, dough-like consistency. At this stage, lymphedema may be mistaken for other causes of lower limb edema, such as congestive heart failure or chronic venous insufficiency[4,13,14].

Moderate lymphedema

In Stage II, or moderate lymphedema, adipocyte hypertrophy occurs in response to persistent fluid accumulation in the interstitial space. At this stage, the edema does not resolve with limb elevation and becomes non-soft due to skin thickening. As the condition progresses, there is continued deposition of fibroadipose tissue and further thickening of the overlying skin.

Severe lymphedema

In stage III, or severe lymphedema, there is greater evidence of fibrous tissue deposition in the interstitial space and trophic skin changes such as acanthosis, increased thickness, and verrucous lesions.

Initially, the skin develops a dimpled, *peau d'orange texture, which,* as it progresses, becomes hardened, hyperkeratotic, and leathery in texture. As the condition progresses, lymphostatic elephantiasis may develop, characterized by the presence of hyperkeratotic verrucous lesions[13]. These changes contribute to the appearance of the pathognomonic sign of chronic lymphedema—Stemmer's sign—defined by the inability to pinch a skin fold at the base of the second toe.

In chronic and severe lymphedema, the presence of skin fissures increases the risk of trophic changes associated with secondary infections and ulcerations. Patients may present with recurrent episodes of cellulitis, lymphangitis, impetigo, and clear fluid leakage, known as lymphorrhea[13]. Non-healing ulcers in lymphedema warrant investigation for malignant transformation, particularly the development of lymphangiosarcoma[14].

Diagnostic

The diagnosis of lymphedema is primarily clinical. A thorough medical history and physical examination revealing typical characteristics can confirm the diagnosis, especially if there is a classical etiology present. Edema following lymph node resection, a history of trauma, absence of a systemic cause for generalized edema, and skin changes typically associated with lymphedema strongly support the diagnosis[14]. However, according to Jayaraj et al.[16], classical clinical signs of lymphedema were present in only 17% of cases confirmed by lymphoscintigraphy, highlighting their limited reliability.

Several imaging tests evaluate the anatomy and function of peripheral and central lymphatic vessels. These tests can evaluate the lymphatic vessels directly, observing their anatomical or functional changes, or indirectly evaluate lymphatic impairment by identifying consequences of lymphatic dysfunction, such as interstitial fibrosis[17].

The investigation usually begins with a venous ultrasound to exclude causes of edema[15]. Although duplex ultrasound cannot visualize lymphatic vessels—only lymph nodes and blood vessels—it plays an important role in identifying dermal and subcutaneous alterations associated with lymphedema[17]. The dermis may show changes in echogenicity due to increased collagen fiber deposition, while the subcutaneous tissue often exhibits fat tissue hyperplasia and hypertrophy, which disrupts the normal echogenic line patterns observed on ultrasound[18].

Computed tomography and magnetic resonance imaging of limbs affected by lymphedema can be useful in identifying indirect signs of the disease. Edema acquires a characteristic marked by honeycomb distribution, reflecting fluid accumulation around fibrotic and adipose tissue. These imaging modalities also aid in identifying potential causes of lymphedema, such as extrinsic compression of the lymphatic system by tumors. Furthermore, magnetic resonance imaging can provide valuable features that assist in distinguishing lymphedema from other causes of swelling, such as chronic venous insufficiency.

Although the diagnosis of lymphedema is primarily clinical and does not require lymphatic imaging, evaluating the anatomy and function of the lymphatic system can confirm the diagnosis, determine the disease stage, and guide treatment planning and follow-up. Currently, lymphoscintigraphy is considered the gold standard imaging modality for diagnosing lymphedema. The procedure involves intradermal injection of technetium-99m-labeled sulfur colloid into the second and third interdigital spaces of the feet, followed by serial imaging using a scintigraphic camera to track lymphatic flow from the feet toward the thoracic region[4].

Differential diagnosis

Peripheral edema is a common clinical finding and may be indicative of a wide range of underlying conditions. As such, the differential diagnosis is often broad. A thorough clinical history is essential at the outset of the diagnostic process, including information on the chronicity and laterality of symptoms, associated manifestations, concurrent skin changes, and current medication use[20].

Causes of lower limb edema can be local or systemic. Among the most common systemic causes are congestive heart failure, renal failure, hypoalbuminemia, and protein-losing nephropathy. Local etiologies include primary and secondary lymphedema, lipedema, deep vein thrombosis, and chronic venous disease[20].

One of the main differential diagnoses of lymphedema is chronic venous disease (CVD), as it produces a bilateral chronic edema in the ankle and sole of the foot with characteristics similar to those of lymphedema[20]. Clinical suspicion typically arises in patients presenting with soft, pitting, reddish edema, predominantly affecting the leg, particularly the medial aspect of the ankle and calf. The diagnosis can be confirmed through lower limb venous Doppler ultrasound or by assessing the ankle-brachial index[21]. However, despite being a differential diagnosis, the relationship between CVD and lymphedema has been studied. Up to 30% of CVD cases have associated lymphatic system involvement. Some authors have used the term phlebolymphedema to characterize this mixed involvement[22].

Edema of cardiac origin usually begins in the pre-tibial region, in some severe cases reaching proximal regions of the lower limb. When the patient acquires a supine position, there may be sacral edema. The skin is shiny, often associated with symptoms of stasis dermatitis, and edema is soft[23]. In chronic cases, edema may harden, although it occurs less frequently than in cases whose etiology is venous insufficiency[24].

Lipedema is a chronic disease characterized by increased adipose tissue in the limbs, which occurs mainly in women. A family history of lipedema is common, with approximately 60% of patients reporting an affected first-degree relative. Current evidence suggests an autosomal dominant inheritance pattern with incomplete penetrance[25]. Patients relate the onset of the condition to periods of hormonal variation, such as adolescence, pregnancy, and menopause. In this type of swelling, the hands and feet are not affected, and the adipose hypertrophy is bilateral and symmetrical. Stemmer's sign, positive in lymphedema, is often negative in lipedema. Symptoms such as pain disproportionate to pressure and touch, feeling of heaviness and tension in the affected limbs, a marked tendency to form bruises, worsening of symptoms over the days, hypothermia of the skin, telangiectasia, and visible veins around the fat deposits are associated. When clinical examination is not sufficient to differentiate the case with lymphedema, imaging tests such as lymphoscintigraphy may be requested to evaluate changes in the lymphatic system[26].

Edema of traumatic origin

Trauma is a common cause of acute lower limb edema, with swelling resulting from capillary injury, inflammatory response, or hematoma formation. Evaluation begins with a history consistent with trauma, and subsequent management is individualized based on the mechanism and severity of the injury, which may range from contusions and sprains to fractures[20].

The Morel-Lavallée injury or closed degloving is an uncommon cause of acute, subacute, or even chronic lower limb edema. Injury most commonly occurs in high-velocity trauma through the shear mechanism, where the deep fascia separates from the skin and superficial fascia. This mechanism has also been reported to occur in direct lower limb trauma, especially in athletes, and rarely in abdominoplasties and liposuction. Although it can affect any region of the lower limbs, it most commonly occurs in proximal areas. Due to its delayed onset—often days after trauma—and prolonged course, it is frequently misdiagnosed as chronic edema[27]. However, it has been identified that patients who have suffered from circumferential dehiscence in the lower limbs have a high probability of developing lymphedema. Thus, in addition to being a differential diagnosis, the Morel-Lavallée injury is also one of the possible etiologies of secondary lymphedema[28].

Conclusion

Orthopedic surgeons frequently face the challenge of differentiating causes of chronic lower limb edema in clinical practice. Given the increasing prevalence of lymphedema, lymphatic drainage dysfunction should always be considered in the diagnostic process. Characteristic clinical manifestations, a history of predisposing conditions, and appropriate imaging studies are essential for accurate diagnosis. In this context, the identification of orthopedic conditions associated with lymphedema contributes to improved therapeutic strategies and prognostic outcomes.

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