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REVIEW ARTICLE

Phlebolymphedema–A Common Underdiagnosed and Undertreated Problem in the Wound Care Clinic

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Abstract This article focuses on the pathophysiology of phlebolymphedema, as well as proper diagnosis and treatment. It is hoped that this article will improve care of patients in wound care clinics and motivate wound care physicians to consider adding care of lymphedema patients to their clinical practice.

The correction and treatment of chronic swelling is inescapable in the wound care clinic, and it is impossible to do good wound care and not encounter patients with various forms of lymphedema. Yet most physicians have very little formal training or knowledge of treatment and diagnosis of lymphedema.

The most common form of lymphedema worldwide may be filarial infection, but the most common in the Western world is phlebolymphedema. Phlebolymphedema is a mixed-etiology swelling due to chronic venous insufficiency (CVI) and lymphatic insufficiency. Phlebolymphedema is most commonly due to inability of the lymphatic system to adequately drain the interstitial fluid that accumulates in severe chronic venous hypertension. Additionally, there are a host of contributing factors that can increase demand on the lymphatic system and lead to development of phlebolymphedema. Lymphatic insufficiency due to damage to the lymphatic system can also result in phlebolymphedema. Often multiple factors are at play, including systemic disease (eg, congestive heart failure, cirrhosis, or nephropathy), which compounds the problem and leads to inability of the lymphatic system to drain interstitial fluids and macromolecules. Thus, *phlebolymphedema is due to insufficiency of the venous or lymphatic system (or both), in combination with possible systemic contributors, leading to accumulation of interstitial protein-rich fluid in the interstitial space.*

This article focuses on the pathophysiology of phlebolymphedema, as well as proper diagnosis and treatment. It is hoped that this article will improve care of patients in wound care clinics and motivate wound care physicians to consider adding care of lymphedema patients to their clinical practice.

Incidence

Lymphedema is a lifelong condition for which no cure exists. An estimated 300 million people are affected by lymphedema worldwide. Filariasis is a paracytic infection and is the most common cause of lymphedema worldwide, affecting 100 million people.[1] Phlebolymphedema, the most common form of lymphedema in the Western world, is a secondary lymphedema that develops in patients with CVI. Contributing factors to lower extremity swelling are

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increased survival of heart failure patients, numerous medications associated with edema, and increased incidence of obesity. With the aging of the baby boomers and the lack of education of caregivers in proper treatment of lymphedema, the incidence will almost certainly increase in upcoming decades. Lymphedema has been considered an "orphan" disease because it does not fall into any medical specialty. Consequently, few physicians are well versed in its pathophysiology or treatment.[2]

Pathophysiology of CVI

CVI is caused by dysfunction of the one-way valvular system in the perforators and deep venous plexus of the lower extremity. Valvular dysfunction results in backflow of venous blood to the superficial venous system. This loss of valvular function may result from age-related decrease in valvular competency, occult or previous deep venous thrombosis (DVT), surgery, or other etiologies. Incidence is approximately 6% to 7% of patients at 50 years of age, with an increase to >20% at age 70. CVI has a slight female preponderance.[3] Up to 76% can be diagnosed by clinical presentation alone, but duplex ultrasound can also be used and is done routinely by some clinicians.[4]

Pathophysiology of Lymphedema

The problem of lymphedema starts at the capillary. Review of capillary physiology reminds us that at the precapillary end of the arteriole, the hydrostatic pressure drives fluid (called the *ultrafiltrate*) out of the capillary. Toward the venule side of the capillary, the oncotic pressure inside the capillary is the main force pulling fluid back into the capillary. About 10% of the ultrafiltrate is not reabsorbed back into the capillary. The ultrafiltrate also contains small amounts of proteins and cellular debris. It is the job of the lymphatic system to capture and drain this fluid, filter and concentrate it in the lymph nodes, and then return it to the vascular system. The actual flow of lymph fluid varies greatly in the human body. Lymph flow is based on demand and cardiovascular hemodynamics. It is not uncommon for lymph flow to vary more than 20-fold above baseline flow when the lymphatic system is at a maximum.[5] Normally there is a large reserve capacity to the lymphatic. Normal healthy tissues lymphatics work at only 5% to 10% of capacity.[6] Actual amount of lymph fluid returned through the thoracic duct is estimated to be 2 to 4 L daily. However, the total flow into the lymphatic system prior to concentration by lymph nodes produces a volume that is at least 8 L in a normal adult.[7] The removal of proteins from the interstitium is an essential function. Without functional lymphatics, we would die in about 24 hours.[5]

Drainage into the lymphatic system starts in the lymphatic precollectors, which contain single-layer endothelial cells with anchoring filaments and valves. Stretch of these anchoring filaments opens clefts between cells to expand, allowing entry of interstitial fluid and macromolecules. From the lymphatic precollectors and collectors, lymph flows through lymphatic capillaries. Thereafter, it flows into the lymph nodes, which concentrate and filter the lymph. Eventually the lymph returns to the cardiovascular system via the thoracic duct.

Interstitial fluid pressure and degree of activity of the lymphatic pump are the main factors driving flow through the lymphatic system. The lymphatic pump is driven by several factors. These factors are contraction of muscles in the body portion, movement of body parts, arterial pulsations, compression by objects outside the body, and the lymphangion micropump. The micropump is located throughout the lymphatic capillary and collecting system. The lymphangion micropumps are crude pumps of the lymphatic system that have their own contractile activity and bicuspid valves, which prevents lymphatic backflow.[5] The lymphangions contain actomyosin filaments and have their own rhythmic contractility and action potentials. This system is similar to the gastrointestinal system. The rate of lymphatic peristalsis varies greatly, from 1 to 30 pulsations per minute. The lymphangions have a series of one-way valves, allowing flow of fluid only one way. The degree of lymphatic flow varies widely. During exercise or periods of high drainage, flow may increase 10-fold to 30-fold. During periods of rest, however, lymphatic flow may be very sluggish. The effectiveness of lymphangion pump action on lymphatic flow is debated, but it is likely that the lymphangion and lymphatic contraction play some role in determining lymph flow rates.

In summary, the lymphatic system is a dynamic system that handles capillary ultrafiltrate with great variance depending on the need. The lymphatic system has limits in volume of fluid it can handle. The lymphatic system contains fragile vessels that can be damaged easily from infection, trauma, tissue inflammation, or radiation. Damage to lymphatic vessels leads to development of lymphedema with a swollen extremity or body portion.

Use of diuretics for patients with lymphedema will merely increase concentration of proteins and macromolecules in the interstitial space and speed the inflammatory process that leads to irreversible skin and soft tissue changes and increased risk of cellulitis. Therefore, use of diuretics solely for reduction of swelling in patients with lymphedema is contraindicated.

Development of Phlebolymphedema (Secondary Lymphedema in Venous Insufficiency)

To understand how patients with venous hypertension develop secondary lymphedema, we need to review venous pathophysiology. In the recumbent position, arterial pressure may be approximately 100 mm Hg and venous