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EDITORIAL

A new classification of lymphedema

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ABSTRACT

The classification of lymphedema into primary and secondary has been criticized over the years and should be updated based on advances in general knowledge of lymphedema. The present editorial proposes a new classification into primary lymphedema (congenital - emerges before 2 years of age; early - emerges between 2 and 35 years of age; late - emerged after 35 years of age), secondary lymphedema and mixed lymphedema (primary mixed lymphedema and secondary mixed lymphedema). The main additions are the primary mixed congenital lymphedema while maintaining the same periods of occurrence (early and late congenital lymphedema), however adding secondary harm to the lymphatic system, and secondary mixed lymphedema, in which the patient suffers new harm to the lymphatic system, such as that resulting from the occurrence of erysipelas, in addition to the initial harm that caused the lymphedema. The classification of primary mixed lymphedema and secondary mixed lymphedema makes the diagnosis more comprehensive, enabling a more accurate treatment approach and prognosis. This new classification is essential for a better understanding of the diagnosis of lymphedema.

Keywords
Lymphedema, classification, epidemiology, physiological processes.

Lymphedema is a specific type of edema resulting from a failure in the formation or drainage of lymph. The main epidemiological classification is divided into two major groups: primary and secondary lymphedema. In primary or congenital lymphedema, the lymphatic system is abnormal since birth and may or may not lead to the formation of edema at some point in life.[1] In secondary lymphedema, the lymphatic system is intact at birth, but harm occurs to this system during the course of one's life, leasing to the formation of edema[1,2].

The incidence of primary lymphedema is one out of every 100,000 livebirths, but few epidemiological studies have evaluated this condition[3]. This condition is denominated primary congenital lymphedema when emerging prior to two years of age, early primary lymphedema when emerging between two and 35 years of age and late primary lymphedema when emerging after 35 years of age. The early primary type is the most prevalent, accounting for approximately 85% of cases[4].

Secondary lymphedema has several causes. The major cause is cancer treatment that damages the lymphatic system, as can occur following treatment for breast cancer, cervical cancer and skin cancer (melanoma)[5,6]. Radiotherapy combined or not with surgery that involves the lymph nodes and lymphatic vessels is a risk factor. Physical injury or surgical trauma that causes damage to the lymphatic system can lead to lymphedema. Infection by erysipelas is

associated with the development of this condition and filariasis is a major cause of secondary lymphedema in tropical countries. Besides these major causes, there are others that are less prevalent.

The classification of lymphedema into primary and secondary with these existing characteristics has been criticized over the years and should be updated based on advances in general knowledge of lymphedema.

One of the first etiological classifications of lymphedema was published in 1935 based on the analysis of 300 cases of lymphedema, which were divided into two main groups (primary and secondary), depending on the presence or absence of clinical evidence of infection. Congenital cases were defined as early lymphedema and inflammatory cases were defined as secondary lymphedema[7]. Kinmonth progressed in relation to Allen's classification and divided all cases into primary and secondary lymphedema. Three types of primary lymphedema were recognized: congenital (when emerging prior to two years of age), praecox (emerging between two and 35 years of age) and late (emerging after 35 years of age). Secondary lymphedema develops as a consequence of the rupture or obstruction of lymphatic pathways[8]. These were the two main etiological classifications of lymphedema.

Other classifications evaluating the clinical stage, severity of the case and whether there is damage to the lymphatic system leading to a state of lymphatic hypertension are fundamental to the diagnosis and therapeutic prognosis. A classification in clinical stages defines stage 0 or subclinical, stage 1 when the edema occurs during the course of a day but regresses with rest, stage II when the edema does not regress completely with rest and stage III, in which greater deformities occur[12]. Some authors have added further information. However, this classification remains the most widely used in clinical practice. Regarding severity, the volume of the edema is classified as mild (less than 20% increase in volume in comparison to the contralateral limb), moderate (20 to 40% increase in comparison to the contralateral limb) and severe > 40% increase in comparison to the contralateral limb)[13]. Another classification that is fundamental to the establishment of treatment employed is whether the lymphedema has a hypertensive pattern[14]. Although all these classifications contribute to the diagnosis and treatment, the most precise diagnosis is achieved when these data are combined with genetic aspects[15,16].

Another classification of primary lymphedema according to the International Society for the Study of Vascular Anomalies uses St. George's algorithm and considers combined vascular malformations and lymphatic anomalies. This classification divides types of lymphatic anomalies into lymphatic malformations and primary lymphedema and divides generalized syndromic lymphedema into dysplasia with internal/systemic involvement, congenital onset lymphedema and late onset lymphedema[9]. Another classification using magnetic resonance lymphography without contrast classifies primary lower limb lymphedema into hyperplasia, aplasia, hypoplasia and normal patterns[10]. The grouping of patients by precise phenotyping facilitates molecular investigation, as well as the understanding of hereditary patterns and the natural history of different types of primary lymphedema[11]. All these classifications have contributed new information to the diagnosis of the condition.

The main criticism is that all primary lymphedemas are congenital. The division into congenital, early and late does not enable a clear definition of early and late lymphedema, which are also congenital. Moreover, this classification does not define all clinical conditions in many patients. Over the years, knowledge on the causes and progress in the treatment of lymphedema have led to a novel concept of mixed lymphedema, which is a combination of both congenital and secondary lymphedema. The new concept is based on observations that the occurrence of an additional pathophysiological factor in either the congenital or secondary type can predispose the individual to the aggravation of lymphedema. In terms of therapy, these data are fundamental to both therapeutic planning and with regards to the expected results.

Thus, here we are proposing a new classification of lymphedema into primary lymphedema (congenital - emerges before 2 years of age; early - emerges between 2 and 35 years of age; late - emerged after 35 years of age), secondary lymphedema and mixed lymphedema (primary mixed lymphedema and secondary mixed lymphedema), as shown in **Table 1**. Primary mixed lymphedema is defined as primary mixed congenital lymphedema, while maintaining the same periods of occurrence (early and/or late congenital lymphedema) with initial harm of lymphatic system,

Table 1. A new epidemiological classification of lymphedema

Primary lymphedema	Secondary lymphedema	Mixed lymphedema/additional lymphatic damage
Congenital – emerges prior to 2 years of age	All causes	Primary mixed lymphedema (associated with primary)
Early – emerges between 2 and 35 years of age		Secondary mixed lymphedema (associated with secondary)
Late – emerges after 35 years of age		

but with the occurrence of another associated lesion, which we call a secondary damage to this system, for example, infection, several episodes of erysipelas, leading to aggravation this lymphedema. Secondary mixed lymphedema is defined as lymphedema where the patient suffers new harm to the lymphatic system, such as that resulting from the occurrence of erysipelas, in addition to the initial harm that caused the lymphedema.

Studies have shown that when there is more than one pathophysiological factor, the probability of developing lymphedema increases. In clinical practice, the therapeutic response differs when lymphedema is associated with several physiological factors. Therefore, this new classification is fundamental to a better understanding regarding the diagnosis of lymphedema.

Conflict of Interest

The authors declare no conflict of interest.

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