ORIGINAL ARTICLE

Lymphoscintigraphy of the lower limbs: a retrospective study of 154 cases from March 2009 to June 2010

Linfocintilografia de membros inferiores: estudo retrospectivo de 154 casos no período de março de 2009 a junho de 2010

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ABSTRACT

Introduction: Lymphoscintigraphy of the lower limbs (LLL) is an effective method to assess lymphatic function. **Objective:** To present the case of 154 patients undergoing LLL between March 2009 and June 2010. **Methods:** Images of the pelvis and lower limbs were acquired after simultaneous intradermal administration of 1.0 mCi of 99mTc-Dextran 500 in 0.1 mL in the interdigital space of the first and second toes, bilaterally. **Results:** 129 (83.77%) patients were female, mean age was 51.48 years, with 32 patients (20.78%) aged between 40 and 49 years. 58 patients (37.66%) had body mass index between 25 and 30 kg/m², 92 patients (59.74%) reported edema, lymphedema or swelling as the reason for examination. 93 patients (60.39%) without previous vascular surgery or procedure, 108 patients (70.13%) without previous inflammation, erysipelas or trauma. 103 patients (66.88%) presented with bilateral swelling upon examination, with 48 patients (31.17%) reporting edema that worsened in the evening. 77 patients (50%) with symptoms for over a year. 31 patients (20.13%) were hypertensive. Scintigraphic findings: 149 patients (96.75%) with some abnormality upon examination, 38 with severe bilateral delay in lymphatic transit time, 85 (55.19%) with normofunctioning lymph nodes, 62 patients with bilateral radiotracer drainage via small saphenous veins, 84 patients (54.55%) without collateral vessels, 92 (59.74%) without lymphatic retention, 85 patients (55.19%) without dermal backflow. 15 patients (9.74%) showed lymph nodes in the popliteal region. **Conclusions:** Lower limb lymphoscintigraphy is available as a method to detect lymphedema and changes in lymphatic drainage, and is important for initial investigative screenings, early stage assessments of edema, and for monitoring therapeutic, clinical or surgical interventions.

Key words: Scintigraphy; Lower Extremity; Lymphedema; Technetium; Nuclear Medicine.

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RESUMO

Introdução: *a linfocintilografia de membros inferiores (LMMII) é método eficaz para avaliar a drenagem linfática.* ***Objetivo:*** *apresentar 154 pacientes submetidos à LMMII entre março/2009 e junho/2010.* ***Métodos:*** *foram adquiridas imagens da pelve e MMII após administração intradérmica simultânea de 1,0 mCi de 99mTc-Dextran 500 em 0,1 mL no espaço interdigital do primeiro e segundo pododáctilos bilateralmente.* ***Resultados:*** *foram examinadas 129 (83,77%) mulheres; média de 51,48 anos de idade; 32 (20,78%) na faixa etária entre 40 e 49 anos; 58 (37,66%) com índice de massa corporal entre 25 e 30 kg/m2; 92 (59,74%) com edema, linfedema ou inchaço como motivo do exame; 93 (60,39%) não submetidos a cirurgia ou procedimento vascular prévios; 108 (70,13%) sem processo inflamatório, erisipela ou trauma prévios; 103 (66,88%) com edema bilateral ao exame; 48 (31,17%) com piora do edema no período noturno; 77 (50%) com evolução há mais de um*

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*ano; 31 (20,13%) hipertensos. Achados cintilográficos: 149 (96,75%) com alguma alteração ao exame; 38 com atraso bilateral acentuado no tempo de trânsito linfático; 85 (55,19%) com cadeias linfonodais normofuncionantes; 62 com drenagem do radiotraçador via safena parva bilateralmente; 84 (54,55%) sem vasos colaterais; 92 (59,74%) sem retenção linfática; 85 (55,19%) sem refluxo dérmico; 15 (9,74%) com linfonodos em região poplítea. **Conclusões:** a LMMII é método disponível para detecção do linfedema e alterações na drenagem linfática, sendo importante para triagem inicial investigativa, avaliação de edemas em fases iniciais e monitoramento de intervenções terapêuticas, clínicas ou cirúrgicas.*

***Palavras-chave:** Cintilografia, Extremidade Inferior; Linfedema; Tecnécio; Medicina Nuclear.*

INTRODUCTION

Chronic edema of the lower limbs (LL) is a common complaint that may be the initial manifestation of several underlying diseases, among which lymphedema. Interest in the study of chronic edema of the LL is increasing due to the growing number of people affected, as well as due to improvements in diagnostic methods, successful surgical treatments for chronic deep venous insufficiency, and the development of microvascular surgery, which has made lymphovenous anastomosis (LVA) and lymphatic vessels transplant possible.

The lymphatic system is essential in maintaining interstitial liquid balance and also for immunological functions. LL lymphedema has a chronic and debilitating evolution, with severe functional, aesthetic, and psychosocial repercussions. It is characterized by leg edema due to congestion by protein-rich interstitial fluid caused by disorders related to lymphatic transport. Those disorders in lymphatic drainage are associated with a deficiency in response to infection that may or may not be associated to cellulite, which is thenacute infection of skin and subcutaneous tissue in general caused either by Streptococcus pyogenes or *Staphylococcus aureus* and a common reason for hospitalization.[1]

The initial signs of lymphedema are generally soft and painless edemata. The affected limb may feel heavy, especially at the end of the day and in warm weather, and symptoms may vary throughout the menstrual cycle.[2] It may take from weeks to months for the skin to become thicker and for the edema to harden. As cutaneous lymphatic vessels present a functional deficiency, local immunological response is affected and recurring skin infections are common, causing more textured local lesions and worsened edema. Lack of proper treatment results in the progressive increase in limb size, severe functional disability, and disfiguring edema formation, with psychological repercussions.[3]

The disease affects 140 to 300 million people all over the world and frequency has increased with the growing number of surgeries and oncological and radiotherapeutic procedures performed.[4]

Primary lymphedema may be congenital (Milroy's disease), manifest before 35 years of age (lymphedema praecox) or after (lymphedema tarda). It is more common among women, commonly starting at the menarche[2], and may range from hyperplasia, hypoplasia due to reduced lymph trunks (in number or in caliber), to aplasia, or the total absence of subcutaneous lymph trunks. In primary lymphedema, no precipitating factors are involved in the spontaneous swelling of the affected limb.

Secondary lymphedema may be related to a number of causes, such as lymph node dissection, radiotherapy, damage or obstruction of the lymphatic vessels by neoplasms (extrinsic compression by abdominal or pelvic mass), trauma, filariosis, and other parasitic infections. Its clinical expression generally develops insidiously over months or years after the initial aggression. Early and accurate assessment is extremely relevant for defining adequate therapy.

Lymphoscintigraphy of the lower limbs (LLL) is an efficient method to assess lymphatic drainage first performed in the 1950s.[5,6] Since then, significant advances have been made regarding the gamma cameras technology used and in the selection of optimal size for pharmacological particles administered. It is now used routinely and prominently.

The aim of this retrospective study is to describe 154 patients submitted to LLL between March 2009 and June 2010 and their correlated underlying lymphatic abnormalities according to physical exam and lymphoscintigraphy findings.

MATERIALS AND METHODS

From March 2009 to June 2010, 205 patients underwent LLL, 154 (75.12%) of which were included in this study after they filled correctly and fully the questionnaire handed to them moments before the exam. The questionnaire characterized patients according to sex, age, weight, height, reason for the examination, reports of trauma, history of vascular surgery or procedure, swelling, inflammatory process or erysipelas, medication currently in use, and current underlying diseases.

LLLs were performed in a gamma camera with double rectangular detector and high-resolution collimators with parallel holes, 20% window centered on the 140 keV photopeak, with the patient in supine position and image acquisition of anterior projection of both the pelvis and LLs, after simultaneous intradermal administration of 37 MBq of 99mTc-Dextran 500 in volume of 0.1 mL in the interdigital space between the first and the second toes, bilaterally. Dynamic images were collected every minute, for 12 minutes, for quantitative analysis of the lymphogram obtained from constructed areas of interest in the inguinal area, and immediate raster images and late static images after one hour and after three hours for qualitative analysis.

Figure 1 - Image of patient with erysipelas for the past six years, showing poorly healing wounds on the left ankle, bilaterally.

Figure 2 - Image showing the intradermal administration technique of 1.0 mCi of 99mTc-Dextran 500 in a volume of 0.1 mL in the interdigital space between the first and the second toes, on the left foot.

Image analyses were used to verify any abnormalities on lymphatic channels, absence of lymph nodes and/or lymphatic channels, lymph nodes of the deep lymphatic system in the region (e.g. in popliteal region), collateral vessels, lymphatic retention, or dermal reflux.

The following criteria were considered to assess lymphatic transport time: 1. Lymph nodes from the inguinal lymph node chain evidenced in early dynamic images: lymphatic transport time preserved. 2. Lymph nodes of inguinal lymph node chain highlighted in images 15 minutes after radiopharmaceutical injection: slight delay of lymphatic transport. 3. Lymph nodes of inguinal lymph node chain highlighted in images 30 minutes after radiopharmaceutical injection: moderate delay in lymphatic transport time. 4. Lymph nodes of inguinal lymph node chain highlighted in images 1 hour after radiopharmaceutical injection: marked delay in lymphatic transport time.

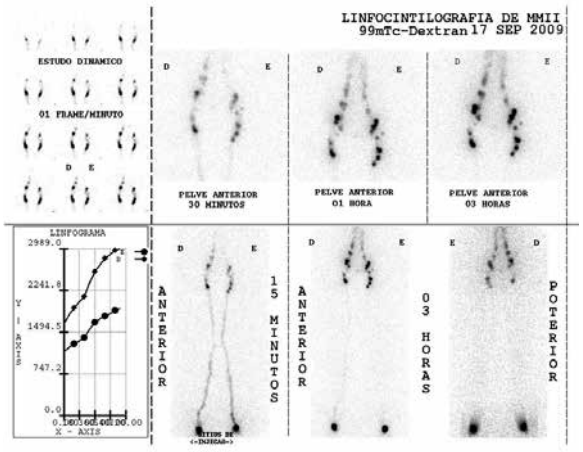

Figure 3 - LLL with no alterations in the transport time of the radiopharmaceutical substance, evidencing drainage of the radiotracer in the lymphatic system via saphena magna and femoral veins, with no signs of lymphatic retention and/or or dermal reflux; within normal limits.

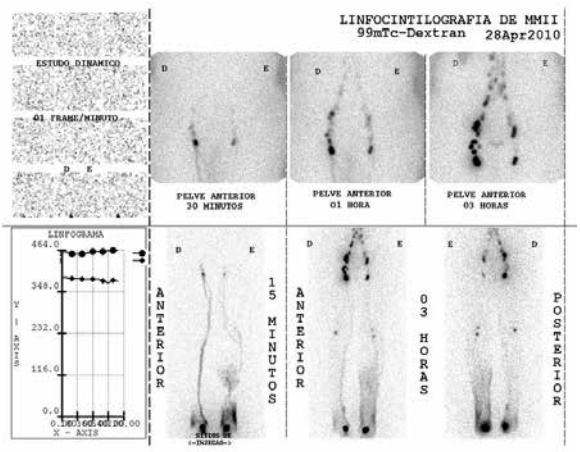

Figure 4 - LLL evidencing discrete delay in lymphatic transport time bilaterally. Left side inguinal lymphatic chains less impounding. Right LL: radiopharmaceutical drainage through the lymphatic system via saphena magna and femoral veins quite visible, with collateral vessels in its proximal third evidencing a lymph node in popliteal fossa projection, as well discrete signals of lymphatic retention and dermal reflux in ankle projection. Left LL: lateralization of the radiotracer drainage through the lymphatic system via saphena parva, with collateral vessels in its proximal half, and moderate dermal reflux and lymphatic retention in the distal half.

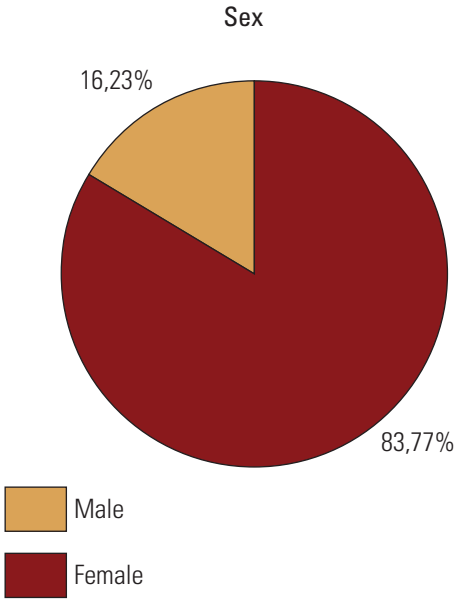

Figure 6 - Sex stratification of patients in the study.

RESULTS

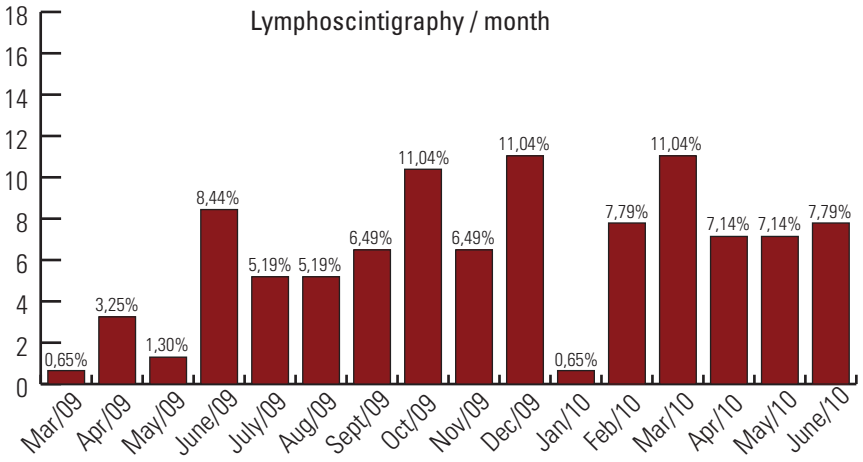

Figure 5 - Monthly frequency of LLLs performed during the study period. .

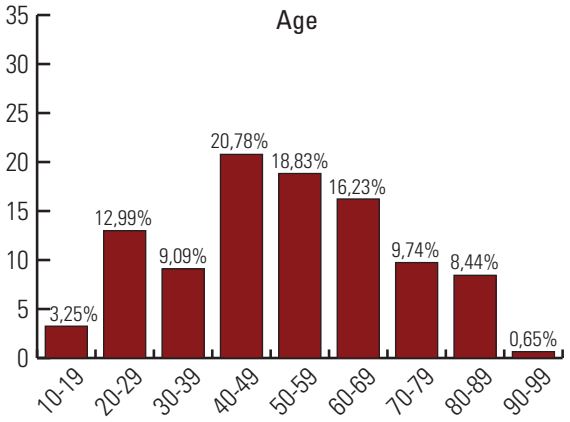

Figure 7 - Stratification of patients by age group intervals.

Patients' ages ranged from 12 to 91 years, with average age of 51.48 years.

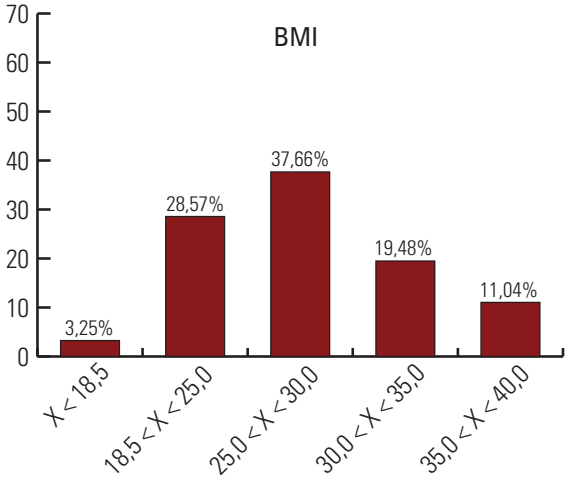

Figure 8 - Stratification of patients based on Body Mass Index.

Out of the 154 patients, 92 reported edema, lymphedema or swelling as the reason for having the exam; 31 mentioned edema linked to pain, and 7 patients reported pain.

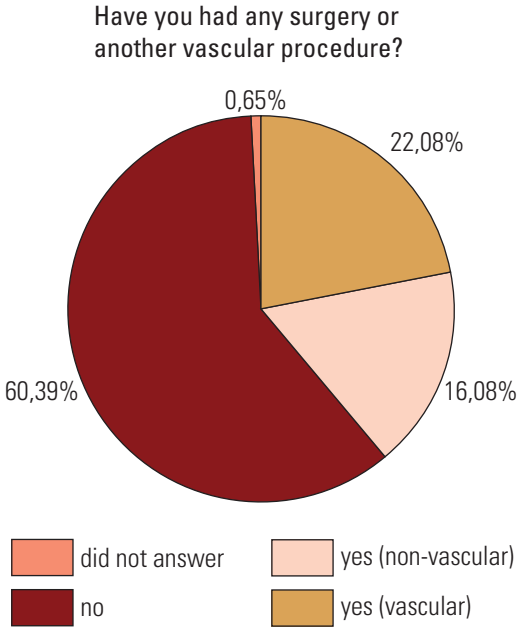

Figure 10 - Percentage of patients previously submitted, or not, invasive procedures to lower limbs.

From the total of 154 patients, 93 had never been undergone any surgery or vascular procedure, while 34 had had surgeries in the LL more than a year previous.

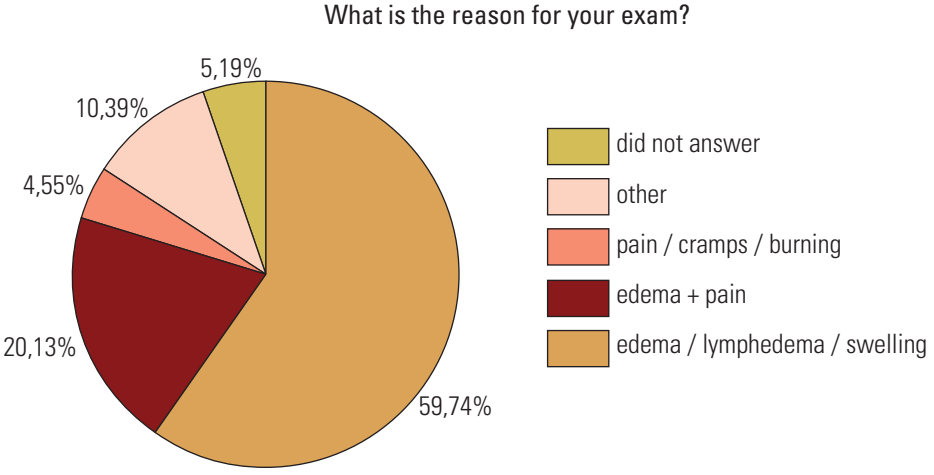

Figure 9 - Main causes patients name as reasons for undergoing LLL.

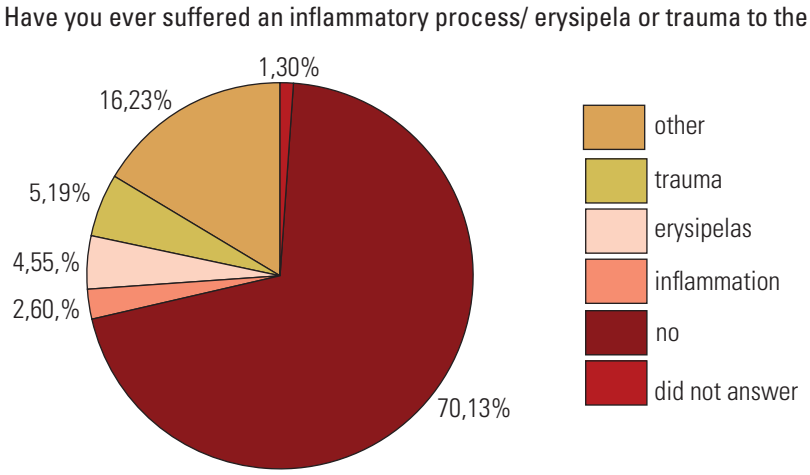

Figure 11 - Stratification of patients based on history of trauma, erysipelas, and inflammation.

Approximately 108 patients had never presented with an inflammatory process, erysipelas, or trauma in the LL. Among those who had, the occurrence had been over a year before.

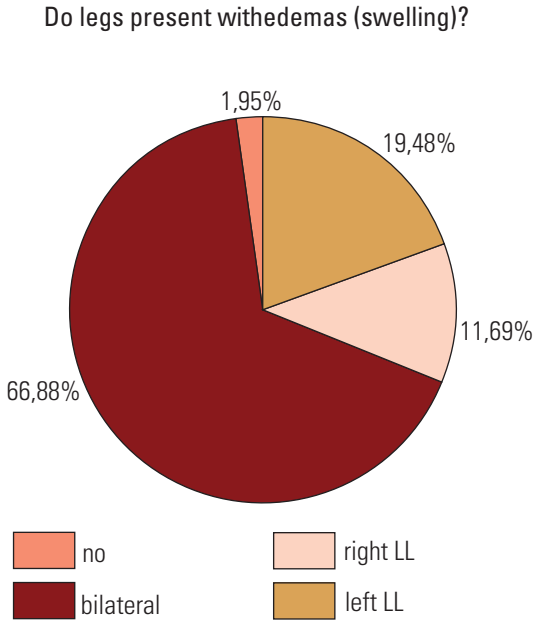

Figure 12 - Stratification of patients based on edema (swelling) when LLL was performed.

Bilateral edema was present in 103 out of the 154 patients at the moment of the exam, while 30 of them presented edema in the left and 18 in the right.

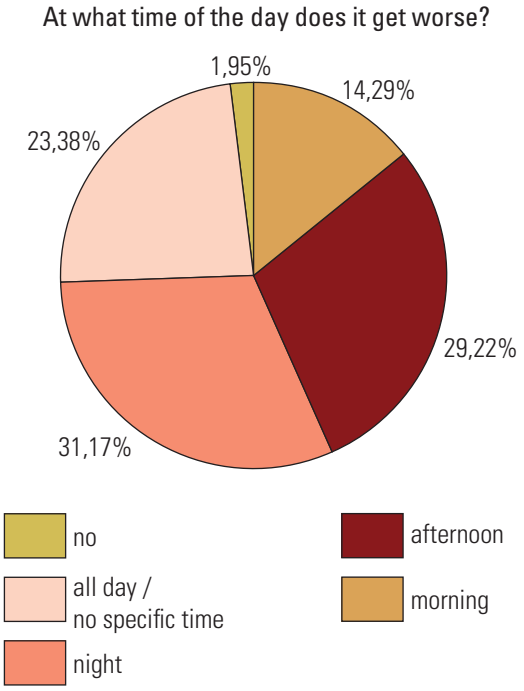

Figure 13 - Correlation between edema worsening and time of day.

Out of the 154 patients, 48 reported worsening of edema at night, 45 in the afternoon, and 22 in the morning.

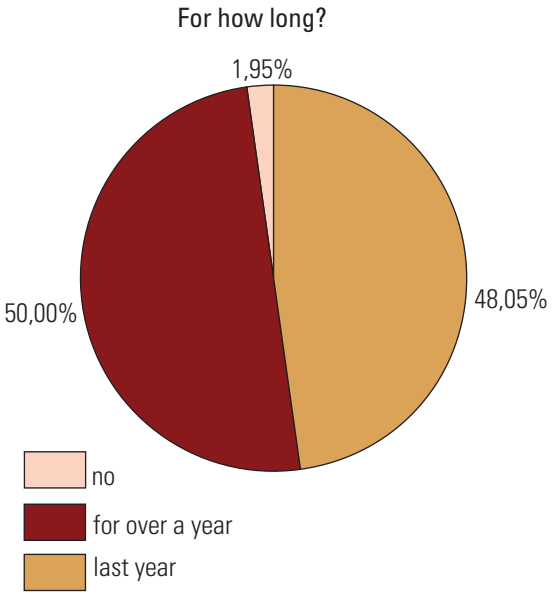

Figure 14 - Stratification of patients in the study based on the occurrence of edema of the LL

Approximately 77 patients had presented with the clinical profile for over a year 77 (50%). Among the 154 patients, 55 (35.71%) did not have any underlying disease, 31 (20.13%) were hypertensive, 8 (5.19%) were cardiac patients, 7 (4.55%) were diabetic, and 9 (5.84%) had some type of thyroid dysfunction.

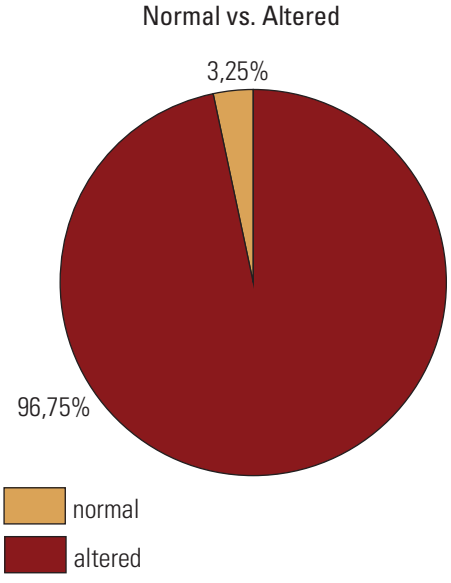

Figure 15 - Percentage of LLLs considered normal or altered.

Out of 154 patients, 149 presented some alteration in the scintigraphic study.

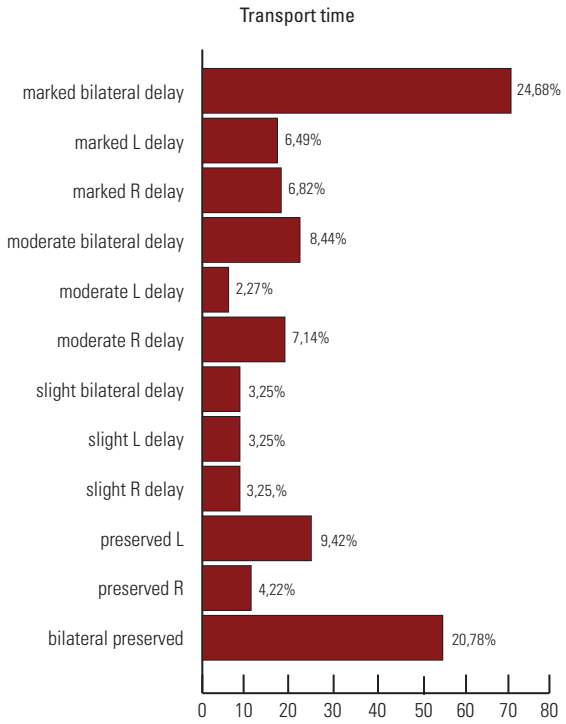

Figure 16 - Frequency of lymphatic transport time variations for every limb studied and evidenced by LLL.

Marked bilateral delay in lymphatic transport time was found in 38 out of the 154 patients.

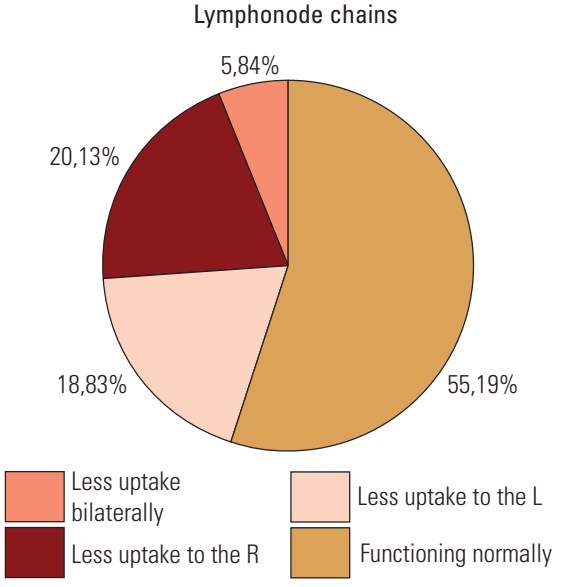

Figure 17 - Frequency of unilateral, right or left and bilateral involvement, according to scintigraphic analysis.

Out of the 154 patients, lymph node chains functioned normally in 85.

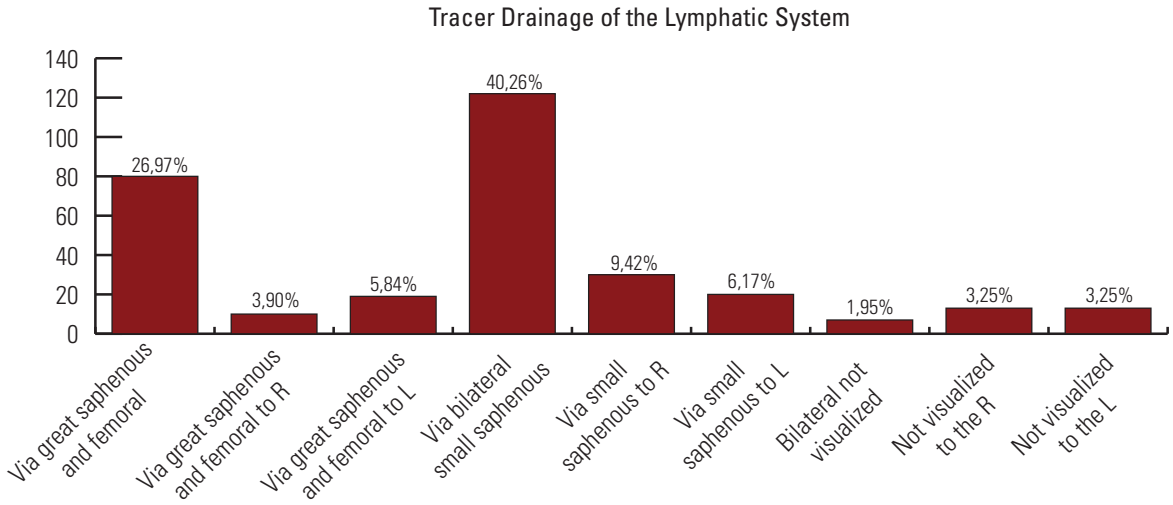

Figure 18 - Distribution of radiotracer drainage by the lymphatic system located in different regions of the LL by number and percentage of patients undergoing LLL.

In 62 patients, radiotracer drainage by tge lymphatic system happened through the saphena parva, bilaterally.

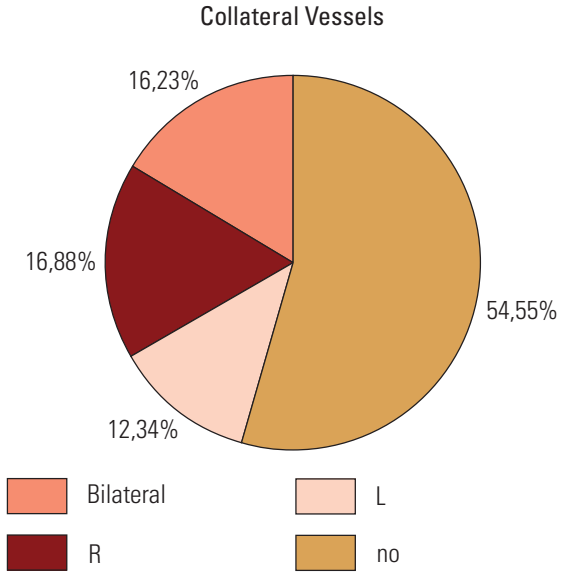

Figure 19 - Stratification of visibility of collateral paths for lympahatic drainage of the LL both unilaterally and bilaterally, per patient evaluated.

Collateral vessels were not present in 84 patients and 25 had them bilaterally, 26 on the right and 19 on the left.

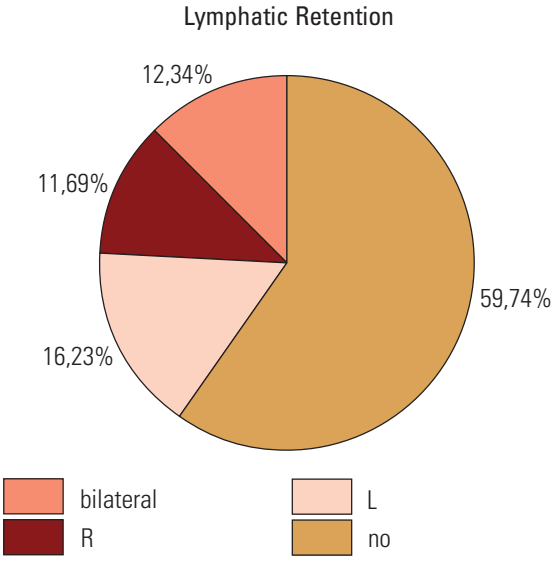

Figure 20 - Stratification of patients based on lymphatic retention distribution.

There were no signs of lymphatic in 92 patients and the other 19 had bilateral lymphatic retention, 18 on the right, and 25 on the left.

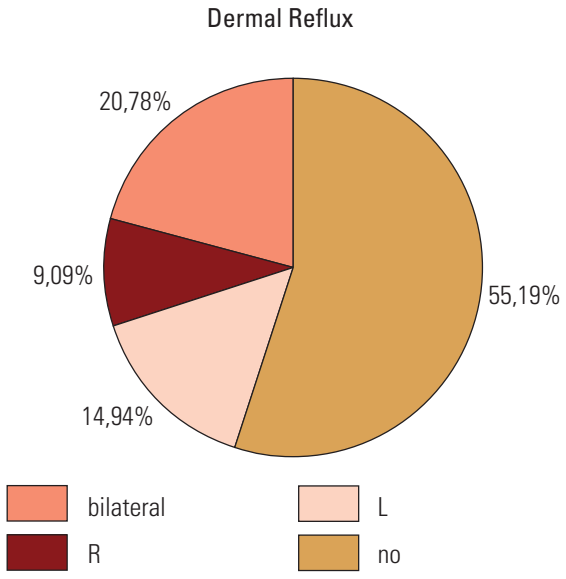

Figure 21 - Stratification of patients based on the presence and laterality of dermal reflux.

Out of the 154 patients, 85 patients presented no dermal reflux and 32 had dermal reflux bilaterally, 14 on the right and 23 on the left. Out of the 154 patients, 15 (9.74%) revealed lymph nodes in popliteal region on one side or bilaterally.

DISCUSSION

In chronic edema of the LL, anamnesis and clinical examination are the cornerstones of the initial approach to rule out cardiac, renal, hepatic, endocrine or post-traumatic systemic causes. Local causes include primary and secondary lymphedema, lipodystrophy, deep vein thrombosis, and chronic venous disease, as well as post-operative complications of surgical procedures, cellulite, Baker's cyst and cyclic idiopathic edema.[2] Diagnosis of pathological circulation impairment is frequently reached by exclusion of other potential causes that can lead to edema. Lymphedema of the LL has a complex pathogenesis, arising from congenital abnormalities, obstruction or damage of lymphatic channels or, even, from functional alterations of the lymphatic system.

LLL is a technique to distinguish the lymphatic causes for edema of the LL from other disorders such as obesity, venous disease, and hypoalbuminemia. Scintigraphic examination of the lymphatic drainage of the LL in cases of venous disease, however, is also relevant, considering that the cycle edema-infection-fibrosis can lead to further lymphatic drainage deterioration, also affecting lymphatic pathways. Besides, some forms of lymphedema are more prone to respond positively to treatment and LLL can help identify such cases.[7]

LLL is a simple, non-invasive method, linked to an effective low dose, acceptable even for children. It is low-cost and can provide precise physiological information on the lymphatic system and show functional deficiencies in lymphatic transport, even before morphological alterations such as edema, fibrosis or epidermic alterations emerge. This means that a significant number of patients, even with no prior manifestation of edema or signs of lymphedema, present suggestive scintigraphic findings for clinically compensated primary lymphedema, which predisposes them to erysipelas. LLL has a 100% specificity and sensitivity ranging between 90 and 95%.[8]

In patients with primary lymphedema, delay or absence of drainage of the radiopharmaceutical are common, with absent or poorly visible lymphatic vessels, unidentifiable regional lymph nodes and, at times, dermal reflux in early images. Those findings are considered diagnostic in the absence of a clinical background suggesting secondary causes.

Patients with secondary lymphedema are more prone to present at the scintigraphic study prominent lymphatic vessels or lymphangiectasia, collateral vessels, delay transporting the radiopharmaceutical and dermal reflux in late images.

There may be mixed etiologies for lymphedema, for example, a secondary factor that causes subclinical lymphatic hypoplasia. These cases are, many times, revealed through the scintigraphic patterns of primary and secondary lymphedema.

The results obtained via LLL may vary according to the radiopharmaceutical used, volume and activity injected, pH, electric charge, and hydrophilicity. In this case study, simultaneous intradermal administration of 37 MBq of 99mTc-Dextran 500 in 0.1 ml volume was used in the interdigital space of the first and second toes, bilaterally, an easily reproducible method.

The transport of the radiopharmaceutical is accelerated by mechanical stimulation (massaging, physical stress), as well as by the increased hydrostatic pressure on the interstitial fluid by edema or orthostatic position.

The results presented here suggest a strong correlation between the abnormalities in lymphatic drainage and clinical examination findings such as cellulite, even though it is not possible to tell whether cellulite was the cause or an effect of the lymphatic abnorma-

lities found. The fact that some patients with no previous history of cellulite present alterations upon LLL suggests that lymphatic alterations precede cellulite.

Furthermore, damage to lymphatic drainage pathways seems to be permanent, conferring increased risk of swelling (edema) and infection. Thus, patients with cellulite found on clinical examination must be assessed with lymphoscintigraphy to check for lymphedema diagnosis. In patients with at least two previous episodes of cellulite, lymphograms with significant lymphatic alterations are found, and post-cellulite edema episodes are underestimated and underreported.[1] De Godoy *et al.*[9] estimate that 77% of the patients who had at least two episodes of erysipelas bear scintigraphic abnormalities due to the lymphatic involvement.

Baulieu et al.[10] analyzed LLL of 32 patients with tibial fractures treated surgically and discovered that untraced inguinal lymph nodes enables prediction of late LL edema in the post-operative phase. This study suggests that LLL is able to identify patients with high risk of developing lymphedema. When performed early LLL, allows for the implementation of preventive strategies to minimize that risk.

The main objectives of the treatment are remission of complaint, preventing disease progression and reducing the size of the affected limb. Conservative therapies are available, including pharmacological therapies and surgery. In milder cases, slight elevation of the limb and compression socks may be successful. Other conservative actions include massage and special exercise to stimulate lymphatic drainage. At first, the combination of those actions is normally used. Surgery is often reserved for refractory cases and aggressive therapy with antibiotics is necessary when there is infection on the limbs so as to avoid new lymphatic obliterations. Patients with more than two events of cellulite in 12 months and scintigraphic pattern that confirms alteration in lymphatic drainage must be properly assessed, and antibiotic prophylaxis considered.[1]

CONCLUSION

Clinical differentiation between lymphatic and non-lymphatic edemata is usually difficult and causes patients to undergo a number of inconclusive, costly, and even unnecessary investigations. It is essential to establish an adequate algorithm applicable to the resources locally and that may contribute to the early and accurate diagnosis of lymph circulation disorders. Early intervention and efficient therapy can result in a consequent satisfactory development that prevents the affected limb from developing tissue degeneration or formation of chronic lesions.

As a safe, trustworthy, and low cost method to confirm the direct involvement of the lymphatic system as an etiological factor in the pathogenesis of LL edema is effectively found in the LLL technique.

Lymphedema and alterations in lymphatic drainage are very frequent entities in the population in general, which makes LLL an important tool not only for initial investigative screening but also to assess initial phases of edemata or even for the follow-up and monitoring of therapeutical, clinical or surgical interventions.

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