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Does lymphoscintigraphy have a role in the diagnosis and management of lipedema?

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Abstract

Lipedema is a chronic and progressive connective tissue disorder characterized by symmetric accumulation of adipose tissue, predominantly in the lower limbs, often associated with pain, easy bruising, and reduced response to lifestyle interventions. Despite increasing recognition, the condition remains frequently misdiagnosed or mistaken for obesity or lymphedema. To investigate the role of lymphoscintigraphy in the diagnostic and therapeutic management of patients with clinically confirmed lipedema and assess its potential utility in detecting associated lymphostatic disorders. A retrospective observational study was conducted on 108 patients clinically diagnosed with lipedema between January 2019 and August 2023. Among them, 31 patients underwent lymphoscintigraphy due to suspected mixed pathology or surgical candidacy. Data on lymphatic involvement were collected and analyzed to determine correlations with clinical staging. In 58% of the selected cases, lymphoscintigraphy revealed no detectable lymphatic abnormalities. Of these, approximately 70% showed latent compensatory lymphatic patterns. The remaining 39% had confirmed alterations of the superficial and/or deep lymphatic system, suggesting a mixed clinical picture (lipo-lymphedema) with potential surgical contraindications. Lymphoscintigraphy is not essential for routine diagnosis of lipedema, which remains clinical. However, it is valuable in identifying cases with coexisting lymphostatic components and guiding surgical decisions. These findings support a multidisciplinary and individualized approach to diagnosis and treatment.

Key words: lipedema, lipo-lymphedema, lymphoscintigraphy, differential diagnosis, Fat Pain Syndrome, conservative treatment, liposuction risk.

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Introduction

Lipedema is a chronic disorder of loose connective tissue, clinically characterized by a particular form of edema associated with a significant increase in adipose tissue, predominantly affecting the lower limbs. The condition typically begins at the level of the iliac crest and progressively extends to the ankles in advanced stages, leading to increased body weight. A disproportional distribution of adipose tissue is generally observed, primarily affecting the lower extremities; the upper limbs are also often involved, while the abdomen is usually less affected by fat accumulation. More rarely, cases may present with a symmetric distribution of both edema and adipose tissue, without disproportion between the upper and lower limbs and the abdomen.[1] The etiology of lipedema remains unknown. However, it predominantly affects women, with epidemiological studies estimating a prevalence of at least 11% among all women.[1] It typically manifests during periods of hormonal fluctuation, such as puberty, pregnancy, or menopause.[2] Although rare, lipedema has been reported in male patients, usually associated with low levels of male sex hormones or liver dysfunction. A clear gender prevalence exists, and a genetic predisposition is highly likely. A study published in the International Journal of Molecular Sciences confirmed the genetic basis of the disease, identifying a mutation in the *AKR1C1* gene in a family affected by non-syndromic primary lipedema.[3]

Recent research has also focused on extracellular microRNAs isolated from the stromal vascular fraction, comparing patients with lipedema to healthy controls. Results showed significant alterations in seven microRNAs in lipedema patients, potentially involved in adipogenesis, angiogenesis, inflammation, and fatty acid metabolism – all central processes in the disease's pathophysiology.[2,3] Despite growing scientific interest in recent years, especially regarding its pathophysiology, high-level evidence remains limited, making it difficult to establish definitive diagnostic and therapeutic algorithms. Most guidance relies on expert consensus or narrative reviews, and the condition remains largely underdiagnosed and mismanaged. Even in clinical settings, confusion persists between lipedema and other conditions such as lymphedema, lipodystrophy, cellulite, or simply obesity. This misclassification often results in ineffective therapeutic approaches that fail to address the disease's specific characteristics.

Materials and Methods

This study is a retrospective, single-center observational analysis conducted between January 2019 and August 2023. The pathology affects both males and females, but it is usually predominantly female patients who come to the doctor's attention due to greater attention to aesthetics and localized adiposity.

A total of 108 female patients with a clinical and ultrasonographic diagnosis of lipedema were evaluated at our vascular and lymphatic outpatient clinic. Among these, a selected subgroup of 30 patients underwent lymphoscintigraphy. The indication for lymphoscintigraphy was based on the presence of clinical features suggestive of a coexisting lymphostatic condition (e.g., asymmetry, progression of swelling, frequent infections, or suspicion of lipolymphedema), or in cases where surgical intervention (e.g., liposuction) was being considered and a precise evaluation of the lymphatic system was deemed essential to avoid iatrogenic complications.[4-6] The inclusion criteria were: i) female patients ≥18 years of age; ii) clinically confirmed diagnosis of lipedema (using the International Lipoedema Association, ILA, 2022 criteria), and iii) no prior lymphatic surgery or malignancy. The exclusion criteria were: i) isolated lymphedema without clinical signs of lipedema; ii) previous radiotherapy or lymph node dissection. The diagnosis of lipedema was established through clinical examination, supported by Doppler ultrasound in all patients to exclude chronic venous insufficiency and to assess subcutaneous tissue characteristics. Diagnostic confirmation adhered to the ILA criteria.[7] Lymphoscintigraphy was carried out through subcutaneous administration of technetium-99m-labeled nanocolloid, with acquisition protocols including whole-body, static, and dynamic imaging. Lymphatic function was categorized as positive (clear evidence of lymphatic damage) ("YES"), negative (no abnormal findings) ("NO"), or latent (compensatory changes in lymphatic flow) ("NO LAT").[8-11] The "latent" category included cases showing minor asymmetry of tracer distribution, delayed but complete lymphatic transport, or visualization of collateral lymphatic pathways, without dermal backflow. These findings were interpreted as compensatory changes in lymphatic flow. All patients provided informed consent. The study complies with the Declaration of Helsinki.

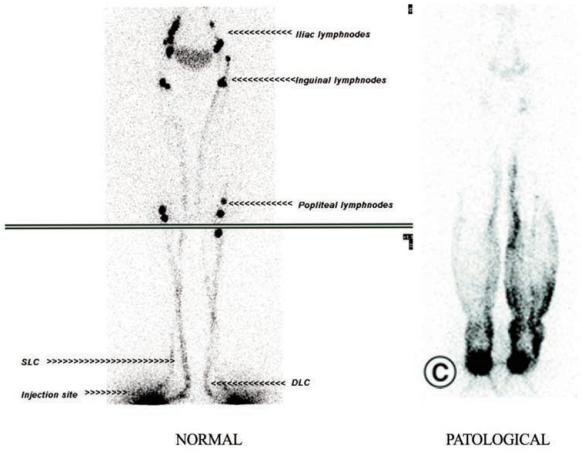

Figure 1. Segmental superficial and deep lymphoscintigraphy of the lower limbs: normal findings on the left side and pathological alterations on the right side.

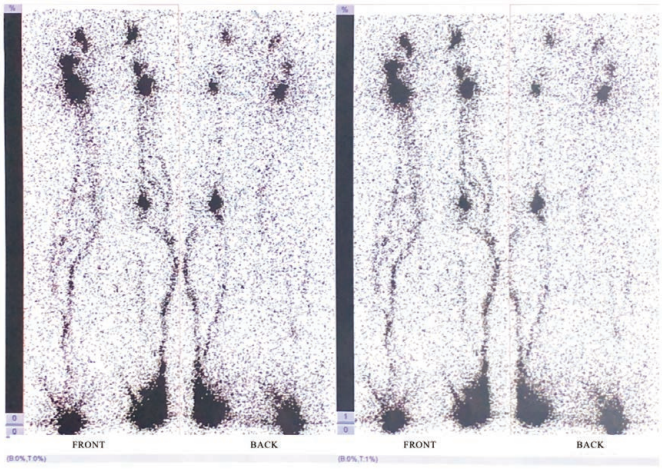

Figure 2. Segmental superficial and deep lymphoscintigraphy of the lower limbs: normal findings on the left side and pathological alterations on the right side.

Radiopharmaceutical and acquisition protocol

The radiopharmaceutical used in our center was 99mTc-human serum albumin nanocolloid (particle size 20-80 nm). A total activity of 1-2 mCi (37-74 MBq) was administered, divided into aliquots of 0.2-0.4 mCi in injection volumes of 0.2-0.3 mL. Imaging was performed using a dual-head large-field gamma camera equipped with LEHR collimators. Whole-body imaging: Acquired in anterior and posterior projections (speed 10 cm/min, matrix 128×128, zoom 1). For lower limbs, acquisition extended from the feet to the liver; for upper limbs, from the neck to the liver. Acquisition of dynamic images (60 s/frame, 64×64 matrix, zoom 1) on the lymph glandular districts occurs for about 20-30 min after radiopharmaceutical administration. At the end of the dynamic study, acquisition of total body images (speed 10 cm/min) is perfomed in anterior and posterior projections after 30 min (early acquisition) and 2h (delayed acquisitions) in case of poor radiotracer migration. Static planar views (300 s, 128×128 matrix, zoom 1) on the injection sites and on the loco-regional lymphoglandular districts can be taken after 3-4 h. Both superficial and deep lymphatic systems were studied during the same session. Static planar imaging: Acquired in anterior and posterior projections, matrix 128×128, zoom 1.33, for 5 minutes. Dynamic imaging: Acquired in anterior and posterior projections, matrix 64×64, zoom 1, with 60 sec/frame for a total duration of 30 minutes. Deep circulation injection: For the study of the deep circulation, one aliquot (37 MBq in injection volumes of 0.2-0.3 mL) of radiopharmaceutical is injected at the level of the deep palmar fascia for the upper limbs or the deep plantar fascia for the lower limbs. Following injection, patients were instructed to perform physical exercise for 20 minutes. Superficial circulation injection: Two aliquots of the radiopharmaceutical were injected (25G needle) subdermally on the dorsum of the hands (2nd and 3rd metacarpal spaces) or feet (2nd and 3rd metatarsal spaces). After injection, patients were again instructed to perform physical exercise for 20 minutes.

Results

A total of 108 female patients were evaluated, of whom 30 underwent lymphoscintigraphy. The average age was 47,5 years (Standard Deviation, SD±14,87 years). Among these 30, 18 patients (60%) had negative lymphoscintigraphy results, of which 11 (36.7%) showed latent signs (NO LAT).[6,11] Twelve patients (40%) had positive findings consistent with lymphatic alterations.[7]

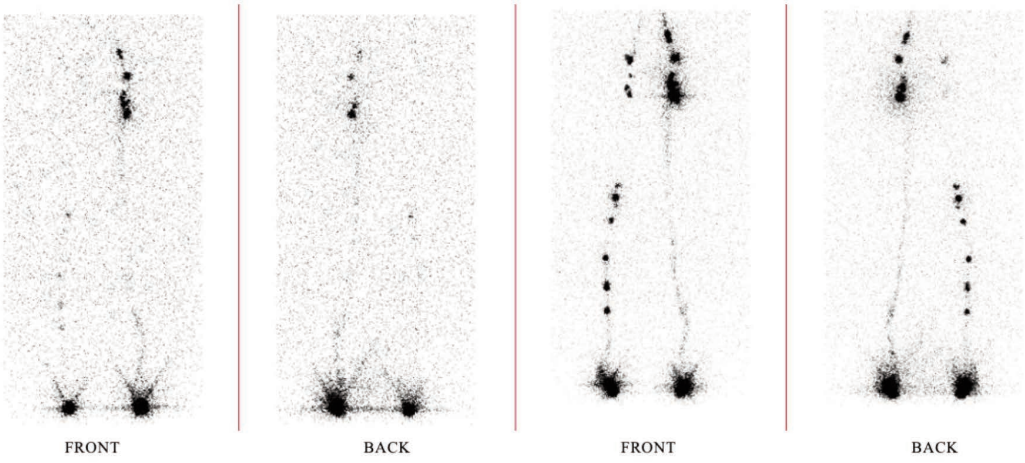

Figure 3. Lymphoscintigraphy showing latent lymphatic alterations.

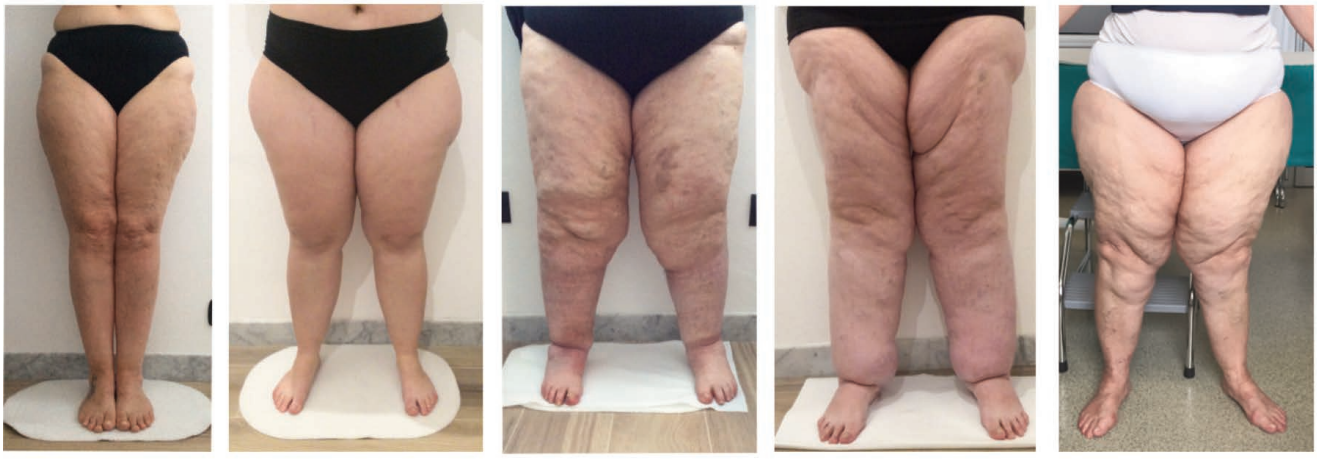

Figure 4. Examples of lower limb lipedema at different disease stages.

These results suggest that in more than half of the patients with suspected mixed pathology, lymphoscintigraphy did not show overt lymphatic damage, supporting eligibility for surgical intervention with minimal lymphatic risk (Figure 1-4, Table 1).[6,12]

Discussion

The findings of this study confirm the central role of clinical evaluation in diagnosing lipedema, as supported by international guidelines and expert consensus.[7,13,14] However, they also highlight the complexity and heterogeneity of the disease, which often overlaps with other conditions such as obesity and lymphedema.[5,12]

Lymphoscintigraphy, while not necessary for diagnosis in typical cases, emerges as a valuable tool in identifying patients with latent or overt lymphatic dysfunction, especially when surgical intervention is being considered. The detection of lymphatic abnormalities in 40% of the patients who underwent lymphoscintigraphy suggests a significant prevalence of mixed pathologies such as lipo-lymphedema.[11] This is clinically relevant, as lymphatic compromise can influence both prognosis and treatment strategy. Surgical procedures like liposuction, although effective in volume reduction and symptom relief, carry the risk of damaging already vulnerable lymphatic structures. Therefore, lymphoscintigraphy can be instrumental in risk stratification and surgical planning.[6] The presence of latent lymphatic compensation in a majority of "negative" cases also invites further investigation into the subclinical dynamics of lymphatic overload in lipedema. It raises the question of whether lipedema represents a spectrum disorder with varying degrees of lymphatic involvement rather than a purely adipose-based pathology.[3,10] Additionally, the psychological burden and quality-of-life impact of lipedema remain underexplored. Awareness remains low even among healthcare providers, as highlighted by recent surveys.[13] Patients often face years of misdiagnosis, inappropriate treatments, and stigma, which can exacerbate both physical and emotional suffering. Future studies should integrate psychosocial metrics and long-term follow-up to better understand the holistic outcomes of different treatment strategies.[12,14]

Table 1. Patients' information.

Patient ID	Age	Sex	Stage	Lymphoscintigraphy
A. J.	41	F	2	NO LAT
A. T	74	F	2	YES
A. K.	38	F	2	NO LAT
B. A.	28	F	2	NO LAT
C. B	45	F	3	NO
C. J.	27	F	2	NO LAT
D. SM. S	54	F	2	YES
D. S. F.	49	F	2	YES
D. G.	69	F	3	YES
C. V.	58	F	3	NO
D. S.	44	F	3	YES
D. A.	49	F	3	YES
F. D.	51	F	3	NO
F. R.	39	F	3	NO LAT
F. G.	32	F	1	YES
G. D.	35	F	2	NO LAT
L. S.	24	F	1	NO LAT
L. A.	68	F	LIPO-LYMPHEDEMA	YES
L. A.	58	F	3	YES
L. S.	51	F	3	YES
M. M.	50	F	1	NO
M. V.	34	F	2	YES
M. A.	24	F	1	NO LAT
M. G.	79	F	2	NO LAT
M. T.	29	F	1	NO
M. S.	52	F	2	NO LAT
N. V.	44	F	1	NO
P. C. V.	60	F	3	NO LAT
P. C.	57	F	3	YES
R. G.	62	F	2	NO LAT

Conclusions

Lipedema is a complex and often misunderstood adipose tissue disorder with clinical, functional, and psychosocial consequences. While its diagnosis remains primarily clinical, imaging modalities such as lymphoscintigraphy provide valuable insight in select cases, particularly where mixed pathologies are suspected or surgical interventions are planned.[6,7] Our findings support the integration of lymphoscintigraphy as a second-level investigation in patients with suspected lipo-lymphedema or when evaluating surgical candidacy. Importantly, the results underscore the necessity of a multidisciplinary approach involving vascular specialists, radiologists, surgeons, endocrinologists, and mental health professionals.[12,15,16] Ultimately, the effective management of lipedema requires early diagnosis, individualized care plans, and ongoing research into its pathophysiology, treatment outcomes, and patient-reported quality of life.

Further research into lipedema's pathophysiology, genetics, and patient-centered outcomes is needed to refine diagnostic tools and optimize care.[1,8,9]

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Informed consent: informed consent was obtained from the patient included in this study.

Patient's consent for publication: the patients gave their written consent to use their personal data for the publication of this case report and any accompanying images.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.