Lymphology 58 (2025) 34-41

LYMPHANGIOSARCOMA, A RARE COMPLICATION OF LYMPHOSTASIS: AN OBSERVATIONAL STUDY ON THE ROLE OF THE PHYSIOTHERAPIST IN EARLY RECOGNITION AND MEDICAL REFERRAL

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ABSTRACT

Lymphangiosarcoma is a rare, malignant angiosarcoma that primarily develops in limbs with chronic lymphedema and presents with dermal lesions. Due to a 5-year survival rate of 22.4%, early detection and treatment are critical for improving prognosis. This study assessed physiotherapists' skills in recognizing suspicious dermal lesions in lymphedema patients with a focus on lymphangiosarcoma. An 11-question online survey was created using Google Forms that included academic training, practical experience, frequency of lymphatic treatments, ability to recognize suspicious dermal lesions, referral frequency to specialists, and opinions on specific training needs. The study was conducted from 9 February to 30 March, 2024 and it targeted Italian physiotherapists who manage patients with lymphedema. Responses were received from 170 physiotherapists. Only 12.9% had university education on dermal lesions in lymphedema patients, while 70.6% had postgraduate training. Additionally, 57.6% felt unable to recognize lymphangiosarcoma. Postgraduate education was correlated with the ability to recognize the pathology ($p=0.047$). Clinical experience and frequency of lymphatic treatments was associated with recognition and reporting of suspected cases ($p<0.05$). Findings suggest the need for increased awareness and specialized training among physiotherapists to improve early detection and treatment of lymphangiosarcoma in lymphedema patients. Enhanced postgraduate education and clinical experience may lead to better patient outcomes.

Keywords: Lymphangiosarcoma, Stewart-Treves syndrome, Lymphedema, Chronic Lymphedema, Dermal lesions

INTRODUCTION

Lymphangiosarcoma is a rare form of angiosarcoma. The first correlation with lymphedema was described in the inaugural volume of the journal "Cancer" in 1948. Investigators Fred Stewart and Norman Treves reported a case series of six female patients with secondary lymphedema following radical breast surgery who had developed this rare tumor in the limb affected by secondary lymphostasis. This pathological relationship was thus called Stewart-Treves Syndrome (1). The deficiency of lymphatic drainage hinders the normal circulation of immunocompetent cells, rendering the affected areas immunocompromised (ICD), making them more vulnerable compared to the rest of the body. Due to a dysregulation of local immune control, such ICDs can become favorable grounds for the

Fig. 1. *Clinical signs of early-stage lymphangiosarcoma in a patient with chronic lymphedema. Suspicious skin lesions are visible and this requires immediate referral for medical attention to facilitate early diagnosis.*

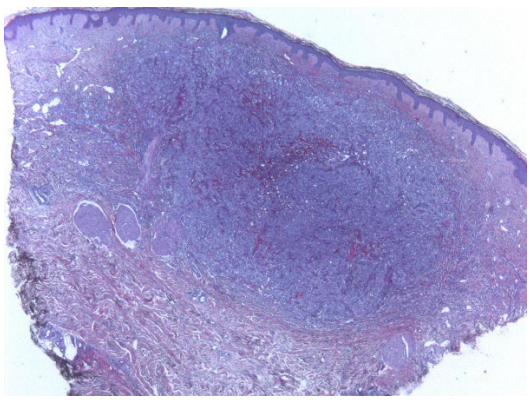

Fig. 2. *Histological image of a tissue sample obtained from a patient affected by lymphangiosarcoma in the setting of lymphedema. Section was prepared using paraffin embedding technique and stained with hematoxylin and eosin. Image displays irregular proliferation of blood vessels which is characteristic of lymphangiosarcoma along with presence of atypical endothelial cells and infiltration of surrounding tissue. Additionally, areas of necrosis and increased cellular density (both indicative of the tumor's aggressiveness) are also observed.*

development of opportunistic infections or constitute a predisposed environment for tumor neoformations (2,3) (*Fig. 1*). Supporting this, ultrastructural and immunohistological analyses conducted on neoplastic cell samples of lymphangiosarcoma have shown endothelial-type oncogenetic differentiation of the lymphatic vessels (4) (*Fig. 2*). Stewart-Treves syndrome is a rare condition. Its prevalence is estimated between 0.07% and 0.45 of patients treated for breast cancer (5). In patients with lower limb lymphedema, lymphangiosarcoma is less common compared to upper limbs, with few cases documented in the literature. In most cases, it occurs in people with secondary lymphedema due to oncological pathology (71.2%), but it can also be associated with secondary lymphedema from filariasis, post-surgical outcomes, radiotherapy treatments, trauma, or primary congenital conditions (6). Lymphangiosarcoma appears on average 10.7 years after the onset of lymphedema (7).

Lymphangiosarcoma is a malignant tumor with a 5-year survival rate from diagnosis of 22.4% (6). It predominantly develops in limbs affected by chronic lymphedema and presents with dermal lesions on the affected limb. Lymphangiosarcoma can initially manifest as a bruise-like lesion that spreads ("spreading bruise") or as a red or purplish swelling, which can later progress by infiltrating tissues and worsening the edema. The growth of the tumor mass can lead to ulcer formation and bleeding (8). The size of these lesions typically ranges from 3 to 6 centimeters, but if untreated, they can grow up to 20 centimeters. Patients commonly report discomfort or pain in the area affected by the lesions (8). To increase survival chances, early identification of lymphangiosarcoma and the timely initiation of treatment are crucial (9-11).

This study arises from the awareness that physiotherapists are among the healthcare professionals who most frequently assess, manage, and treat patients with lymphedema during follow- up periods (12). In high-income countries, particularly in settings where cancer-related lymphedema is prevalent, physiotherapists play an active role in patient monitoring and can contribute to the early detection of

signs or symptoms of possible malignancies, ensuring timely referral to the appropriate specialist. However, in lower-resource settings, the accessibility and role of physiotherapists in this regard may vary. The aim of this cross-sectional observational study, conducted in Italy, is to investigate, through a questionnaire, the competence of physiotherapists working in lymphology in their clinical practice in recognizing suspicious dermal lesions in patients with lymphedema, with particular attention to the dermal manifestations of lymphangiosarcoma.

MATERIALS AND METHODS

2.1. Study Design

The study is a cross-sectional observational type. It is based on the creation of a questionnaire and its administration to a sample of physiotherapists.

2.2. Experimental Setting

In January 2024, the study design was set, and the questionnaire was developed by our research team, following a structured process based on a literature review and clinical experience in the field of lymphedema. The questionnaire was created online using Google Forms. From February 9, 2024, the questionnaire was advertised via email, social channels, and the communication channels of the Bergamo Physiotherapists' Order Commission. Data collection took place from February 9 to April 15, 2024. Each study participant was able to respond and complete the survey only once.

2.3. Participants

The population involved in the study consists of Italian physiotherapists who treat patients with lymphatic diseases in their clinical practice. Inclusion criteria for participants included: being a physiotherapist regularly registered with the Italian Physiotherapists' Order (FNOFI) and being a physiotherapist who treats patients with lymphatic issues. Exclusion criteria included: non-physiotherapist population and physiotherapists who do not treat lymphatic conditions. The inclusion/exclusion criteria were determined in the questionnaire.

2.4. Survey Development

The questionnaire consists of a total of 11 questions. The first two questions concerned the participant selection criteria as above. Then questions examined: university and post-graduate academic training on dermal lesions in lymphedema, years of clinical experience, average frequency of monthly lymphatic treatments, ability to recognize suspicious dermal lesions, frequency of specialist medical referrals, and opinion regarding the need for more specific training. The classification of clinical experience into specific time intervals was determined based on a balance between ensuring meaningful differentiation in professional expertise and maintaining sufficient sample distribution across categories. (See Supplemental attachment 1 for questionnaire).

2.5. Data Analysis

Data were archived in MS Excel and analyzed using the free statistical software Jamovi (version 2.3.28). Descriptive data were reported as frequency (%), and inferential statistics were obtained using the chi-square test and Spearman's correlation test, with the significance level set at $p < 0.05$. Spearman's correlation test was applied to ordinal variables to assess associations between the ability to recognize lymphangiosarcoma, years of experience, and the number of monthly lymphatic treatments. The statistical power was calculated using G*Power software and was found to be $1-\beta = 0.95$

RESULTS

3.1. Characteristics of Survey Participants

Sample

At the end of the data collection, 182 completed questionnaires were obtained. After

TABLE 1
Response rates from physiotherapists concerning need for education regarding dermal injuries in undergraduate and/or postgraduate courses

Question: Do you think there is a need for specific training on skin/dermal injuries in lymphedema patients at undergraduate and/or postgraduate level?

	Frequency	Percent	Cumulative Percentage
Absolutely necessary	166	97.6 %	97.6 %
Not much needed	4	2.4 %	100.0 %

applying inclusion and exclusion criteria, 6 participants (3.3% of responses) were excluded because they were not part of the "physiotherapist" population, and another 6 participants (3.4%) were excluded because they were physiotherapists who do not treat patients with lymphedema. Thus, the selected sample consisted of 170 individuals.

Clinical Experience

Of the 170 therapists considered for the survey, 27.1% (n=46 therapists) reported having clinical experience with patients affected by lymphatic diseases ranging from 0 to 5 years, 17.6% (n=30) between 5 and 10 years, 27.6% (n=47) between 10 and 20 years, and another 27.6% (n=47) had more than 20 years of clinical experience.

Frequency of Lymphatic Treatments

Among the participants, 44.7% (n=76 therapists) reported performing an average of fewer than 10 lymphatic treatments per month, 30.6% (n=52) reported between 11 and 30 treatments, 14.7% (n=25) between 31 and 60 treatments, and 10% (n=17) reported performing more than 60 treatments per month.

3.2. Training on Dermal Lesions in Lymphedema

The questionnaire investigated whether the physiotherapists had attended education on dermal lesions during their university and postgraduate courses and their personal opinion on the need for training in this area. Only 12.9% (n=22) had attended lessons on this topic during their university studies. Of the sample, 87.1% (n=148) had never attended education on dermal lesions during their university studies. 70.6% (n=120) reported attending courses on this topic during their postgraduate training, 27.1% (n=46) had never attended education on dermal lesions in patients with lymphedema during postgraduate specialization courses and 2.4% (n=4) had not attended any postgraduate courses related to lymphedema.

Seventy-two-point 4 percent of physiotherapists (n=123) considered specific training on dermal lesions absolutely necessary, 25.3% (n=43) considered it necessary, 1.8% (n=3) considered it somewhat necessary, and only 0.6% (n=1) considered it not necessary at all. (*Table 1*)

3.3. Medical Referral

An important topic explored was the need for physiotherapists to make medical referrals in their practice due to the presence of suspicious dermal lesions or suspected lymphangitis. Forty-eight-point 2 percent of physiotherapists (n=82) reported not referring any patients to a specialist in the past year, 37.1% (n=63) referred between 1 to 3 patients, 5.9% (n=10) referred between 4 to 5 patients, 3.5% (n=6) referred between 6 to 9 patients,

TABLE 2
Characteristics of physiotherapists reporting ability to recognize suspicious dermal lesions considering courses, lymphatic treatments performed per month, and years treating patients with lymphedema

Question: Could you recognize Lymphangiosarcoma or Stewart-Treves Syndrome?				
	No, never seen it	Yes, I have never seen it, but I would recognize it OR Yes, I have already seen one	χ^2	P
Postgraduate courses				
Yes	63	57		
No	32	14	3.96	0.047*
Lymphatic treatments performed (number/ month)				
0-10	54	22	14.4	0.002*
11-30	29	23		
31-60	10	15		
>60	5	12		
Years have you been treating lymphedema patients				
0-5	33	13	17	0.009*
5-10	16	14		
10-20	26	21		
>20	23	24		

***significant p-value <0.05**

and 5.3% (n=9) referred between 10 to 14 patients. None of the participants referred more than 15 patients for suspicious dermal lesions in the past year.

Patients Referred for Suspected Lymphangitis

In the past working year, 41.2% of participants (n=70) reported not referring any patients to a specialist, 33.5% (n=57) referred between 1 and 3 patients, 14.1% (n=24) referred between 4 and 5 patients, 3.5% (n=6) referred between 6 to 9 patients, 5.3% (n=9) referred between 10 to 14 patients, and 2.4% (n=4) referred more than 15 patients for suspected lymphangitis.

Physiotherapists' Satisfaction with Medical Referrals

Following the referral to a specialist, physiotherapists were asked to express their level of satisfaction and the usefulness of the consultation for continuing therapy and for diagnostic doubts. In 32.4% of cases (n=55), physiotherapists found all requested medical consultations exhaustive, 41.8% (n=71) were satisfied with most of the consultations, 17.6% (n=30) were satisfied with less than 50% of the consultations, and 8.2% (n=14) were satisfied with less than 10% of the consultations.

3.4. Physiotherapists' Ability to Recognize Lymphangiosarcoma

Within the questionnaire, therapists were asked to self-evaluate their ability to recognize the possible presence of signs and symptoms of lymphangiosarcoma. 12.9% of therapists

TABLE 3
Comparison of physiotherapists who attended lectures on dermal injuries during either undergraduate or postgraduate education and their medical referrals

Question: In the past year, how many patients have you referred to a physician for suspected dermal lesions?

	0	>1	χ^2	P
Postgraduate courses				
Yes	50	70	7.39	0.007*
No	30	16		
Courses during college				
Yes	11	11	0.605	0.437
No	87	61		

*significant p-value <0.05

(n=22) reported having seen one and being able to recognize it, 29.4% (n=50) reported being able to recognize it despite never having seen one, and 57.6% of participants (n=98) reported not being able to recognize it.

3.5. Statistical Analysis of Correlations

Statistical analysis explored associations between physiotherapists' ability to recognize lymphangiosarcoma and key predictor variables, including years of experience, number of monthly lymphatic treatments, and participation in university and postgraduate courses covering dermal lesions in lymphedema. Spearman's correlation test was used for correlation analysis with significance level set at $p < 0.05$.

Participation in university courses on dermal lesions was not associated with the ability to recognize lymphangiosarcoma ($p = 0.437$) (*Table 2*). However, a significant association was found between participation in postgraduate courses and both a greater ability to recognize lymphangiosarcoma ($p = 0.047$) and a higher frequency of patient referrals to specialists for suspected dermal lesions ($p = 0.007$) (*Table 3*). For ordinal variables, Spearman's correlation showed a relevant correlation between the ability to recognize lymphangiosarcoma and the number of monthly lymphatic treatments ($rS = 0.8$). A correlation was also observed between the ability to recognize lymphangiosarcoma and years of experience in treating lymphatic patients, although the association was weaker ($rS = -0.04$).

These findings suggest that the ability to recognize lymphangiosarcoma may be more influenced by clinical experience and treatment frequency than by university education alone. However, further studies are needed to validate these observations.

DISCUSSION

Our survey shows that there is lack of awareness regarding the clinical signs of lymphangiosarcoma among physiotherapists who perform lymphology-related treatments. Specifically, more than one in two participants report not being able to recognize the signs and symptoms of lymphangiosarcoma. However, physiotherapists seem to be aware of the importance of having such knowledge, as nearly all respondents considered training on the subject necessary or absolutely necessary. Analyzing responses regarding education on dermal lesions in lymphedema, it emerges that

dedicated training on this topic is still not widely integrated into three-year or five-year university courses with only 12.9% of the sample having had the opportunity to study it during their academic training. However, in postgraduate training programs this topic appears to be more frequently addressed with 70.6% of the sample reporting having received specific education on the subject. This trend suggests that postgraduate education may contribute to improving the ability to recognize less common clinical conditions and facilitate the referral of patients to specialists for further evaluation. Although our study may be one of the first to investigate the role of physiotherapists in recognizing lymphangiosarcoma, findings highlight the importance of advanced training and clinical exposure in enhancing recognition skills. While the data do not directly demonstrate a causal relationship between training and improved early diagnosis, they suggest that physiotherapists could play a relevant role in facilitating specialist referrals and improving patient outcomes in the management of lymphedema-related complications. Further research is needed to better define their contribution in this regard.

Study Limitations

This study has some limitations. First, the sample size is relatively small. Second, it was not possible to determine the total number of individuals who received the questionnaire and, consequently, to calculate the participation rate. This introduces a potential participation bias, as physiotherapists who chose to respond may be those with a greater interest in lymphology or more experience in managing lymphedema, potentially influencing the findings. Additionally, the questionnaire did not collect information regarding demographics, type of university training, or work environment (e.g., facilities affiliated with the national health system, private clinics, outpatient settings), limiting the analysis of potential correlations with these factors. Another limitation is that the questionnaire was self-reported and self-administered, which may have led to responses that do not accurately reflect participants' actual clinical practice. A significant limitation is also the cross-sectional nature of this study, which allows for the identification of associations between the analyzed variables but does not establish causal relationships. Future research should employ longitudinal study designs to assess how postgraduate training and clinical experience influence the ability to recognize lymphangiosarcoma over time. Moreover, expanding the research to a larger and more diverse sample, including physiotherapists from different geographical and cultural contexts, would help determine the generalizability of the findings. From a clinical practice perspective, the integration of more structured training programs could be a crucial step toward improving the early recognition of this pathology.

CONCLUSION

This study highlights the limited awareness among physiotherapists regarding the clinical signs of lymphangiosarcoma despite their involvement in the management of patients with lymphatic disorders. More than half of the participants reported being unable to recognize this condition, although they acknowledged the importance of specific training on the subject.

Data analysis indicates that undergraduate university education does not systematically address dermal lesions in lymphedema, whereas postgraduate training programs appear to provide more structured education on this topic. While the findings do not establish a direct causal relationship between advanced training and improved diagnostic ability, they suggest an association between postgraduate education and a greater likelihood of recognizing and referring suspicious lesions to medical specialists.

However, this study has some limitations including relatively small sample size and the cross-sectional nature of the research, which allows for the identification of associations between variables but does not establish causation. Additionally, potential participation bias may have influenced the results, as physiotherapists who responded to the survey may have

been those with a greater interest in lymphology.

Given these factors, further longitudinal studies are needed to better understand the actual impact of training and clinical experience on the ability to recognize lymphangiosarcoma. Expanding the sample to include diverse geographic and healthcare settings could also help assess the generalizability of the findings. Finally, the implementation of more structured training programs could represent a crucial step in enhancing awareness and improving the clinical management of this pathology in patients with lymphedema.

DISCLOSURE OF CONFLICT OF INTEREST

All authors declare no competing financial interests exist.

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