

LYMPHSCINTIGRAPHIC EVALUATION OF MANUAL LYMPHATIC DRAINAGE FOR LOWER EXTREMITY LYMPHEDEMA

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ABSTRACT

To evaluate the effect of manual lymphatic drainage on technetium-99m-labeled dextran ($^{99m}\text{TcDx}$) transport, 16 patients with lymphedema of lower extremities underwent two lymphoscintigraphy exams by injecting $^{99m}\text{TcDx}$ intradermally into the first interdigital space of the affected extremity. The first was a control examination at rest followed by an examination which included a manual lymphatic drainage session after the injection of the $^{99m}\text{TcDx}$. Images were obtained 45 minutes and three hours after the injection of the radioisotope. Extremity volumes were also measured before and after the drainage session. The findings from the examinations were assessed in a quantitative, semiquantitative and qualitative manner and compared without and with drainage. The analyses of the extremities' circumference before and after the drainage by paired t-test revealed a significant decrease. The analyses of the quantitative, semi-quantitative and qualitative evaluations evidenced no significant difference, without or with drainage, within the 45-minute and three-hour periods. Thus, manual lymphatic drainage caused an effective reduction in the circumference of the extremities but did not have a significant effect in the transport of $^{99m}\text{TcDx}$.

Keywords: lymphedema, lower extremity, massage, lymphoscintigraphy

A variety of congenital and acquired alterations in the lymphatic system compromise lymph transport and cause lymphedema (1). After an initial phase in which edema is the main clinical manifestation, protein accumulation induces a chronic inflammatory response associated with fibrosis, increased susceptibility to recurrent infections and major social and work impairments (2).

Multiple therapeutic alternatives have been used to treat lymphedema, including physical, pharmacological, and operative methods. The aim of both physical and pharmacological methods is to improve interstitial fluid and macromolecular drainage from areas with lymph accumulation to areas with normal drainage, restoring function, reducing complications, and improving the esthetic aspect of the extremity (3).

Complex physical therapy has been considered the treatment of choice for the reduction of lower limb lymphedema. This modality includes manual lymphatic drainage, exercises, skin care, and multilayer bandaging followed by elastic compression (4-7).

Lymphoscintigraphy is the gold standard technique to visualize the lymphatic system, evaluate its function (8,9) as well as responses to treatment (10-13). In a previous study using lymphoscintigraphy, we showed that sequential pneumatic compression reduced lower limb volume, but removal of macro-

molecules was not enhanced by this method (11,13). In the present study we demonstrate the effects of manual lymphatic drainage on the transport of dextran labeled with ^{99m}Tc in patients with lower limb lymphedema.

METHODS

The clinical protocol was approved by the Ethics Committee of the Federal University of São Paulo. Eighteen sequential patients with lower limb lymphedema were randomly assigned for this study. They attended the outpatient Vascular Surgery Clinic from the ABC School of Medicine teaching hospital. Exclusion criteria included the presence of acute infections in the affected limb and refusal to undergo lymphoscintigraphy or to sign the informed consent. Two patients were withdrawn because the second lymphoscintigraphy was not performed.

Therefore, 16 patients completed the study. They were all female, with ages varying from 26 to 80 years old (mean = 46.5 years old). According to Kinmonth's classification of lymphedema (14), four were secondary and 12 primary, ten of them considered early and two late primary lymphedemas. Ten patients presented with bilateral lymphedema while in six the disease affected only one lower extremity. All patients presented grade II lymphedema according to Mowlem's classification (15). Clinical history of lymphedema was present from three to 47 years.

Lymphoscintigraphy

All lymphoscintigrams were performed at the Nuclear Medicine Division of the Department of Image, Federal University of São Paulo.

Control lymphoscintigraphy was performed with the patient at rest, in dorsal decubitus, with no manipulation of the lower extremity. An intradermal injection of 185 MBq of dextran labeled with ^{99m}Tc was administered in the first interdigital space of

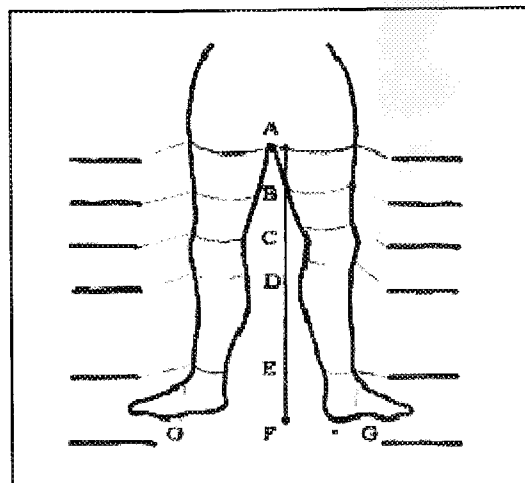


Fig. 1. Sites for circumferential measurements obtained in the lower extremities.

both feet, at a maximum volume of 0.3 mL. Initial images were obtained after 45 minutes, evaluating lower extremities and inguinal regions. Three hours after the injection, final images were obtained and patients were discharged home.

After seven days, all patients returned for a second lymphoscintigraphy, to demonstrate the effects of the manual lymphatic drainage. Initially, lower extremities were measured circumferentially at six different points, named A, B, C, D, E and F, as shown in Fig. 1. Radiotracer was injected as described earlier and manual lymphatic drainage was initiated immediately, lasting 40 minutes. Images were acquired at 45 minutes and three hours after radiotracer injection, using the same technique as described for the control exams.

The same physiotherapist was responsible for the manual drainage for all patients in the present study. Liquid vaseline was applied to the skin and low pressure movements were performed with the fingers. Wide circular movements were initiated in the inguinal region contralateral to the extremity to be evaluated, for four minutes. Then, the ipsilateral inguinal region was drained in a similar fashion for four minutes. The anterior

TABLE 1
Semiquantitative Evaluation Worksheet of Lymphoscintigraphy by Each Observer

Variables	Right Extremity				Left Extremity			
	0	3	5	9	0	3	5	9
Transport kinetics								
Dermal reflux								
Lymph nodes								
Lymphatic vessels								
Transport index								
Total semiquantitative index								

Criteria				
Variables	0	3	5	9
Transport kinetics	Normal	Minor decrease	Major decrease	No flow
Dermal reflux	Normal	Minor reflux	Major reflux	No flow
Lymph nodes	Normal	Visible, decreased	Barely visible	Not seen
Lymphatic vessels	Normal	Visible, decreased	Barely visible	Not seen

aspect of the thigh was drained by ascending movements toward the projection of the saphenous vein and its accompanying lymphatics for eight minutes. The leg was manually drained in a similar fashion as at the thigh, for eight minutes. The patient was placed in ventral decubitus for the drainage of the posterior aspect of the limb. Movements were started from the proximal thigh toward the medial aspect of the limb, for eight minutes. Finally, the calf was drained in a similar fashion for eight additional minutes.

After returning to the dorsal decubitus, the initial lymphoscintigraphic images were acquired and new circumferential measurements were obtained at the pre-established points (*Fig. 1*). The patient was maintained resting at dorsal decubitus for three hours. Then, the last lymphoscintigraphic images

were acquired. All images were stored for subsequent semiquantitative and qualitative evaluation by three independent physicians, two of them specialists in nuclear medicine and one vascular surgeon, all blinded for the patient and phase of the exam.

Quantitative Lymphoscintigraphic Evaluation

Comparison between control lymphoscintigraphy and the exam after manual lymphatic drainage was performed using radiotracer clearance calculation at the inguinal, thigh, popliteal and leg regions (11,13,16), applying the following formula:

Tracer clearance (%) = (radioactivity count at 45 min - radioactivity count at 3 hours) X 100 / radioactivity count at 45 min

A negative clearance signifies a lower

TABLE 2
Qualitative Evaluation Worksheet by Independent Observers
Based on Lymphoscintigraphic Findings

LEG	Right	Left
Lymphatic tract aspect (1-Linear; 2-Tortuous; 3-absence)		
Number of lymphatics (1-none; 2-single; 3-multiple)		
Popliteal lymph nodes (1-yes; 2-no)		
Dermal reflux (1-absence; 2-moderate; 3-intense)		
Collateral circulation (1- yes; 2- no)		
THIGHS	Right	Left
Lymphatic tract aspect (1-Linear; 2-Tortuous; 3-absence)		
Number of lymphatics (1-none; 2-single; 3-multiple)		
Inguinal uptake (1-yes 2-no)		
Dermal reflux (1-absence; 2-moderate; 3-intense)		
Collateral circulation (1- yes; 2- no)		

local tracer clearance, while a positive value signifies a greater clearance from the region (11,13).

Semiquantitative Analysis

Semiquantitative evaluation employed data from the dynamic tracer transport with data from the independent observers, according to the criteria defined by Kleinhans et al (11,13,17) for the calculation of transport index. In summary, this index was calculated by multiplying the values corresponding to the radioactivity detection time at the inguinal nodes, in minutes, times a constant of 0.04 (for example, 1.8 for the appearance within 45 minutes or 7.2 after three hours). The values were then summed to the total score by the three independent observers, thereby obtaining the total semiquantitative index for control exams as

well as for those after drainage at 45 minutes and three hours for each extremity (Table 1).

Qualitative Analysis

Qualitative analysis (18) was based on the observer's opinion, by grading the aspects of the lymphatic tract, the number of lymphatics, dermal reflux, presence of collateral circulation, and presence or absence of inguinal uptake (Table 2).

Statistical Analysis

Paired *t*-test was used to analyze the circumferential measurements of the lower limbs before and after manual drainage. The Wilcoxon test was used to compare the clearance values between exams with and without drainage. For the semiquantitative evaluation, concordance analysis between the

TABLE 3
Lower Extremity Measurements at Predetermined Sites (A, B, C, D and G)
Before and after Manual Drainage. Difference Between Means and Results of the Paired T Test

Site	Difference between means	Standard deviation from the differences	95% confidence interval		p value
			Lower limit	Upper limit	
A	0.563	0.727	0.175	0.950	0.007
B	0.844	0.569	0.540	1.147	0.001
C	0.719	0.576	0.412	1.026	0.001
D	1.031	0.464	0.784	1.279	0.001
E	0.688	0.544	0.398	0.977	0.001
G	0.625	0.619	0.295	0.955	0.001

three independent observers was employed and the mean index values were evaluated by analysis of variance for repeated factors, time (45 min and three hours) and drainage (with and without). The McNemar exact binomial test was used for the qualitative evaluation to detect if the proportion of lower extremities with changes in values was different from the extremities without changes in lymphscintigrams with and without drainage at 45 minutes and three hours (19,20).

RESULTS

Lower Extremity Measurements

Comparative analysis between before and after manual lymphatic drainage demonstrated a significant reduction in volume for all segments of the leg and thigh (Table 3).

Quantitative Analysis

The quantitative analysis of lymphscintigraphic tracer clearance showed

no significant differences between before and after manual drainage at the leg ($p=0.422$), popliteal ($p=0.875$), thigh ($p=0.695$) and inguinal regions ($p=0.249$).

Semi-Quantitative Analysis

There was an excellent correlation coefficient for the index between observers (> 0.95). The mean variance between indexes, with two repeated factors, time (45 min and 3 hours) and drainage (with and without drainage) showed that only the time factor was significant ($p=0.043$) while interaction between drainage and time was not ($p=0.633$).

Qualitative Analysis

Qualitative analysis of lymphscintigraphic exams showed no significant differences between with and without drainage for 45 minutes and three hours regarding the lymphatic aspects at the leg and thigh, the presence of popliteal lymph nodes, the presence of collateral circulation lymphatics at the thigh, dermal reflux, and inguinal



Fig. 2. Representative lymphoscintigram in a patient with lymphedema in the right lower extremity in whom minimal difference was detected before (A) and after drainage (B).

uptake. *Fig. 2* shows a representative image in which no improvement was detected after drainage. In only six cases was an improvement detected after drainage, as shown in *Fig. 3*.

DISCUSSION

Limb volume reduction and improvement of lymphatic vessel function are the main goals of the treatment of lymphedema. Manual lymphatic drainage has been considered as an effective technique for the management of lymphedema. We demonstrated that limb volume reduction, the most obvious signal of clinical improvement observed after manual lymphatic drainage (21,22), is mainly due to fluid shifts with no significant effect on macromolecular clearance. Our findings are similar to our previous study (11,13) and to other reports (23,24) in which sequential intermittent pneumatic compression also reduced limb volume by mobilizing water but not protein. Földi, et al (10) performed lymphoscintigraphy after four weeks of complex physical therapy

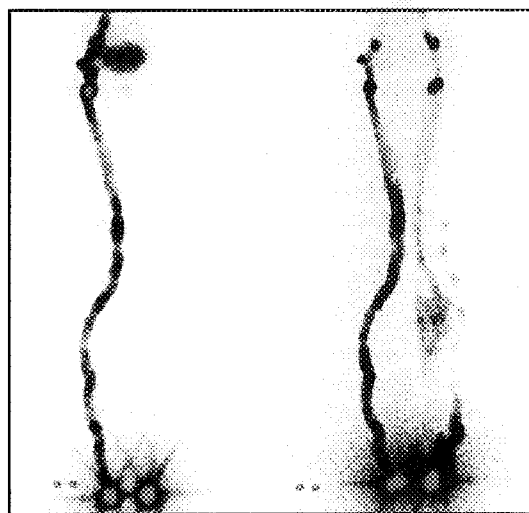


Fig. 3. Representative lymphoscintigram in a patient with lymphedema in the left lower extremity in whom a noticeable improvement was detected after drainage (B).

detecting lymph nodes in areas where they were not seen before, decreased dermal reflux and improved tracer clearance. They did not evaluate the isolated effects of manual lymphatic drainage. Leduc et al (25) performed manual lymphatic drainage in normal volunteers showing improved tracer clearance and lymphatic flow by lymphoscintigraphy. However, they did not have controls and did not evaluate patients with lymphedema, in sharp contrast with our study. In another study not comparable to ours, Ferrandez, et al (12) evaluated manual lymphatic drainage with a single lymphoscintigraphy in patients with upper extremity lymphedema from breast cancer, showing benefits in tracer clearance.

Caution must be exercised in analyzing our results. The present findings are limited to our study protocol. Our main goal was to evaluate the effects of a single session of manual lymphatic drainage, which is an important element of complex physical therapy, the recommended approach for the clinical management of lymphedemas (4-7). The effects of a more complete approach or

even more sessions of manual lymphatic drainage remain to be evaluated.

Measuring lower limb circumferences showed that a single session of manual lymphatic drainage promoted significant benefits in agreement with several other reports (10,21,22,25,26). Although technical aspects of manual lymphatic drainage are poorly described, there are common principles. Initially, proximal lymph trunks are emptied toward normal adjacent lymph areas, thereby allowing that lymph from the lower limb to meet empty lymph reservoirs. Only then massage was performed at the thigh and leg (2,10,22,27,28).

Our lymphoscintigrams were interpreted by three methods: quantitative, semiquantitative and qualitative (29,30). Qualitative analysis addressed radiotracer transport in relation to time (31). The use of semiquantitative analysis addressed the time for the radiotracer to reach regional lymph nodes, attributing score for the visual aspects of the images, allowing the calculation of a transport index (17). The qualitative analysis involved several types of information based on the images, including the number and aspects of lymphatics, the presence of dermal reflux and collateral circulation (18,30,32). The most frequently used method is the qualitative analysis, with a sensitivity varying between 70% and 94.8%, a specificity of 100% and an accuracy greater than 90% (29). We believe that by using three methods, an increased precision was achieved. All three methods agreed that a single session of manual lymphatic drainage promoted no significant benefits by lymphoscintigraphic evaluation, in spite of the clear clinical benefit of promoting lower extremity volume reduction.

REFERENCES

1. Głowiczki, P, HW Wahner: Clinical diagnosis and evaluation of lymphedema. In: *Vascular surgery*. Rutherford, R (Eds), Sixth Edition, Chapter 167, Saunders, WB, Philadelphia, 2005, 2396-2415.
2. Casley-Smith, JR, M Földi, TJ Ryan, et al: Lymphedema: Summary of the 10th International Congress of Lymphology: working group discussions and recommendations. *Lymphology* 18 (1985),175-180.
3. Mortimer, PS: Therapy approaches for lymphoedema. In: *XII World Congress of the International Union of Phlebology; 1995*; London. Proceedings. *Angiology* 48 (1997), 87-91.
4. The diagnosis and treatment of peripheral lymphedema. Consensus document of the International Society of Lymphology Executive Committee [commented on *Lymphology* 28 (1996), 137-40]. *Lymphology* 28 (1995), 113-117.
5. Guedes, HJ, MFC Andrade: Diagnóstico e tratamento do linfedema periférico. *Cir. Vasc. Angiol.* 12 (1996), 62-65.
6. Witte, MH, CL Witte, M Bernas. ISL Consensus document revisited: Suggested modifications. *Lymphology* 31 (1998), 138-140.
7. Bernas, MJ, CL Witte, MH Witte: The diagnosis and treatment of peripheral lymphedema Draft revision of 1995 Consensus document of International Society of Lymphology. *Lymphology* 34 (2001), 84-91.
8. Williams, WH, CL Witte, MH Witte, et al: Radionuclide lymphangioscintigraphy in the evaluation of peripheral lymphedema. *Clin. Nucl. Med.* 25 (2000), 451-464.
9. Witte, CL, MH Witte, EC Unger, et al: Advances in imaging of lymph flow disorders. *Radiographics* 20 (2000), 1697-1719.
10. Földi, E, M Földi, H Weissleder: Conservative treatment of lymphedema of the limbs. *Angiology* 36 (1985), 171-180.
11. Perez, MDCJ: Compressão pneumática intermitente seqüencial no linfedema dos membros inferiores: avaliação linfocintilográfica com dextran marcado com tecnécio 99m [tese]. São Paulo: Universidade Federal de São Paulo, 1996.
12. Ferrandez, JC, JP Laroche, D Serin, et al: Aspects lymphoscintigraphiques des effets du drainage lymphatique manuel. *J. Mal. Vasc.* 21 (1996), 283-289.
13. Miranda Jr, F, MDCJ Perez, MLV Castiglioni, et al: Effect of sequential pneumatic compression on both leg lymphedema volume and on lymph transport as semi-quantitatively evaluated by lymphoscintigraphy. *Lymphology* 34 (2001), 135-141.
14. Kinmonth, JB, GW Taylor, GD Tracy, et al: Primary lymphoedema. *Br. J. Surg.* 45 (1957), 1-10.
15. Mowlen, R: The treatment of lymphoedema. *Br. J. Plastic Surg.* 1 (1948), 48-55.

16. Takeishi, Y, J Chiba, S Abe, et al: Heterogeneous myocardial distribution of iodine-123 15-(p-iodophenyl)-3-R, S-methylpentadecanoic acid (BMIPP) in patients with hypertrophic cardiomyopathy. *Eur. J. Nucl. Med.* 19 (1992), 775-782.
17. Kleinhans, E, RG Baumeister, D Hann, et al: Evaluation of transport kinetics in lymphoscintigraphy: follow up study in patients with transplanted lymphatic vessels. *Eur. J. Nucl. Med.* 10 (1985), 349-352.
18. Gomes, SCN. Linfocintilografia superficial de membros inferiores com dextran 500 Tc99m. Estudo em pacientes portadores de filariose e de linfopatia não filariótica [tese]. Recife: Universidade Federal de Pernambuco, 1990.
19. Winer, BJ: Statistical principles in experimental design. (Eds), McGraw-Hill Kogakusha, Tokyo, 1971, 907.
20. Sprent, P: Applies nonparametric statistical methods. Champman & Hall (Eds.), London, 1993, 1342.
21. Casley-Smith, JR, M Boris, B Lasinski: Treatment for lymphedema of the arm-the Casley-Smith method: A noninvasive method produces continued reduction. *Cancer* 83(12 Suppl) (1998), 2843-2860.
22. Casley-Smith, JR, JR Casley-Smith: Modern treatment of lymphoedema I. Complex physical therapy: The first 200 Australian limbs. *Australas J. Dermatol.* 33 (1992), 61-68.
23. Partsch, H, A Mostbeck, G Leitner: Experimentelle Untersuchungen zur Wirkung einer Druckwellenmassage (Lymphapress) beim Lymphödem. *Phlebologie u Proktologie* 80 (1980), 124.
24. Baulieu, F, JL Baulieu, L Vaillant, et al: Factorial analysis in radionuclide lymphography: Assessment of the effects of sequential pneumatic compression. *Lymphology* 22 (1989), 178.
25. Leduc, O, P Bourgeois, A Leduc: Manual lymphatic drainage: Scintigraphic demonstration of its efficacy on colloidal protein reabsorption. In: XI International Congress of Lymphology. Partsch, H (Ed), Amsterdam, 1988, 551-554.
26. Daane, S, P Poltoratszy, WB Rockwell: Postmastectomy lymphedema management: evolution of complex decongestive therapy technique. *Ann. Plastic Surg.* 40 (1998), 128-134.
27. Vodder, E: Lymph drainage ad modum Vodder. *Aesthet Med* 14 (1965), 190-191.
28. Stillwell, GK: Treatment of postmastectomy lymphedema. *Mod. Treat.* 6 (1969), 396-412.
29. Weissleder, H, R Weissleder: Lymphedema: Evaluation of qualitative lymphoscintigraphy in 238 patients. *Radiology* 167 (1988), 729-735.
30. Perez, MDCJ: Linfocintilografia radioisotópica, tomografia computadorizada e ressonância magnética nas doenças linfáticas. In: *Doenças Vasculares Periféricas*. Maffei, FHA, S Lastória, WB Yoshida, et al, (Eds.), Medsi, São Paulo, 2002, 545-52.
31. McNeill, GC, MH Witte, CL Witte, et al: Whole-body lymphangioscintigraphy: Preferred method for initial assessment of the peripheral lymphatic system. *Radiology* 172 (1989), 495-502.
32. Guedes-Neto, HJ: Estudo linfocintilográfico qualitativo dos membros superiores de doentes com linfedema secundário a tratamento cirúrgico para o câncer de mama [Tese]. São Paulo: Faculdade de Ciências Médicas da Santa Casa de São Paulo, 2002.

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