ePlasty

ORIGINAL RESEARCH

PEER REVIEWED

Treatment of Lymphedema in Patients With Advanced Cancer Receiving Palliative Care: A Single-Center Experience

Keisuke Shimbo, Haruka Kawamoto, Isao Koshima

Keywords Palliative Care
Upper Extremity Lymphedema
Lower Extremity Lymphedema
Lymphaticovenular Anastomosis
Compression Therapy
Advanced Cancer

May 2024
ISSN 1937-5719
Index ePlasty 2024;24:e29

Abstract

Background. Lymphedema can develop during the progression of neoplastic diseases and is a devastating complication in patients with cancer receiving palliative care. This study aimed to investigate the course of treatment for lymphedema in patients receiving palliative care to assess posttreatment outcomes.

Methods. This single-center, retrospective cohort study reviewed the maintained database of patients with lymphedema who presented to our department from January 2015 through December 2022. A combination of skin care, compression therapy, and lymphaticovenular anastomosis was used to treat lymphedema in patients with cancer receiving palliative care. The upper or lower extremity lymphedema indices, calculated based on 5 upper or 4 lower extremity circumferences and body mass index, were compared at the first and last visits.

Results. Of the 202 patients with lymphedema, 38 patients with 45 affected limbs (upper extremities: 11 patients, 12 limbs; lower extremities: 27 patients, 33 limbs) were included in the analysis. There were no significant changes in edema based on the upper or lower extremity lymphedema indices in the upper ($P = .931$) or lower extremities ($P = .767$) between the first and last visits. No pain relief was observed after the treatment. In the treatment differences, the rate of change in edema was -3.6 ± 10.8% for the compression garment and +5.7 ± 11.5% for the lymphaticovenular anastomosis, showing no significant difference ($P = .157$).

Conclusions. All treatments had limited therapeutic effects, such as reduced edema and pain relief, and there were no significant differences between them.

Introduction

Lymphedema is the accumulation of abnormal tissue fluid resulting from impaired lymphatic drainage and is predominantly cancer-related due to surgery and/or radiation therapy.[1] Upper extremity lymphedema (UEL) is most often seen in patients with breast cancer and lower extremity lymphedema (LEL) in those with gynecologic cancer.[2] Additionally, lymphoedema can develop in the progression of neoplastic diseases, with reports of edema including lymphedema in 11% of patients with cancer receiving palliative care.[3] It is a devastating complication for patients with cancer, and previous studies have found that patients with cancer and lymphedema were more likely to have a lower quality of life (QOL) and greater emotional distress than those without lymphedema.[4-6]

The therapeutic interventions for lymphedema in patients receiving palliative care are limited, and the primary goal is to improve the patient's QOL rather than to reduce edema.[6] However, there is no established standard of care or treatment for lymphedema in patients receiving palliative care to improve their QOL, and knowledge of the condition is somewhat limited among the majority of health professionals. Therefore, we treated lymphedema in patients according to their condition at our hospital based on the hypothesis that the alleviation of edema leads to an improvement in symptoms and QOL. Our treatments included skin care and compression therapy, which are parts of complete decongestive therapy (CDT), and lymphaticovenular anastomosis (LVA), which is a surgical treatment. Although LVA is a safe and effective treatment,[7,8] only nonsurgical treatments, such as CDT, have been reported for the treatment of lymphedema in patients receiving palliative care.[6] Additionally, not only is the therapeutic efficacy of LVA for patients receiving palliative care unknown but also there is a significant lack of information regarding the treatment course of lymphedema for other strategies.

Consequently, this study investigated the course of treatment for lymphedema in patients receiving palliative care with the aim of evaluating posttreatment outcomes and identifying best practices.

Methods and Materials

Study Design

This single-center retrospective cohort study was conducted in accordance with the Declaration of Helsinki as revised in 2013 and was approved by our hospital's institutional review board. We retrospectively reviewed the data of patients with lymphedema who presented to our department from January 2015 through December 2022.

Participants

Inclusion criteria were as follows: presence of cancer-related lymphedema requiring palliative care and patients treated for lymphedema in our department. Exclusion criteria were as follows: (1) diagnosis of edema of etiologies other than lymphedema, such as hypoproteinemia, chronic renal failure, or deep vein thrombosis; (2) age <18 years; and (3) significant cognitive or psychiatric disorders.

All patients received self-care instructions centered on skincare under the guidance of a trained lymphatic therapist. For compression therapy, easy-to-wear low-pressure compression garments are often applied, whereas standard-pressure ones are applied depending on the patient's clinical state. In this study, standard-pressure compression garments (Sigvaris) were adjusted to a pressure of 20 to 30 mm Hg, and low-pressure ones were used with elasticated tubular support bandages (tg Grip, NAK Corporation) at pressures of less than 20 mm Hg. LVA was only performed in patients with a stable clinical status who wished to undergo surgery with the permission of their palliative care physician. Multisite LVA with a small incision (approximately 1.5 cm) based on lymphatic mapping provided by indocyanine green imaging was performed under local anesthesia. The lymphatic vessels and size-matched venulae were anastomosed using 11-0 or 12-0 nylon monofilament. Compression therapy was resumed 3 days after LVA using low-pressure compression garments. Treatment for lymphedema in patients receiving palliative care was classified into the following 4 categories, depending on the patient's condition and wishes: (1) skin care only, (2) low-pressure compression garment and skin care, (3) standard-pressure compression garment and skin care, and (4) LVA, low-pressure compression garment, and skin care. All patients were seen for follow-up every 1 to 2 months whenever possible, depending on their general condition. The above treatments were performed considering the patients' conditions and respecting their wishes.

Measurement

The patients were classified into 2 groups: those with UEL and those with LEL, and data were collected on basic patient characteristics, etiology, cancer treatment information, lymphedema and treatment information, and circumference values at specific points of the affected limb.

Quantitative Variables

The circumference of the affected limb was measured at 5 points in the upper extremity (dorsum manus, wrist, 5 cm from the cubital fossa in the forearm, 10 cm from the cubital fossa in the upper arm, and axilla), and 4 points in the lower extremity (foot, ankle, 5 cm below the knee, and 10 cm above the knee). These measurements were taken with the patient in the supine position at the first and last visits by the lymphatic therapist engaged with the patient. Changes in lymphedema volume at the first and last visits were assessed using the UEL or LEL index. The indices were calculated by dividing the sum of the squared circumference at 5 points in the upper extremity or 4 points in the lower extremity by the body mass index (BMI).[9,10] Changes in edema since the last visit were evaluated from medical records. The rate of change in edema between the first and last visits due to the different treatment methods was measured using the following formula:

[(UEL or LEL index at first visit)–(UEL or LEL index at last visit)] × 100 / (UEL or LEL index at first visit).

Statistical Analysis

Continuous variables were presented as means ± standard deviations, whereas categorical variables were reported as frequencies and percentages. UEL and LEL groups were not compared, but changes in edema within groups and between treatment methods were compared using a 2-tailed Student *t* test. Statistical significance was set at $P < .05$.

Results

Overall, 202 patients with lymphedema (101 in the UEL and LEL groups each) were identified during the study period, and 38 met the inclusion criteria. Of these, 11 patients (12 affected limbs) were in the UEL group and 27 patients (33 affected limbs) were in the LEL group (**Figure 1**). The proportion of patients receiving palliative care in the LEL group (26.7%) was higher than that in the UEL group (10.9%). The average age of the patients was 67.7 ± 14.8 years, with the majority (73.7%) being female, and BMI was 24.4 ± 4.6 kg/m^2. The stage of cancer of all patients was IV; the etiology of UEL was breast cancer (100%) and that of LEL was mostly gynecological cancer (44.4%) (**Table 1**). A history of lymph node dissection was higher in the case of UEL than in the case of LEL (75.0% vs 18.5%), and most patients had undergone chemotherapy (81.6%) and/or radiation therapy (73.7%). The International Society of Lymphology stages[11] of all patients were almost evenly distributed from stages I to IIB. The overall patient mortality rate was 92.1%, with a mean follow-up period of 2.5 ± 3.4 months and a mean time from first visit to death of 6.5 ± 6.9 months.

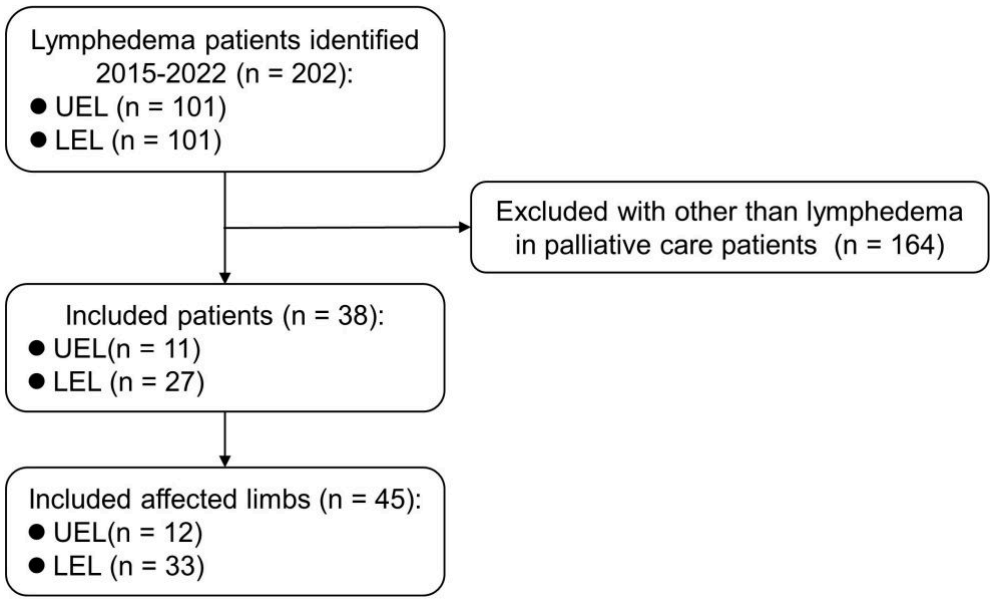

Figure 1. Flowchart of eligible patients. UEL, upper extremity lymphedema; LEL, lower extremity lymphedema.

Table 1. Characteristics of Patients in Upper and Lower Extremity Lymphedema Groups

Characteristic	Total	UEL	LEL
Total patients, n	38	11	27
Affected limbs, n	45	12	33
Affected limb			
Right, n (%)	24 (53.3)	4 (33.3)	20 (60.6)
Left, n (%)	21 (46.7)	8 (66.7)	13 (39.4)
Age, y ± SD	67.7 ± 14.8	65.5 ± 16.6	68.7 ± 13.7
Sex			
Male, n (%)	10 (26.3)	1 (9.1)	9 (33.3)
Female, n (%)	28 (73.7)	10 (90.9)	18 (66.7)
BMI, kg/m^2 ± SD	24.4 ± 4.6	20.3 ± 2.1	23.9 ± 4.2
Smoking, n (%)	13 (34.2)	3 (27.3)	10 (37.0)
Diabetes, n (%)	2 (5.3)	0 (0)	2 (7.4)
Etiology, n (%)			
Breast cancer		11 (100)	–
Gynecologic cancer		–	12 (44.4)
Urologic cancer		–	7 (25.9)
Other cancer		–	8 (29.6)
Cancer stage IV, n (%)	38 (100)	11 (100)	27 (100)
Lymph node dissection, n (%)	14 (36.8)	9 (75.0)	5 (18.5)
Cancer treatment, n (%)			
Radiotherapy	28 (73.7)	8 (72.7)	20 (74.1)
Chemotherapy	31 (81.6)	9 (81.8)	22 (81.5)
Mean time from cancer surgery to first visit, y ± SD	7.2 ± 7.0	10.7 ± 8.0	3.4 ± 2.1
Mean time from onset of edema to first visit, mo ± SD	15.6 ± 37.1	42.4 ± 61.8	5.2 ± 6.6
History of cellulitis, n (%)	5 (11.1)	2 (16.7)	3 (9.1)
Pain, n (%)	19 (50.0)	4 (36.4)	15 (55.6)
ISL stage			
I	15 (33.3)	7 (58.3)	8 (24.2)
IIA	16 (35.6)	2 (16.7)	14 (42.4)
IIB	13 (28.9)	2 (16.7)	11 (33.3)
III	1 (2.2)	1 (8.3)	0 (0)
Mortality	35 (92.1)	11 (100)	24 (88.9)
Mean time from first visit to death, mo ± SD	6.5 ± 6.9	8.3 ± 4.7	5.7 ± 7.6

death, mo ± SD			
Mean follow-up, mo ± SD	2.5 ± 3.4	3.5 ± 3.7	2.1 ± 3.2

UEL, upper extremity lymphedema; LEL, lower extremity lymphedema; ISL, International Society of Lymphology.

The treatment and outcomes of the UEL and LEL groups are shown in **Table 2**. All patients underwent self-care centered on skin care, and low-pressure compression garments were the most common treatment for UEL (50.0%) and LEL (63.6%). LVA was performed in 1 patient in the UEL group (8.3%) and 4 patients in the LEL group (12.1%). The 5 patients who underwent LVA had a mean of 3.8 anastomoses and a mean operative time of 2 hours and 58 minutes. LVA was performed at multiple locations for UEL, ranging from the dorsum of the hand to the proximal forearm, and for LEL, from the dorsum of the foot to the proximal lower leg. There were no significant changes in edema in the UEL ($P = .931$) or LEL ($P = .767$) groups between the first and last visits. Although 16.7% of patients with UEL and 9.1% of patients with LEL had a history of cellulitis, no cellulitis developed after treatment. Furthermore, pain was present in 36.4% of patients with UEL and 55.6% of patients with LEL at the first visit, but no relief was observed after treatment. Based on the chart review, edema had increased for most patients in the UEL (66.7%) and LEL groups (69.7%) since their last visits (**Figure 2**).

Table 2. Treatment and Outcomes for Upper and Lower Extremity Lymphedema

Variable	**UEL**	**LEL**
Treatment, n (%)		
Skin care only	2 (16.7)	8 (24.2)
Low-pressure compression garment + skin care	6 (50.0)	21 (63.6)
Standard-pressure compression garment + skin care	3 (25.0)	0 (0)
Surgery (LVA) + low-pressure compression garment + skin care	1 (8.3)	4 (12.1%)
UEL/LEL index		
First visit	120.9 ± 16.8	185.4 ± 27.0
Last visit	120.1 ± 22.4	182.3 ± 39.0
P value	.931	.767
Cellulitis after treatment, n (%)	0 (0)	0 (0)
Pain relief, n (%)	0 (0)	0 (0)
Change in edema from last visit, n (%)		
Increase in edema	8 (66.7)	23 (69.7)
Generalized edema	2 (16.7)	3 (9.1
Lymphorrhea	1 (8.3)	2 (6.1)
No change in edema	1 (8.3)	8 (24.2)
Reduction in edema	1 (8.3)	1 (3.0)
Unknown	2 (16.7)	1 (3.0)

UEL, upper extremity lymphedema; LEL, lower extremity lymphedema; LVA, lymphaticovenular anastomosis.

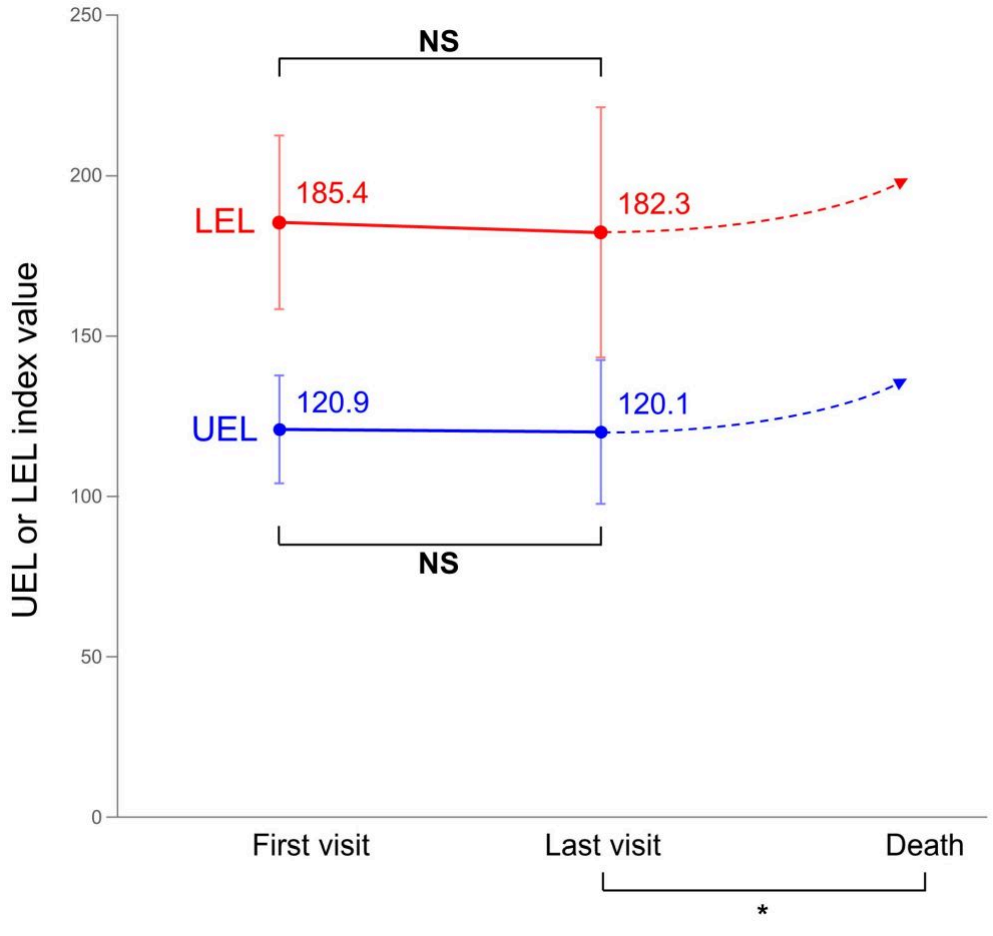

Figure 2. Changes over time in the UEL or LEL index. *Predicted from medical records. LEL, lower extremity lymphedema; NS, not significant; UEL, upper extremity lymphedema.

Changes in edema due to different treatment methods are shown in **Table 3**. Patients who only performed self-care centered on skincare were not followed up. The rate of change in edema between the first and last visits was -3.6% ± 10.8% for the compression garment and +5.7% ± 11.5% for the LVA with compression garment, indicating no significant difference (*P* = .157).

Table 3. Changes in Edema Due to Different Treatment Methods

Variable	Compression garment (n = 18)	LVA with compression garment (n = 4)	*P* value
Edema rate of change*	-3.6 ± 10.8%	+5.7 ± 11.5%	.157
Mean follow-up, mo ± SD	4.2 ± 3.4	3.5 ± 3.9	.745

*[(UEL or LEL index at first visit) – (UEL or LEL index at last visit)] × 100 / (UEL or LEL index at first visit).

LVA, lymphaticovenular anastomosis; UEL, upper extremity lymphedema; LEL, lower extremity lymphedema.

Discussion

Patients with cancer receiving palliative care often cannot tolerate a full evaluation and treatment for lymphoedema, suggesting the need to develop appropriate palliative approaches.[6] Our findings, within a short mean follow-up period of 2.5 ± 3.4 months, indicated that the therapeutic effect of the treatments of edema did not differ significantly, although they may have had a certain effect on the development of cellulitis. In other words, there was no significant reduction in edema or pain relief during the follow-up period regardless of the treatment strategy. Although LVA has been shown to be an effective and versatile procedure for the treatment of lymphedema,[7,8] the change in edema was increased by +5.7% ± 11.5% in the group treated with LVA and compression garment. This was probably due to an increase in edema with the progression of the neoplastic disease, suggesting that LVA does not have sufficient therapeutic efficacy for lymphedema in advanced cancers.

LVA is a minimally invasive surgical treatment, and the patients who underwent LVA in this study had an uneventful postoperative course. However, based on our results, it is more burdensome than other treatments and may be an inappropriate therapeutic strategy. However, all 5 patients who underwent LVA were satisfied with their treatment and could not completely rule out LVA as a treatment option. Lymphedema can substantially impact the physical experience and psychosocial status of patients receiving palliative care.[12] Professional lymphedema management in palliative care can be neglected, leading to hopelessness and disgust in patients.[6] In such a psychological situation, the fact that they underwent surgery (LVA) may have led to gratitude and satisfaction in our patients. Patient satisfaction should be evaluated in more detail in future studies and compared with other treatments.

CDT consists of 4 components: skin care, exercise, manual lymphatic drainage, and compression therapy.[13] It is the most frequently recommended management modality for lymphedema; 1 study with a small sample size indicated improvements in limb volume, skin quality, and lymphedema-related QOL for CDT in patients with cancer receiving palliative care.[14] However, CDT should be adapted in a palliative setting for patients with advanced cancers according to their treatment tolerance. In this study, skin care and compression therapy were used for lymphedema in most patients receiving palliative care (91.7% in the UEL group and 87.9% in the LEL group). A reduction in edema of -3.6% ± 10.8% was observed with compression therapy using compression garments, even though most of the garments had low pressure (66.7% and 100% in the UEL and LEL groups, respectively). Compression garments are more effective at higher pressures; however, patients receiving palliative care often have difficulty wearing standard pressure garments. Elasticated tubular support bandages, although low-pressure compression garments, are low-cost, easy to slip on, and provide treatment that patients can tolerate even when their general conditions worsen. Although 2 reports of compression therapy applied to patients receiving palliative care had major limitations because they were case reports, both yielded positive results, including a reduction in edema.[15,16] Low-pressure compression garments, such as elasticated tubular support bandages, may be an effective treatment that is easy to adopt on a daily basis for patients receiving palliative care.

Our results showed that edema increased in most patients (66.7% and 69.7% of those with UEL and LEL, respectively) from the last visit until death, although there were no precise measurements. As some patients had generalized edema or lymphorrhea, it was presumed that the edema had increased considerably. Edema in patients at the end of life may have a multifactorial etiology that includes not only lymphedema due to lymphatic congestion[17,18] but also a combination of angioedema due to increased capillary hydrostatic pressure, hypoproteinemic edema due to decreased plasma oncotic pressure, and/or permeability edema due to increased capillary permeability.[19,20] Lymphedema was diagnosed by various examinations at the first visit; however, it is considered that edema increased due to a mixed etiology as the neoplastic disease progressed. Given that edema eventually increases in patients at the end of life, it may not be controlled by treatment or care. Therefore, it may be desirable to present the treatment methods for lymphedema that can be provided at all institutions, respect the patient's wishes, and select the treatment that the patient can tolerate.

Limitations

Our study has 2 critical limitations. First, it was a retrospective cohort study with a small sample size and a short follow-up period, which may have caused a significant bias. Second, there was a lack of patient-reported outcomes regarding the symptoms and treatment of lymphedema, which may have affected the interpretation of the results. In particular, it is important to evaluate the improvement in patients' QOL, which will be considered in future research.

Conclusions

In this study, a combination of skincare, compression therapy, and LVA was used to treat lymphedema in patients with cancer receiving palliative care. None of the treatments had limited therapeutic effects, such as reduction of edema and pain relief, and there was no significant difference among them. Because edema may increase with the progression of neoplastic diseases, treatment and care respecting the patient's wishes are desirable. Although this study could not identify any best practices from the perspective of health professionals, it highlighted the need for established practice guidelines on this topic aimed at improving patients' QOL.

Acknowledgments

We would like to thank Editage (www.editage.com) for English language editing.

Authors: Keisuke Shimbo, MD, PhD[1]; Haruka Kawamoto, MD[1]; Isao Koshima, MD, PhD[2,3]

Affiliations: [1]Department of Plastic and Reconstructive Surgery, Hiroshima Prefectural Hospital, Hiroshima, Japan; [2]Department of Plastic and Reconstructive Surgery, Hiroshima University Hospital, Hiroshima, Japan; [3]International Center for Lymphedema, Hiroshima University Hospital, Hiroshima, Japan.

Correspondence: Keisuke Shimbo, MD, PhD; k_s08_10hyogo@hotmail.com

Ethics: Approval was obtained from Research Ethics Committee of Hiroshima Prefectural Hospital (approval number: 202304-4). Informed consent was obtained from all individual participants included in the study.

Disclosures: The authors disclose no relevant conflicts of interest or financial disclosures for this manuscript.

References

1. Szuba A, Rockson SG. Lymphedema: classification, diagnosis and therapy. *Vasc Med.* 1998;3(2):145-56. doi:10.1177/1358836X9800300209

2. Clemens KE, Jaspers B, Klaschik E, Nieland P. Evaluation of the clinical effectiveness of physiotherapeutic management of lymphoedema in palliative care patients. *Jpn J Clin Oncol*. 2010;40(11):1068-72. doi:10.1093/jjco/hyq093

3. Lee CH, Kim JK, Jun HJ, Lee DJ, Namkoong W, Oh JH. Rehabilitation of advanced cancer patients in palliative care unit. *Ann Rehabil Med.* 2018;42(1):166-174. doi:10.5535/arm.2018.42.1.166

4. Ahmed RL, Prizment A, Lazovich D, Schmitz KH, Folsom AR. Lymphedema and quality of life in breast cancer survivors: The Iowa Women's Health Study. *J Clin Oncol.* 10 2008;26(35):5689-96. doi:10.1200/JCO.2008.16.4731

5. Chachaj A, Malyszczak K, Pyszel K, et al. Physical and psychological impairments of women with upper limb lymphedema following breast cancer treatment. *Psychooncology*. 2010;19(3):299-305. doi:10.1002/pon.1573

6. Beck M, Wanchai A, Stewart BR, Cormier JN, Armer JM. Palliative care for cancer-related lymphedema: A systematic review. *J Palliat Med.* 2012;15(7):821-7. doi:10.1089/jpm.2011.0494

7. Shimbo K, Kawamoto H, Koshima I. Comparative study of conservative treatment and lymphaticovenular anastomosis with compression therapy for early-stage breast cancer-related lymphoedema. *J Plast Reconstr Aesthet Surg*. 28 2023;88:390-396. doi:10.1016/j.bjps.2023.11.035

8. Shimbo K, Kawamoto H, Koshima I. Conservative treatment versus lymphaticovenular anastomosis for early-stage lower extremity lymphedema. *J Vasc Surg Venous Lymphat Disord*. 2023;11(6):1231-1240. doi:10.1016/j.jvsv.2023.06.013

9. Yamamoto N, Yamamoto T, Hayashi N, Hayashi A, Iida T, Koshima I. Arm volumetry versus upper extremity lymphedema index: Validity of upper extremity lymphedema index for body-type corrected arm volume evaluation. *Ann Plast Surg.* 2016;76(6):697-9. doi:10.1097/SAP.0000000000000259

10. Yamamoto T, Matsuda N, Todokoro T, et al. Lower extremity lymphedema index: A simple method for severity evaluation of lower extremity lymphedema. *Ann Plast Surg*. 2011;67(6):637-40. doi:10.1097/SAP.0b013e318208fd75

11. Executive C. The diagnosis and treatment of peripheral lymphedema: 2016 consensus document of the International Society of Lymphology. *Lymphology*. 2016;49(4):170-84.

12. Frid M, Strang P, Friedrichsen MJ, Johansson K. Lower limb lymphedema: Experiences and perceptions of cancer patients in the late palliative stage. *J Palliat Care*. 2006;22(1):5-11. doi:10.1177/082585970602200102

13. Executive Committee of the International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2020 Consensus Document of the International Society of Lymphology. *Lymphology*. 2020;53(1):3-19.

14. Cobbe S, Nugent K, Real S. Pilot study: The effectiveness of complex decongestive therapy for lymphedema in palliative care patients with advanced cancer. *J Palliat Med*. 2018;21(4):473-478. doi:10.1089/jpm.2017.0235

15. Pyszora A, Graczyk M, Krajnik M, Dos J. Implementation of modified manual lymphoedema treatment—complex physical therapy (MLT-CPT) in terminal ill patient. *Adv Palliat Med*. 2007;6(2):93-96.

16. Pyszora A, Krajnik M. Is kinesio taping useful for advanced cancer lymphoedema treatment? A case report. *Adv Palliat Med*. 2010;9(4):141-144.

17. Weber E, Agliano M, Bertelli E, Gabriele G, Gennaro P, Barone V. Lymphatic collecting vessels in health and disease: A review of histopathological modifications in lymphedema. *Lymphat Res Biol*. 2022;20(5):468-477. doi:10.1089/lrb.2021.0090

18. Barone V, Borghini A, Tedone Clemente E, et al. New insights into the pathophysiology of primary and secondary lymphedema: Histopathological studies on human lymphatic collecting vessels. *Lymphat Res Biol*. 2020;18(6):502-509. doi:10.1089/lrb.2020.0037

19. Cho S, Atwood JE. Peripheral edema. *Am J Med*. 2002;113(7):580-6. doi:10.1016/s0002-9343(02)01322-0

20. Gradalski T. Edema of advanced cancer: Prevalence, etiology, and conservative management —A single hospice cross-sectional study. *J Pain Symptom Manage*. 2019;57(2):311-318. doi:10.1016/j.jpainsymman.2018.11.005

HMP Global

HMP Education

HMP Omnimedia

HMP Europe