

Clinical Note

Edema of Advanced Cancer: Prevalence, Etiology, and Conservative Management—A Single Hospice Cross-Sectional Study



Tomasz Gradalski, MD, PhD
St Lazarus Hospice, Krakow, Poland

Abstract

Context. Edema of advanced cancer, seldom recognized in the literature, significantly impairs patient quality of life.

Objectives. The purpose was to assess edema frequency, etiology, and impact on common symptoms and present its conservative management.

Methods. A prospective analysis of 784 patients admitted to a hospice was performed, of whom 119 were diagnosed with edema. For 18 patients with short life prognosis, an individually tailored physiotherapy (limb elevation, bandaging, manual lymphatic drainage, and Kinesio Taping) or subcutaneous needle drainage was administered. Forty-six patients with longer prognosis were treated by standardized limb bandaging (5-7 days) and re-evaluated, 28 of them with venous congestion resistant to enteral diuretics received supplementary furosemide infusion.

Results. Among those admitted with edema (96.6% with advanced cancer), 81.5% had bilateral and 10.9% generalized edema, 10.9% had lymphorrhea, 5.9% skin ulcerations, and in 27.7% edema was the main problem. The high mean comorbidity C3-index score (2.97) was observed. The main precipitating factors of the edema were chronic immobilization (79.8%) medications (58.8%), and congestive heart failure (28.6%). Before admission, 47.9% had received diuretics for edema and only 4.2% had physiotherapy. Among those re-evaluated (46 patients [84 limbs]), the mean reduction of limb volume (1.18L; 16.6%; $P < 0.001$) was accompanied by a decrease of edema symptoms/signs intensity and ESAS-Core by median 1 point ($P < 0.002$).

Conclusion. Limb edema of advanced cancer occasionally treated by physical therapy concerns patients with numerous comorbidities and precipitating factors. It can be managed sufficiently with decongestive or supportive physiotherapy, depending on patients' life prognosis, symptom burden, edema stage, and progression. *J Pain Symptom Manage* 2019;57:311–318. © 2018 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words

Edema, lymphedema, end-of-life care, palliative care, physical therapy, diuretic effect, comorbidity

Introduction

Edema (accumulation of vascular pericapillary fluids) in patients at the end of life is a common distressing symptom seldom recognized in literature. The reported prevalence of edema reaches 11% of palliative care population.¹ It may have multifactorial etiology—a combination of lymphatic congestion (lymphedema), increased capillary hydrostatic pressure (vascular edema), decreased plasma oncotic

pressure (hypoproteinemic edema), and/or increased capillary permeability (permeability edema).² In advanced cancer, recent retrospective chart review of 63 patients referred to palliative care edema service revealed that the most frequent issue was lower limb edema of mixed etiology, due to suspected blockage of lymphatics and/or patient's immobility.³ Besides possible lymphatic congestion due to the lymphatic spread of cancer, oncological iatrogenic influence also plays a significant role in the development of

Address correspondence to: Tomasz Gradalski, MD, PhD, St Lazarus Hospice, 31-831 Fatimska 17, Krakow, Poland.
E-mail: tomgr@mp.pl

Accepted for publication: November 6, 2018.

edema: lymph node dissection, taxane-based chemotherapy, and/or radiotherapy may impair the main and collateral lymphatic pathways.⁴ In cancer patients, multimorbidity is common, as key risk factors for cancer are also major risk factors for other serious chronic conditions.⁵ The presence of chronic inflammation, hyperkinetic circulation related to severe anemia, vascular congestion in decompensated heart failure, venous insufficiency, renal/hepatic failure, hypoalbuminemia, drugs, or even obesity may lead to lymphatic overflow, dynamic failure, and congestion of lymphatics.⁶ Patients with edema of advanced cancer are likely to have poor life quality—often suffering from pain (67%) or skin tightness (43%) in the affected limb.⁷ This condition engages an entire multidisciplinary palliative care team in the process of information, guidance, education, assessment, evaluation, and coordinated management.⁸ Various therapeutic approaches are suggested: physiotherapy, pharmacotherapy, and even minimally invasive needle drainage techniques. Complex decongestive therapy (CDT), the most often recommended form of management in lymphedema, which is based on skin care, manual lymphatic drainage (MLD), limb compression (recommended various types of edema⁹), and remedial exercises, sometimes cannot be received well in advanced cancer and should be adapted in a palliative setting to the patient's reduced tolerance to treatment. Inadequate therapeutic strategy may result in unnecessary effort, injury for the patient, or an unsatisfactory outcome.¹⁰ In two observational studies, this individually tailored program of various CDT techniques was effective for a cohort of palliative cancer patients with limited survival.^{11,12} In practice, typically simple, low-maintenance, and low-cost bandaging applied initially only on the distal part of the limb was sufficient in preventing uncontrollable fluid redistribution. A substantial number of terminally ill patients can tolerate only supplementary therapeutic techniques, such as Kinesio Taping or MLD. These techniques may play a beneficial role in improving symptom load due to lymphedema or in quality of life¹³; however, they have unproven value in edema volume reduction.¹⁴ In two case studies, either limb compression bandaging was initiated unilaterally with close symptom monitoring¹⁵ or Kinesio Taping was applied secondary to compression trial failure.¹⁶ The standard physical therapy for these patients is still being debated, as controlled studies are lacking. Diuretic pharmacotherapy is ineffective in pure lymphatic insufficiency; however, it may be helpful in coexistent dynamic failure, "low-protein" edemas.¹⁷ Diuretics, rarely mentioned in palliative care, may decrease vascular and tissue congestion, but unfortunately, fluid mobilization may precipitate patient's

dehydration and accelerate the accumulation of proteins within the edematous tissue, thus facilitating further edema consolidation. Combining parenteral diuretics with limb compression has been shown to be safe: in a recent case series,¹⁸ stable levels of blood pressure, laboratory kidney profiles, and serum albumin have been seen. In advanced cases resistant to pharmacotherapy/physiotherapy (e.g., anasarca with trunk and genital involvement), a trial of "off-label" controlled subcutaneous needle drainage was occasionally suggested^{19–21} (with recommended addition of prophylactic antibiotics²²) but also increase the risk of hypoproteinemia or infection and continued compression therapy is usually needed afterward.

Providing prospective research within this vulnerable population remains challenging due to difficult recruitment processes, high attrition rate, heterogeneous therapeutic regime applied, or not validated assessment methods.²³ The first purpose of this study has been to prospectively assess the frequency, suspected etiology, and impact on common symptoms. The second has been to assess the edema conservative management strategy affordable in a hospice setting.

Methods

Sample

A prospective screening for permanent, nontransient within one week, Stage II–III edema according to the International Society of Lymphology classification²⁴ was performed on all 784 (96.9% with advanced cancer) admissions between July 2016 and November 2017 to a free-standing, acute (mean time of care seven days) 42-bed hospice. Patients on admission were stratified according to expected life prognosis (Gold Standard Framework, GSF²⁵) and presence of edema symptoms, based on literature screening: limb pain, swelling, heaviness, weakness, paresthesia, function loss, and overall well-being impairment related to edema.

Edema Management

Conservative management for edema was initiated for all patients with edema who reported any edema symptoms on admission. Two main therapeutic strategies were implemented according to the clinical stage of advanced disease. For patients with life prognosis of days (GSF Stage D), a supportive therapy was considered, based on an individually tailored combination of symptom management, physical techniques (limb elevation, compression bandaging, MLD, and Kinesio Taping), and controlled subcutaneous needle drainage performed on a daily basis, depending on patients' preferences and condition. Patients with a longer prognosis (GSF Stages A–C) continued general symptomatic management prescribed before the admission and received standardized intensive

(“reducing”) five- to seven-day edema management: two to three layers of short-stretch bandage compression (8 and 10 cm in width, Rosidal, Lohmann, and Rauscher, Germany) were applied by two skilled physiotherapists in the form of a spiral with a 50% overlap to the entire limb. In addition, in patients with signs of systemic and/or pulmonary venous congestion, and when edema was resistant to previously administered diuretics, parenteral furosemide (mean dose 60 mg, range 40–100 mg) was given for an hour in hypersaline intravenous infusion (30 mL 10% NaCl in 250 mL normal saline) concurrently with compression, once a day. Routine daily bedside physical evaluation of fluid congestion was also performed. This “reducing” phase was followed by supportive compression bandaging applied as needed (every one to 3 days for 8 hours) up to the dying phase or to hospice discharge; all patients on parenteral diuretics were switched to oral torsemide (starting range 2.5–10 mg a day).

Evaluation

On admission, the primary diagnoses, potential edema risk factors and comorbidities (using a cancer-specific measure of comorbidity—C3 Index),²⁶ the edema localization suspected etiology, and therapeutic history were collected by the attending

physician. Close question interview was also performed to identify edema symptoms burden.

Before and after the 5 to 7 days of edema management (independent variable), limb volumes (dependent variable, calculated by every 4 cm circumferential tape measurements) were obtained twice by the same physiotherapist. Parallel to that, the attending physician additionally measured the edema symptom burden: sum of the limb-related negative symptoms intensity and overall well-being impairment (by the five-item Likert scale: none, little, moderate, severe, very severe) and Edmonton Symptom Assessment System—Core (ESAS-C).²⁷ ESAS-C is a shortened ESAS version designed for patients in their last days of life, with an improved completion rate. It equals the sum of core end-of-life symptom/signs intensity measured on a numeric rating scale: pain, dyspnea, nausea, chest secretions, and agitation (total score ranges from 0—the best to 50—the worst).

Statistics

Means with SDs of normally distributed continuous variables in one sample (preintervention and postintervention) were compared using a paired t-test. A Wilcoxon signed-rank test was used to compare medians with interquartile ranges of non-normally distributed continuous or ordinal data in

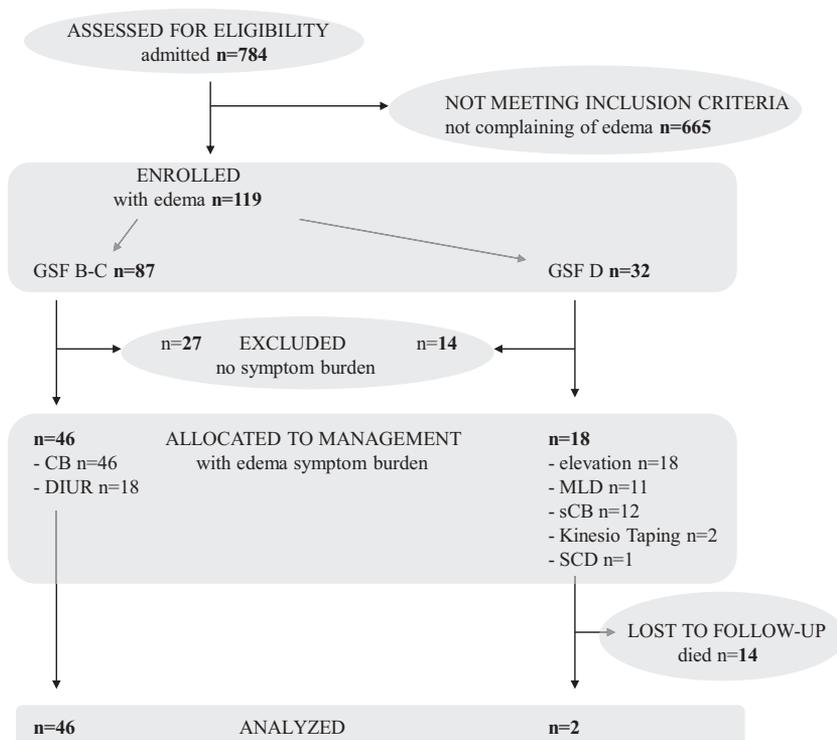


Fig. 1. CONSORT flow diagram of the trial. CB = compression bandaging; DIUR = diuretics; GSF = Gold Standard Framework; MLD = manual lymphatic drainage; sCB = supportive light compression bandaging; SCD = controlled subcutaneous needle drainage.

Table 1
Characteristics of 119 Patients Admitted With Edema

Parameter	Patients, n (%)	Mean (IQR)
Disease stage and life prognosis (GSF)		
A—years	1 (0.8)	
B—months	13 (10.9)	
C—weeks	73 (61.3)	
D—days	32 (26.9)	
Primary diagnosis		
Cancer	115 (96.7)	
Digestive	39 (32.8)	
Female reproductive	32 (26.9)	
Respiratory	16 (13.4)	
Urinary	10 (8.4)	
Other	18 (15.1)	
Congestive heart failure and decubitus ulcers	4 (3.4)	
Cancer metastases		
Distant	88 (76.5)	
Regional	10 (8.7)	
Unknown	17 (14.8)	
Leading comorbidity conditions		
Anemia	113 (95.0)	
Joint or spinal disorders	67 (56.3)	
Hypertension	43 (36.1)	
Malnutrition	41 (34.5)	
Liver—moderate/severe disease	35 (29.4)	
Congestive heart failure	34 (28.6)	
Renal disease	33 (27.7)	
COPD	28 (23.5)	
Venous insufficiency	21 (17.6)	
Comorbidity C3 Index score		2.97 (2.1–3.2)
1	21 (18.3)	
2	37 (32.2)	
3	57 (49.6)	
Length of care (days)		11 (6.0–31.5)
To death	106 (89.1)	11 (6.0–33.5)
To discharge	13 (10.9)	15 (8.0–21.0)

IQR = interquartile range; GSF = Gold Standard Framework.

one sample. The Spearman correlation was used to collate the intensity of symptoms/signs with volume changes. Variance analysis was performed to compare changes in limb volumes and sensation intensity scores between the evaluated subgroups. A *P*-value of 0.05 was considered statistically significant. Data analysis was performed using R software environment for statistical computing and graphics software v. 3.5.0.²⁸ The study was approved by the local ethics committee.

Results

Out of 784 admitted patients, 119 (15.2%; 58.8% females) were diagnosed with edema (mean duration of five weeks (interquartile range 3–18) (Fig. 1). The majority of them had advanced cancer with distant metastases, in GSF Stage C and with bilateral edema, Stage 2 according to the International Society of Lymphology.

Table 2
Edema Stages, Localization, Risk Factors, and Therapies Applied Before Hospice Admission

Parameter	n = 119	%
Edema stage (International Society of Lymphology)		
I	45	37.8
II	58	48.7
III	16	13.4
Edema complications		
Lymphorrhea	13	10.9
Skin ulcerations	7	5.9
Edema localization		
Bilateral	97	81.5
Lower limb/limbs	97	81.5
Upper limb/limbs	12	10.1
Trunk	10	8.4
Head and neck	1	0.8
Generalized	13	10.9
Patients with edema risk factors		
Immobility	95	79.8
Drugs ^a	70	58.8
Lymphatic congestion	61	51.3
Hepatic insufficiency	35	29.4
Heart failure	34	28.6
Renal failure	33	27.7
Prolonged steroidotherapy	26	21.8
Venous insufficiency	21	17.6
Parenteral overhydration	12	10.1
Therapy for edema before the admission	65	54.6
Diuretics	57	47.9
Steroids	13	10.9
Physiotherapy	5	4.2

^aDrugs that may precipitate edema: steroids, B-blockers, anticonvulsants, nonsteroidal anti-inflammatory, calcium channel blockers, alpha-adrenolytics, opioids.

A high mean comorbidity C3-index score of 2.97 was observed (Table 1). In 33 patients (27.7%), edema was the main problem on admission. Anemia (95% patients; median hemoglobin 10.6 g/L; SD 2.0), leukocytosis (38.7%; mean $11.3 \times 1000/\text{mL}$; SD 7.3), hypoproteinemia (34.5%; mean 29.0 g/L; SD 6.8), and hyponatremia (26.1%; mean 135 mmol/L; SD 5.6) were the most frequent laboratory abnormalities seen.

Chronic immobilization, the prolonged use of edematogenic medications, and suspected lymphatic congestion (e.g., neoplastic involvement of lymph nodes or prior oncological treatment) were the most prevalent precipitating factors observed. The majority of patients received one to three medications which could impact peripheral or generalized edema (usually prolonged steroids, B-blockers, and/or anticonvulsants). The mean number of edema risk factors per patient reached 3.39 (SD 1.54). Although over a half of patients with edema were treated for this symptom before admission (usually with diuretics or steroids), they rarely had previously undergone physiotherapy (Table 2).

Forty-one (34.5%) out of 119 patients admitted with edema (27 in GSF Stages B–C) did not report any

Table 3
Limb Volumes, Edema Symptom Burden (Sum of the Negative Edema Symptoms and Overall Well-being Impairment), and ESAS-C Within 46 Evaluated GSF, Stage A–C Patients (84 Limbs)

Parameter		On Admission	Five to Seven Days Later	Difference	P
Limb Volume; Mean (SD)	L %	6.66 (3.14)	5.48 (2.57)	-1.18 (1.4) -16.6 (14.1)	<0.001*
Edema symptoms; median (IQR)					
Pain		2 (0–3)	0 (0–1)	-1 (-2 to 0)	<0.001
Swelling		2 (1–3)	0 (0–1)	-1 (-2 to 0)	<0.001
Heaviness		3 (3–4)	2 (0.3–3)	-1 (-2 to 0)	<0.001
Weakness		2 (2–4)	2 (1–2)	0 (-1 to 0)	0.003
Paresthesia		1 (0–2)	0 (0–1.7)	0 (-1 to 0)	0.004
Function loss		3 (2–4)	2 (1–3)	-0.5 (-1 to 0)	<0.001
Well-being impairment		3 (2–4)	2 (1–3)	-1 (-1 to 0)	<0.001
Edema symptom burden		17 (11–20)	7 (5–14.7)	-5 (-10.8 to -2)	<0.001
ESAS–Core; median (IQR)		12.5 (6–22.5)	8 (3.5–14.5)	-1 (-11.5 to 0)	0.002

ESAS-C = Edmonton Symptom Assessment System–Core; IQR = interquartile range. Significance level within the group: Wilcoxon signed-rank test or *t-test.

edema symptom burden and they were not treated for edema at the hospice facility. Sixty-four patients who complained were managed for edema. Eighteen who were in GSF Stage D had recommended supportive therapy according to patients' preference and tolerance. Limb elevation was most awaited. Less desired were supportive compression bandaging (light, one-layer for 8–12 hours, every one to three days), 30-minute light MLD daily, or Kinesio Taping application every two to four days. The controlled subcutaneous needle drainage was necessary in one case. The edema sensations in this group were in the background of their leading symptoms, such as weakness, restlessness, pain in an area distant from the edema region, dyspnea, dry mouth, and appetite loss. None of the patients reported on admission that edema was the main problem. Reliable symptomatic assessment of the edema therapy in this group occurred to be uncertain due to concomitant symptomatic management changes, patients' diminished mental capacity, and high attrition rate.

In the group of 46 GSF Stage A–C persons (84 limbs in total), 18 patients (33 limbs) received the additional diuretics. The mean limb volume reduction reached 1.18 L (comparable to the GSF Stage D subgroup; $P = 0.2$). The intensity of commonly seen edema symptoms improved in a short time (Table 3). There was a weak correlation between the sum of edema sensations and limb volume changes ($\rho = 0.21$; $P = 0.051$). The reported symptoms or measured limb volume changes did not differ significantly between genders or according to edema burden stratification (edema being the main problem on admission or not). Impeccable adherence to the prescribed treatment was seen: every evaluated patient fulfilled the management as scheduled. There were no signs of adverse venous fluid accumulation due to limb compression.

Discussion

Over 15% of patients admitted to our hospice had visible permanent edema, a proportion that exceeds observations made during previous studies.³ Common in palliative population, this sign demands accurate recognition from the very beginning of caring; however, specifically designed and validated tools are still lacking. Admittedly, the commonly used scales (e.g., ESAS, Palliative Outcome Scale) contain additional items that can be pointed out, but using open questions may be inadequate. In this study, two-thirds of patients with edema experienced a symptom burden due to swelling. Doctors should therefore pay closer attention to this common sign of suffering. Two-thirds of patients admitted with edema had marked edema symptom burden. This burden affected nearly one-tenth of admitted population.

A typical feature seen on admission was bilateral lower extremity involvement, a similar finding to what has been observed earlier. Despite the presence of cancer in nearly all cases in our study group, lymphatic congestion was clinically suspected in a half of them; consequently, nonlymphatic etiology (relative fluid overload, low plasma oncotic pressure, and/or elevated venous pressure) was of equal importance. The bilateral edema localization in four-fifths of patients suggests general, systemic etiology rather than only local lymphatic congestion. The majority of tissue fluid is drained by the lymphatics; thus, all chronic edema represents lymphatic failure, either primary (lymph stasis or lymphedema) or secondary to an excessive lymph load (high microvascular filtration and "dynamic" lymphatic insufficiency). That is why it is sometimes suggested that lymphedema and chronic edema should be considered equivalent.²⁹

Patients' multimorbidity can be measured directly by specific indexes (Charlson, National, Cancer Institute, or recent valid alternative of C3 Index), but its

probability occurrence is also expressed through various laboratory abnormalities. All patients admitted with edema had at least one biochemical abnormality coexisting with a high comorbidity score. The most common edema-predisposing condition in this study was anemia. It can be seen as, among other things, a reflection of congestive heart failure, iatrogenic fluid overload, or renal impairment, but it also by itself perpetuates cardiac output, vasodilatation, and microvascular hyperfiltration, leading to edema.³⁰ The second most prevalent comorbidity in this study was that of articular or spinal disorders often coexisting with chronic noninfectious inflammatory edema. Musculoskeletal impairment additionally predisposes to limb immobility, having a negative effect on lymphatic transport, thus prompting tissue fluid stagnation.

The presence of multiple chronic conditions increases the complexity of therapeutic management, predisposing to polypharmacy. Rarely mentioned and only in case studies, potentially edematogenic medications, in this prospective study for the first time, were observed the second most frequent factor precipitating edema. Hundreds of medications used in palliative care are known as potentially contributing to edema formation or exacerbation; they include anticancer agents (docetaxel), calcium channel blockers (amlodipine), nonsteroidal anti-inflammatory drugs, anticonvulsants (gabapentin, pregabalin), antidepressants (trazodone), or antidiabetics (rosiglitazone, pioglitazone).³¹ Even opioids (particularly at higher doses) may have the potential to cause peripheral edema.³² On the other hand, the influence of some medications (e.g., angiotensin-converting enzyme inhibitors) may play a protective role in vasodilatory edema.³³ Optimal, appropriate polypharmacy in majority of advanced

cancer patients being at risk of developing edema remains challenging for oncologists or palliative care specialists.

Despite a substantial duration of edema before hospice admission, patients in this study only occasionally received compression therapy. As a result, nearly two-thirds of patients demonstrated signs of late-stage edema, often (15%) with severe complications that themselves are more problematic to manage. The first-line medications used to treat edema before palliative care were furosemide and other diuretics; however, they were insufficient, probably also due to lowered oncotic pressure in hypoalbuminemia. Therapeutic approach should be shifted from mere pharmacotherapy to complex management based on suspected edema etiology.

The primary aim of edema management in a palliative setting is to improve patient's comfort, increasing/maintaining functional capacity and enhancing quality of life rather than to resolve the swelling completely. Any treatment modality directed at correcting the underlying disturbance that may also be burdensome with minimal benefit should therefore be avoided.³⁴ This general principle seems to be particularly important within the last days of life, when patients have multiple, often not well-reported symptoms and concerns that may increase over time (drowsiness, fatigue, poor well-being, or dyspnea) in spite of receiving palliative care at the end of life.³⁵ The management of such patients with edema should be cautious to avoid harmful influence on patients' core symptoms of that time (e.g., limb compression may increase skin tightness, red blood cell transfusion in anemia may worsen circulatory overload, or diuretics may augment dry mouth sensation).

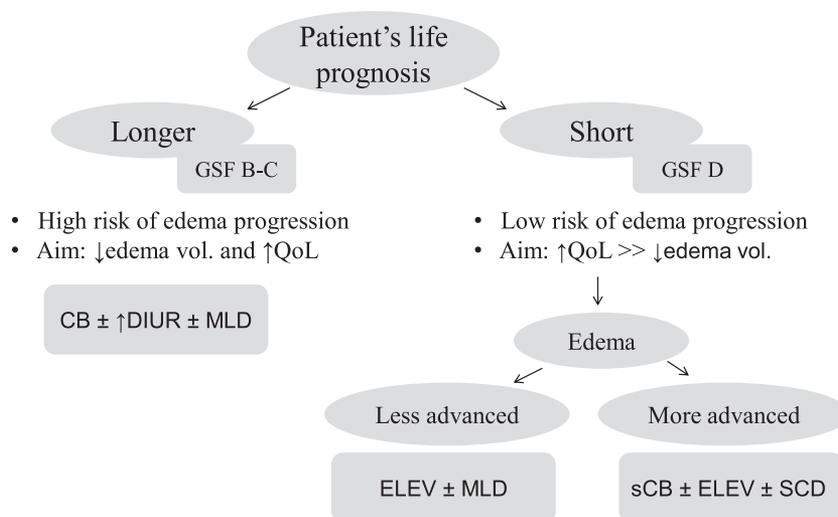


Fig. 2. Recommended edema therapy according to patients' prognosis and edema stage. CB = compression bandaging; DIUR = diuretics; GSF = Gold Standard Framework; MLD = manual lymphatic drainage; sCB = supportive light compression bandaging; ELEV = limb elevation; SCD = controlled subcutaneous needle drainage; ↑ = increase; ↓ = decrease.

The management of GSF, Stage D patients with edema in this study was not easy to assess reliably, not only due to heterogeneous edema therapy, poor patients' cooperation, or high attrition rate, but also due to concomitant symptomatic therapy applied and natural dehydration process observed interfering with limb volumes within the last days of life. For patients with a short life prognosis, in less advanced, stable edema, it would be reasonable to start, according to the author's experience, with a trial of limb elevation and a light MLD (Fig. 2). In more advanced and progressive cases, patients usually need light supportive short-stretch limb bandaging (with cotton/foam padding underneath). In highly advanced lymphatic congestion (particularly in the trunk area) with an increased risk of lymphorrhea and when compression is impossible to apply, a trial of controlled subcutaneous needle drainage should be considered. One patient in this study with advanced arthritis, locally disseminated breast cancer, and pitting upper limb lymphedema could not endure the application of bandage but tolerated well six needle drainage for 8 hours every 2 to 3 days (fluid loss 0.6–0.8 L/day).

Patients with longer prognosis (GSF, Stages A–C), if not treated, may be at a high risk of progression or edema complications (lymphorrhea, infections, or ulcerations), which is why they need CDT components of proved value in volume reduction, based on multi-layer compression bandaging.³⁶

To the author's knowledge, for the first time in prospective observation, standardized several-day compression bandaging could achieve a substantial limb edema reduction that was accompanied by a concomitant improvement in edema symptoms. Short-stretch (<100% elasticity) bandaging is characterized by high working pressure (which, however, drops quickly after application) and low resting pressure, and it is well tolerated and safer in moderately impaired arterial circulation (ankle-brachial pressure index >0.5) or in chronic compensated heart failure.^{37,38}

In this study, none of the re-evaluated patients had pure lymphatic insufficiency. For this reason, in the cases of fluid overload, parenteral diuretic was added to compression therapy. This addition might improve adherence, bringing about an additional "decongestive" effect which could diminish bandage strain on the skin. Furthermore, bandaging combined with diuretics might promote the compensation of an excessively fast vessel fluid withdrawal, acting as a diuresis "safety valve." Questions remain about the optimal use of diuretics in obtaining effective decongestion. Decrease the intensity of dyspnea and chest secretions within ESAS-C in this study indicated for sufficient fluid decongestion. In a hospice setting, observing

simple physical examination findings, such as jugular venous distention and blood pressure, is also valuable.³⁹ In addition, the serial evaluation of hematocrit levels can help gauge the rate of fluid redistribution from the extravascular to the intravascular compartment.⁴⁰ However, owing to the observational nature of this study as well as its small and specific sample size (patients with terminal cancer in a single hospice), any generalization of these therapeutical findings to a greater chronically ill patient population should be made with some caution.

Conclusions

Advanced cancer patients' immobility and inappropriate polypharmacy are the leading predisposing factors for edema development. This condition profoundly concerns patients with numerous comorbidities, causing various negative edema symptoms, like pain, limb swelling, heaviness, paresthesia, and concomitant overall well-being impairment. It is only occasionally treated properly by physical therapy. The edema can be managed sufficiently with decongestive or supportive therapy, depending on patients' life prognosis, symptom burden, edema stage, and progression. In those patients with longer life expectancy, compression bandaging with adequate diuresis maintenance may reduce limbs volume and improve negative sensations and edema-related overall well-being.

Disclosures and Acknowledgments

This research received no specific funding/grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors declare no conflicts of interest.

References

1. Lee CH, Kim JK, Jun HJ, Lee D-J, Namkoong W, Oh JH. Rehabilitation of advanced cancer patients in palliative care unit. *Ann Rehabil Med* 2018;42:166–174.
2. Cho S, Atwood JE. Peripheral edema. *Am J Med* 2002; 113:580–586.
3. Real S, Cobbe S, Slattery S. Palliative care edema: patient population, causal factors, and types of edema referred to a specialist palliative care edema service. *J Palliat Med* 2016;19: 771–776.
4. Penn IW, Chang YC, Chuang E, et al. Risk factors and prediction model for persistent breast-cancer-related lymphedema: a 5-year cohort study. *Support Care Cancer* 2018 Aug 14. <https://doi.org/10.1007/s00520-018-4388-6>. Epub ahead of print.
5. Sogaard M, Thomsen RW, Bossen KS, Sørensen HT, Nørgaard M. The impact of comorbidity on cancer survival: a review. *Clin Epidemiol* 2013;5(Suppl 1):3–29.
6. Farrow W. Phlebolympheidema—a common underdiagnosed and undertreated problem in the wound care clinic. *J Am Col Certif Wound Spec* 2010;2:14–23.

7. Keeley V. Oedema in advanced cancer. In: Twycross R, Jenns K, Todd J, eds. *Lymphoedema*. Oxford: Radcliffe Medical Press, 2000:338–358.
8. Moller UO, Stigmar K, Beck I, Malmstrom M, Rasmussen BH. Bridging gaps in everyday life – a freelisting approach to explore the variety of activities performed by physiotherapists in specialized palliative care. *BMC Palliat Care* 2018;17:20.
9. Dissemond J, Storck M, Kroger K, Stucker M. Indications and contraindications for modern compression therapy. *Wien Med Wochenschr* 2018;168:228–235.
10. Cheville AL, Andrews K, Kollasch J, Schmidt K, Basford J. Adapting lymphedema treatment to the palliative setting. *Am J Hosp Palliat Care* 2014;31:38–44.
11. Gradalski T, Rybak D. The effect of complex decongestive therapy (CDT) on advanced cancer patients with lymphoedema.—presented in abstracts at 9th Congress of the European Association for Palliative Care. *Eur J Palliat Care* 2005;131.
12. 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;21:473–478.
13. 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;40:1068–1072.
14. Muller M, Klinberg K, Wertli MM, Carreira H. Manual lymphatic drainage and quality of life in patients with lymphoedema and mixed oedema: a systematic review of randomised controlled trials. *Qual Life Res* 2018;27:1403–1414.
15. Pyszora A, Graczyk M, Krajnik M, Dos J. Implementation of modified manual lymphoedema treatment - complex physical therapy (MLT-CPT) in terminally ill patient. *Adv Pall Med* 2007;6:93–96.
16. Pyszora A, Krajnik M. Is Kinesio Taping useful for advanced cancer lymphoedema treatment? A case report. *Adv Pall Med* 2010;9:141–144.
17. Towers A, Hodgson P, Shay C, Keely V. Care of palliative patients with cancer-related lymphoedema. *J Lymphoedema* 2010;5:72–80.
18. Gradalski T. Diuretics combined with compression in resistant limb edema of advanced Disease. A case series report. *J Pain Symptom Manage* 2018;55:1179–1183.
19. Clein LJ, Pugachev E. Reduction of edema of lower extremities by subcutaneous, controlled drainage: eight cases. *Am J Hosp Palliat Care* 2004;21:228–232.
20. Jacobsen J, Blinderman CD. Subcutaneous lymphatic drainage (lymphocentesis) for palliation of severe refractory lymphedema in cancer patients. *J Pain Symptom Manage* 2011;41:1094–1097.
21. Sabar R, Safadi W. Relieving the burden: palliative centesis of an oedematous scrotal wall due to anasarca in end-stage heart failure. *BMJ Case Rep* 2013. <https://doi.org/10.1136/bcr-2013-009388>.
22. Landers A, Thomson M. Quantitative study of the subcutaneous needle drainage of lymphoedema in advanced malignancy. *J Lymphoedema* 2017;12:22–26.
23. Gradalski T, Ochalek K, Rybak D. Lymphedema or rather end-of-life edema? *J Palliat Med* 2018;21:585.
24. The Diagnosis and treatment of peripheral lymphedema: 2016 Consensus Document of the International Society of Lymphology. *Lymphology* 2016;49:170–184.
25. Walshe C, Caress A, Chew-Graham C, Todd C. Implementation and impact of the Gold Standards Framework in community palliative care: a qualitative study of three primary care trusts. *Palliat Med* 2008;22:736–743.
26. Sarfati D, Gurney J, Stanley J, et al. Cancer-specific administrative data-based comorbidity indices provided valid alternative to Charlson and National Cancer Institute Indices. *J Clin Epidemiol* 2014;67:586–595.
27. Reid C, Gibbins J, Burcombe M, et al. The use of the Edmonton Symptom Assessment Scale to measure symptoms at the end of life. *BMJ Support Palliat Care* 2012;2:A29.
28. R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2017. Available from <https://www.R-project.org/>. Accessed May 15, 2018.
29. Moffatt CJ, Doherty DC, Franks PJ, Mortimer PS. Community-based treatment for chronic edema: an effective service. *Modellymphatic Res Biol* 2018;16:92–99.
30. Anand IS, Chandrashekhara Y, Ferrari R, Poole-Wilson PA, Harris PC. Pathogenesis of oedema in chronic severe anaemia: studies of body water and sodium, renal function, haemodynamic variables, and plasma hormones. *Br Heart J* 1993;70:357–362.
31. Tesar E, Armer JM. Effect of common medications on breast cancer-related lymphedema. *Rehabil Oncol* 2018;36:7–12.
32. Gardner-Nix J. Opioids causing peripheral edema. *J Pain Symptom Manage* 2002;23:453–455.
33. Messerli FH. Vasodilatory edema: a common side effect of antihypertensive therapy. *Am J Hypertens* 2001;14:978–979.
34. Beck M, Wanchai A, Steward BR, Cormier JN, Armer JM. Palliative care for cancer-related lymphedema: a systematic review. *J Palliat Med* 2012;15:1–7.
35. Hiu D, dos Santos R, Chishholm GB, Bruera E. Symptom expression in the last seven days of life among cancer patients admitted to acute palliative care units. *J Pain Symptom Manage* 2015;50:488–494.
36. Gradalski T, Ochalek K, Kurpiewska J. Complex decongestive lymphatic therapy with or without Vodder II manual lymph drainage in more severe chronic postmastectomy upper limb lymphedema: a randomized noninferiority prospective study. *J Pain Symptom Manage* 2015;50:750–757.
37. Dissemond J, Assenheimer B, Bultemann A, et al. Compression therapy in patients with venous leg ulcers. Review Article. *J Dtsch Dermatol Ges* 2016;14:1072–1087.
38. Andriessen A, Apelqvist J, Mosti G, et al. Compression therapy for venous leg ulcers: risk factors for adverse events and complications, contraindications - a review of present guidelines. *J Eur Acad Dermatol Venereol* 2017;31:1562–1568.
39. Palazzuoli A, Ruocco G, Ronco C, McCullough. Loop diuretics in acute heart failure: beyond the decongestive relief for the kidney. *Crit Care* 2015;19:296.
40. Marenzi GC, Lauri G, Grazi M, et al. Circulatory response to fluid overload removal by extracorporeal ultrafiltration in refractory congestive heart failure. *J Am Coll Cardiol* 2001;38:963–968.