

EFFICACY OF COMPLETE DECONGESTIVE THERAPY AND MANUAL LYMPHATIC DRAINAGE ON TREATMENT-RELATED LYMPHEDEMA IN BREAST CANCER

RASHMI KOUL, M.D.,* TAREK DUFAN, M.D.,* CATHERINE RUSSELL, B.P.T.,[†]
WANDA GUENTHER, R.M.T.,[†] ZOAN NUGENT, PH.D.,[‡] XUYAN SUN, M.Sc.,[‡]
AND ANDREW L. COOKE, F.R.C.P.C.*

*Department of Radiation Oncology, CancerCare Manitoba, Winnipeg, MB, Canada; [†]Winnipeg Regional Health Authority Breast Health Center, Winnipeg, MB, Canada; [‡]Epidemiology and Cancer Registry, CancerCare Manitoba, Winnipeg, MB, Canada

Objective: To evaluate the results of combined decongestive therapy and manual lymphatic drainage in patients with breast cancer-related lymphedema.

Methods and Materials: The data from 250 patients were reviewed. The pre- and posttreatment volumetric measurements were compared, and the correlation with age, body mass index, and type of surgery, chemotherapy, and radiotherapy was determined. The Spearman correlation coefficients and Wilcoxon two-sample test were used for statistical analysis.

Results: Of the 250 patients, 138 were included in the final analysis. The mean age at presentation was 54.3 years. Patients were stratified on the basis of the treatment modality used for breast cancer management. Lymphedema was managed with combined decongestive therapy in 55%, manual lymphatic drainage alone in 32%, and the home program in 13%. The mean pretreatment volume of the affected and normal arms was 2929 and 2531 mL. At the end of 1 year, the posttreatment volume of the affected arm was 2741 mL. The absolute volume of the affected arm was reduced by a mean of 188 mL ($p < 0.0001$). The type of surgery ($p = 0.0142$), age ($p = 0.0354$), and body mass index ($p < 0.0001$) were related to the severity of lymphedema.

Conclusion: Combined decongestive therapy and manual lymphatic drainage with exercises were associated with a significant reduction in the lymphedema volume. © 2007 Elsevier Inc.

Lymphedema, Breast cancer, Combined decongestive therapy, Manual lymphatic drainage.

INTRODUCTION

One of the complications of breast cancer treatment is lymphedema of the ipsilateral arm. No consistent operational definition of clinically significant lymphedema has been published. The lack of consensus leads to confusion regarding the incidence of lymphedema after breast cancer treatment and difficulty in measuring treatment efficacy. The management of lymphedema in breast cancer patients has been based on results from case studies, clinical experience, anecdotal information, and only a few randomized trials. Several therapeutic interventions exist to treat this potentially distressing and disabling condition, but no consensus has been reached as to what constitutes optimal or definitive treatment of lymphedema (1). The aim of this study was to evaluate the results of the first 2 years of a program for patients with lymphedema secondary to breast cancer, who have completed a minimum of 1 year of follow-up.

METHODS AND MATERIALS

The Winnipeg Regional Health Authority (WRHA) and CancerCare Manitoba jointly established the WRHA Breast Health Center in 1999 in response to the need for the centralization of breast diagnostic services for women of Winnipeg and Manitoba. Approximately 800 women annually are diagnosed with breast cancer in the Province of Manitoba, population approximately 1.1 million (2). Included in this program was the development of a comprehensive service for the assessment and management of lymphedema resulting from the treatment of breast cancer. The WRHA is the only public provider for the lymphedema treatment program at two sites. In the present study, we combined the WRHA Breast Health Center records and treatment information from the CancerCare Manitoba medical records for patients referred for lymphedema treatment during the first 2 years of the program and who had ≥ 1 year follow-up.

Patient assessment and treatment

All patients were seen at the outpatient lymphedema clinic that was staffed by two qualified therapists certified in the Vodder

drainage technique and combined decongestive therapy (CDT) (3). Patients underwent complete physical examination and were evaluated for symptoms such as numbness, tightness, stiffness, and heaviness. On initial assessments, both arms were measured. Circumferential measurements were done at the wrist (base of the styloid process of the ulna) and every 4 cm to the top of the arm (axillary fold), as well as two measurements to the hand that were not included in the volume measurements. Every calculation was squared, and then all measurements for that arm were totaled and divided by π (3.1416). This is a modified truncated cone formula. The severity of lymphedema was defined as the absolute volume difference in milliliters between the normal and affected arms. The demonstration of a treatment effect was simply the difference in arm volume over time.

The affected arm was measured at the start of treatment and weekly during the intensive phase of treatment (CDT) (4). During the intensive phase, treatment lasts for 1 h daily for up to several weeks depending on the severity and response. CDT consists of four components. The first is manual lymphatic drainage (MLD), which causes volume reduction by removing excess fluid and protein. MLD is a skin-stretching form of massage performed to open the lymphatics in unaffected regions to drain fluid from the affected regions and increase lymphatic activity. Second, compression therapy is applied to mobilize the edema fluid after each MLD session for 23 h/d, including weekends. Bandages and specific padding are applied in a precise way to the affected limb using a graded pressure. The bandage material used determines the depth of the compression effect. Short-stretch bandages are primarily used in our institution. Bandage application causes high pressure during activity and relatively low pressure in the limb when the body is resting. The third and fourth components are remedial exercises for the arm and shoulder and deep breathing to help promote venous and lymphatic flow. Patients are instructed about skin and nail care. The home program involves 1 h of training on self-lymphatic drainage and education on scrupulous skin care and remedial exercises. In our study, none of the patients received pneumatic compression therapy.

Once the intensive phase was complete, the patient was measured for a custom garment and attended a few sessions to maintain the fluid volume loss until the compression garment was ready to wear (20–30 mm Hg). During the maintenance phase, which is permanent, the patient was instructed to wear the garment daily while awake and to remove it at bedtime. The patient was encouraged to do self-lymph drainage at least once daily. Patients were interviewed by telephone at 3 months after treatment, and follow-up measurements were done at 6 and 12 months.

Statistical analysis

We applied the paired *t* test to the absolute volume in milliliters to evaluate treatment effectiveness. Our data satisfied the assumptions of the paired *t* test. Absolute concordance (degree of differ-

Table 1. Excluded patients (*n* = 81)

Reason	<i>n</i>
Lymphedema resolved before 12 mo	12
Deceased	19
Recurrence	9
Lost to follow-up	12
Noncompliant	26
Leg lymphedema	3

Table 2. Patient, tumor, and treatment characteristics

Characteristic	Value
Patient	
Age (y)	
Mean	54.3
Range	29–82
BMI (kg/m ²)	
Mean	29.1
Range	18–47
Tumor	
Breast involved	
Right	87 (63)
Left	51 (37)
T stage	
Tis	3 (2)
T1	81 (58)
T2	46 (33)
T3	8 (6)
T4	1 (1)
Nodal involvement	
N0	80 (58)
N+	58 (42)
Metastasis	
M0	135 (98)
M+	3 (2)
AJCC stage	
I	65 (47)
II	44 (32)
III	22 (16)
IV	7 (2)
Treatment	
Surgery type	
Modified mastectomy	61 (44)
Lumpectomy and axillary dissection	61 (44)
Other (simple mastectomy, tumor excision alone)	16 (12)
Radiotherapy	91 (66)
Radiation fields	54 (60)
2	37 (40)
>2 (locoregional)	
Chemotherapy	68 (49)

Abbreviation: AJCC = American Joint Committee on Cancer. Data presented as number of patients, with percentages in parentheses, unless otherwise noted.

ence between the volumes before and after treatment) was also assessed through the paired *t* test. Severity was assessed using the Wilcoxon two-sample test.

RESULTS

Patient characteristics

The program received 250 patient referrals during the study period from surgeons, medical and radiation oncologists, and general practitioners. For the purposes of this study, lymphedema was defined as present if the patient was referred and the affected arm was not smaller than the unaffected arm. Of the 250 patients, 81 were excluded because follow-up measurements at 1 year were not available (Table 1), 31 were excluded because the affected arm was smaller than the normal arm at baseline, and 138 patients were included in the study.

Table 2 summarizes the baseline characteristics of all 138 subjects. The mean age at presentation was 54.3 years, the

mean body mass index (BMI) was 29.1 kg/m², and the mean time from the date of first cancer surgery to the date of the first therapy assessment was 73 months. Of the 138 patients, 61 (44%) were treated with modified radical mastectomy, 61 (44%) underwent lumpectomy and axillary nodal dissection, and 16 (12%) underwent either simple mastectomy or excision of tumor alone without axillary dissection. In patients with modified mastectomy, the mean volume in the affected arm was 2931 mL compared with 2673 mL in patients with lumpectomy and axillary dissection only. Ninety-one patients (66%) received external beam radiotherapy to the breast and locoregional area. Of those who received radiotherapy, 40% underwent locoregional radiotherapy, 60% breast radiotherapy alone; 49% received systemic chemotherapy.

Treatment outcomes

Patients received treatment at the discretion of the therapist, depending on the severity, response, and patient compliance. Of the 138 patients, 55% were treated using all four CDT components, 32% received MLD alone delivered by the therapists, and 13%, with mild lymphedema, received instructions and counseling for the home program, which included self-administration of simple lymph drainage and exercises. All the patients treated with CDT were prescribed compression bandages during the intensive phase.

The mean pretreatment volume of the affected arm was 2929 mL (range, 1474–5879 mL) and for the normal arm was 2531 mL (range, 1320–4299 mL). The mean difference in arm volumes at baseline was 398 mL, and the standard deviation was 469 mL.

The volume measurements in the normal and affected arm are outlined in Fig. 1. A treatment effect was measured as a reduction in the absolute volume of the affected arm. At the end of 1 year, the absolute volume of the affected arm was reduced by a mean of 188 mL (median 166) to 2741 mL ($p < 0.0001$). This was a 47% absolute reduction in the lymphedema volume. During the same period, no significant change occurred in the mean volume of the normal arm (2531 vs. 2509 mL). Patients who

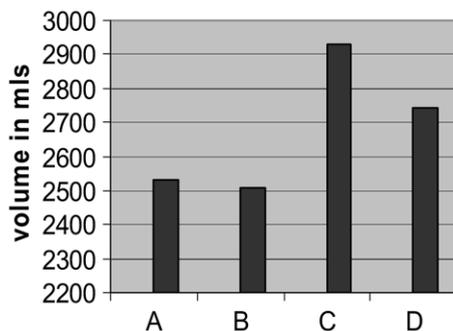


Fig. 1. Comparison of arm volumes before and after treatment. (A) Pretreatment normal arm volume. (B) Posttreatment normal arm volume (A – B = 22 mL, $p = 0.35$). (C) Pretreatment affected arm volume. (D) Posttreatment affected arm volume (C – D = 188 mL, $p < 0.0001$).

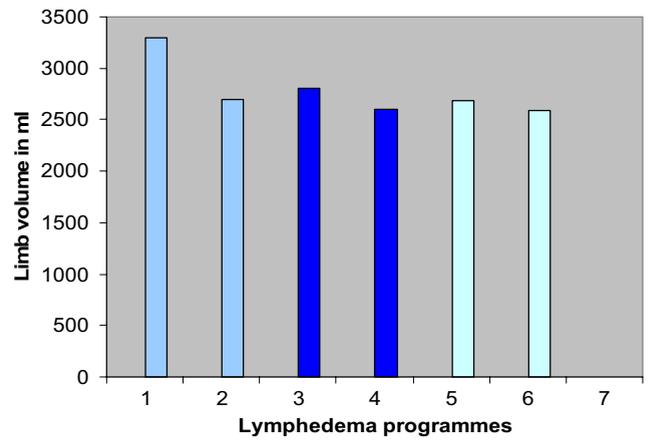


Fig. 2. Comparison of limb volume in various lymphedema programs. Bars 1 and 2, pretreatment and posttreatment volume in CDT program with absolute improvement of 55.7%. Bars 3 and 4, pre- and posttreatment volume in MLD program with absolute improvement of 41.2%. Bars 5 and 6, pre- and posttreatment volume in home program with absolute improvement of 24%.

received CDT, MLD, or the home program had a pre- and posttreatment volume of 3074 mL and 2852 mL, 2778 mL and 2613 mL, and 2685 mL and 2587 mL, respectively. The volume improvement was 223 mL, 164 mL, and 98 mL after CDT, MLD, and the home program (Fig. 2), for a 55.7%, 41.2%, and 24% absolute reduction in lymphedema volume, respectively ($p < 0.0001$).

Because all patients in the study had lymphedema, we could not examine possible risk factors and the likelihood of developing lymphedema. However, we did examine the possible risk factors and the severity of lymphedema at baseline. The disease severity was calculated as the difference between the absolute volumes of the affected and unaffected arms. The type of surgery (mastectomy vs. lumpectomy; $p = 0.0142$), age ($p = 0.0354$), and BMI ($p < 0.0001$) were related to the lymphedema severity. The relationship to BMI might have been spurious, because we measured the severity as an absolute, not a relative, volume. The severity of lymphedema was not related to the number of nodes removed, chemotherapy, radiotherapy, or whether the nodes were irradiated (Table 3). The number of CDT or MLD sessions provided to the patients was related to mastectomy (vs. lumpectomy) and chemotherapy.

DISCUSSION

The awareness of lymphedema has evolved during the past two decades. Lymphedema is an external manifestation of lymphatic system insufficiency and deranged lymph drainage. Breast cancer treatment is the most common cause of secondary lymphedema. Loss of the cross-sectional lymphatic transport system occurs, leading to accumulation of fluid. Some believe that a reduction in barrier function occurs because of the loss of lymph node function. This encourages penetration of bacteria and stimulates repair

Table 3. Univariate analysis of baseline characteristics and their relation to severity

Variable	Test	<i>p</i>
BMI	Spearman's correlation ρ +0.34; n = 137	<0.0001
Age	Spearman's correlation ρ = +0.18; n = 137	0.0354
Nodes removed	Spearman's correlation ρ = -0.005; n = 137	0.98
Radiation fields treated (n)	Median test	0.55
RT	Wilcoxon two-sample test	0.26
Chemotherapy	Wilcoxon two-sample test	0.56
Surgery type	Wilcoxon two-sample test (MRM vs. lumpectomy and nodal dissection)	0.014

Abbreviations: RT = radiotherapy; MRM = modified radical mastectomy.

mechanisms that generate cytokines, which in turn causes lymphedema (5).

Lymphedema may result in cosmetic deformity, loss of function, physical discomfort, and recurrent episodes of erysipelas. Patients with lymphedema are at risk of clinical, as well as psychological consequences that are debilitating and patients may be frustrated as they face a major problem, yet cannot find an answer to reduce a swollen limb (6). Treatment of lymphedema is difficult, multidisciplinary in nature, and, even in the best outcomes, costly and time-consuming (7). With aggressive chemotherapy and sophisticated radiotherapy, breast cancer survivors are living longer and lymphedema is becoming a chronic problem (8).

The American Cancer Society has estimated that 10–15% of these breast cancer survivors will be diagnosed with lymphedema in their lifetime. Some investigators have observed incidences of 30–40%. A 1998 review of seven large studies reported an incidence range of 6–30% (9). In part, because it can develop weeks, months, or years after treatment, it has been difficult to accurately determine the causes of lymphedema and to establish its true incidence. Minor, stable degrees of lymphedema may go unreported and unreported. Some long-term studies have failed to show a relationship between age, number of lymph nodes removed, or weight and an increased risk of lymphedema (10). Surgery, radiotherapy, and tumor growth have been found to increase the risk of lymphedema (11). Retrospective analyses have been done to evaluate the risk of lymphedema after breast conservation surgery. No unanimous agreement has been reached regarding the risk factors for lymphedema. Some data have suggested that nodal radiotherapy is the only significant risk factor for developing lymphedema (12). Other investigators noted that a greater BMI at surgery increased the risk (13). In our study, a greater BMI at the initial assessment of lymphedema affected the severity.

The goal of lymphedema therapy is to reduce swelling, restore function, and improve the cosmetic outcome of the affected limb. In published reports, several common modalities have been used, in various combinations, but the quality of data demonstrating efficacy of the different treatments has been inconsistent.

Most breast cancer patients undergo some form of surgery. Axillary dissection is often done as a staging procedure to guide adjuvant treatment. Although the trial of

sentinel lymph node biopsy demonstrated an overall reduction in the incidence of lymphedema (14), sentinel nodal biopsy is not likely to eliminate the risk of lymphedema in patients with involved nodes because the standard of care, to date, is Level I-II axillary nodal dissection in these patients (15, 16). Furthermore, even patients without node dissection may develop lymphedema, as did 12% of our patients.

Lymphedema has been measured inconsistently, in part because many technical problems in measuring lymphedema exist. Using bony landmarks to define segments that are not equidistant and measuring the arm circumference are inaccurate methods of estimating the volume because of the arm's irregular and nonconstant shape. Another method commonly used to measure lymphedema is water displacement. The limb is submerged in a volumetric cylinder filled with water. The arm volume is measured by displacement (17). Tissue tonometry has been used in some centers in Europe. Skin compressibility correlates with the circumference and volume of the arm and the amount of lymphedema (18).

The reliability of these tests has been tested. However, segmental circumference measurement has been the most frequently used technique because of the ease with which it can be applied. It also allows therapists to determine which part of the affected arm is worst and needs maximal manipulation. Thus, therapists can determine the volume difference, which can be used for grading purposes. In our study, the therapists calculated the limb volume using a modified truncated cone formula using segmental circumference measurement. This has been found in other reports to closely correlate with the water displacement method yet is less burdensome (19). Several common rehabilitative interventions have been used to reduce edema. Combined physical therapy known as CDT involves a two-stage treatment program. The first phase consists of skin care, MLD, range of motion exercises, and compression, typically applied with multilayered bandage wrapping. The second phase aims to maintain and optimize the results obtained in the first phase. It consists of compression using a low-stretch stocking or sleeve, continued remedial exercises, and self drainage. Other therapies include elevation alone, massage, and application of external pressure in the form of a garment or pneumatic compression.

Manual lymphatic drainage may provide a statistically significant reduction in lymph volume and improvement in arm parameters and symptoms related to edema (20). Williams *et*

al. (21) studied women in a randomized control crossover study and found that MLD significantly reduced the limb volume and dermal thickness. The quality of life and emotional functions were also improved using this technique (21). Anderson *et al.* (22), in a prospective randomized study, compared MLD and the use of a compression garment and exercise. The data suggested that MLD did not contribute significantly to reduce edema. Compression bandaging alone can sometimes yield good results (22). Numerous studies of combined MLD and compression bandaging have been reported and the data have indicated that compression bandaging with and without MLD is still an effective intervention in reducing arm volume.

McNeely *et al.* (23) concluded that compression bandaging on its own should be considered the primary treatment option for reducing lymphedema volume. Additional benefit may result from application of MLD for women with moderate lymphedema. However, this finding needs additional evaluation in a research setting (23).

The use of medical compression stockings has been a component of combined physical decongestion treatment of lymphedema for the past four decades. The essential condition for the therapeutic success of compression is a perfect fit and the selection of stocking material (24). Circular knit and flat bed knit are the two main garments available on the market. Circular knit material tends to curl inward causing constriction. The width and compression of the stocking can be varied by changing the loop size and yarn tension. Flat knit material can be negotiated easily and lies flat on the skin, thus reducing the risk of tissue injury. For our group of patients, we have consistently used short-stretched, open mesh bandages, which maintained a perfect fit, provided optimal compression, and were inexpensive compared with other bandages available on the market or on the Internet. The Elvarex compression garment is popular in Europe. It is a flat, firm, knitted fabric with high-working pressure and low elasticity. The open wide mesh stitch pattern offers high air permeability and a micro-massaging effect on the skin (25). The use of the Elvarex as an initial monotherapy is not recommended because a decrease in arm volume renders the fitted garment useless. We recommend the use of other therapies to reach a nadir arm volume before the patient purchases the Elvarex.

The International Society of Lymphology updated their consensus statement in 2003 and emphasized the accurate diagnosis and staging of lymphedema is essential for appropriate therapy. A thorough medical examination and evaluation of other confounding factors such as comorbid

conditions are indispensable. The most effective therapy according to the American Cancer Society, National Lymphedema Network, and medical experts in the field consists of a combination of CDT, including MLD, compression bandaging, a program of remedial exercises, and vigilant skin care and hygiene regimen. CDT should be used as the primary treatment, and failure is confirmed only when intense nonoperative treatment in a specialist clinic is unsuccessful. Multiple large series of patients with mild to severe lymphedema who underwent an intensive 2–3 weeks of CDT have documented striking results. Despite this success, neither CDT nor its components have been subjected to proper randomized clinical trial. In our study, CDT was offered according to the discretion of the therapists to patients with moderate to severe lymphedema. These patients had a maximal response after treatment. Patients who were enrolled in the home program had mild lymphedema and had a less dramatic response to therapy.

The therapeutic benefit of CDT has been documented for >30 years and is in use as the standard treatment in North America. Drugs, such as diuretics, benzopyrones, antimicrobials, and mesotherapy (injection of hyaluronidase), have not been proved to have therapeutic value against uncomplicated lymphedema (26). Surgical techniques such as the Charles debulking and microlymphatic venous anastomosis have also been used, but long-term follow-up data are not available to prove their efficacy (27).

However, because of these conflicting results, no consensus has yet been reached regarding a standard treatment of lymphedema. At our center, the treatment options are often selected individually on the basis of the severity, degree of comorbidity and the life style and social situation of the patient.

CONCLUSION

A program offering some or all components of CDT to patients with lymphedema after treatment of breast cancer was associated with a significant reduction in the mean and median arm volume evident at 1 year after the beginning of treatment. Our patients had a 47% absolute reduction in lymphedema volume. The lack of a control group did not allow us to exclude the possibility that these reductions would have occurred spontaneously. One-third of the patients in this study had never undergone radiotherapy, indicating that surgery alone is a risk factor. Because the treatment was allocated in a nonrandom fashion, we could not comment on the contribution of each component of CDT for lymphedema.

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