Decongestive Lymphatic Therapy for Patients with Breast Carcinoma-Associated Lymphedema

A Randomized, Prospective Study of a Role for Adjunctive Intermittent Pneumatic Compression

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BACKGROUND. Disruption of the lymphatic circulation through breast carcinoma-associated axillary lymph node dissection, with or without radiation therapy, reportedly is the most common cause of lymphedema in developed countries. There is no cure for breast carcinoma-associated lymphedema. Although intermittent pneumatic compression (IPC) has been acknowledged as a potential component of the multidisciplinary therapeutic strategy in the treatment of patients with breast carcinoma-associated lymphedema, prospective study of its adjunctive safety and efficacy is required.

METHODS. IPC was assessed as a component of the initial therapeutic regimen for newly treated patients with breast carcinoma-associated lymphedema. Twenty-three patients who had not previously been treated for lymphedema were randomized to receive either decongestive lymphatic therapy (DLT) alone or DLT with daily adjunctive IPC. Patients with stable, treated, breast carcinoma-associated lymphedema also were assessed in the maintenance phase of therapy. Twenty-seven patients were randomized either to DLT alone or to DLT coupled with daily IPC. In both studies, objective assessment included serial measurement of volume by water displacement, tissue tonometry to assess elasticity of the skin, and goniometry to measure joint mobility.

RESULTS. During initial treatment, the addition of IPC to standard DLT yielded an additional mean volume reduction (45.3% vs. 26%; $P < 0.05$). During maintenance DLT alone, there was a mean increase in volume (32.7 $\pm$ 115.2 mL); with DLT and IPC, there was a mean volume reduction (89.5 $\pm$ 195.5 mL; $P < 0.05$). In both studies, IPC was tolerated well without detectable adverse effects on skin elasticity or joint range of motion.

CONCLUSIONS. When IPC is used adjunctively with other, established elements of DLT, it provides an enhancement of the therapeutic response. IPC is well tolerated and remarkably free of complications. ***Cancer* 2002;95:2260–7.**

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Lymphedema can be defined as the generalized or regional accumulation of protein-rich interstitial fluid that occurs primarily as a consequence of malformation, underdevelopment, or acquired disruption of the lymphatic circulation. With chronic impairments in lymphatic drainage, the ensuing edematous state is characterized over time by the secondary proliferation of fibroblasts, keratinocytes, and adipocytes; the accumulation of collagen; and the destruction of elastin fibers within the skin.

Edema of the arm after axillary lymph node dissection reportedly is the most common cause of lymphedema in developed countries.[1] In general, without regard to the individual surgical approach or the elapsed time since treatment, approximately one in four women develops arm edema after treatment for breast carcinoma.[2] Once it is established, lymphedema has an inexorable tendency to progress.[3] Although the risk of developing lymphedema after therapy for breast carcinoma has been associated with anatomic risk factors, such as the extent of axillary lymph node dissection and the patient's exposure to axillary radiation, this awareness has reduced, but not eliminated, the problem of breast carcinoma-associated lymphedema.[2] The advent of upper extremity edema has a distinct detrimental effect on the perceived quality of life for breast carcinoma survivors.[4] Patients with arm edema secondary to breast carcinoma therapy experience a substantial degree of functional impairment, psychological morbidity, and diminished quality of life.[4–7]

With the remarkable advances that have accrued both in the early detection of breast carcinoma and in the successful application of effective adjuvant therapies, it is increasingly imperative that suitable treatment measures be developed for the sequelae of breast carcinoma therapy, like lymphedema, that impair patients' functional status or perceived quality of life.

There is no cure for breast carcinoma-associated lymphedema. A variety of physiotherapeutic interventions have been proposed for the control of symptoms and to minimize complications. In 1998, the American Cancer Society conducted an international conference to address the need to prioritize diagnostic and treatment strategies for patients with breast carcinoma-associated lymphedema.[8] The resulting recommendations emphasized the aggressive use of a variety of physiotherapeutic interventions to control lymphedema symptoms and to minimize complications.[8] Since that time, prospective investigation of the standard elements of decongestive lymphatic therapy (DLT), including manual lymphatic massage, multilayer compressive bandaging, and the use of compressive garments, has validated the utility of these interventions for the control of acquired lymphedema.[9,10]

Although intermittent pneumatic compression (IPC) has been acknowledged as a potential component of the multidisciplinary, therapeutic approach to treating patients with breast carcinoma-associated lymphedema,[8] conclusive, prospective documentation of the beneficial role of this modality has not been provided.[11] Accordingly, we undertook a prospective, randomized study to investigate the safety and relative efficacy of pneumatic compression therapy for the treatment of patients with breast carcinoma-associated upper extremity lymphedema when used adjunctively with compression bandaging and manual lymphatic massage.

MATERIALS AND METHODS

Design of the Trial

The prospective evaluation of pneumatic compression therapy in patients with breast carcinoma-associated lymphedema was undertaken in two phases. In the first phase (Study 1), adjunctive IPC was assessed for its role as a component of the initial decongestive therapy prescribed for patients with previously untreated lymphedema. This was a 10-day, randomized study with a 30-day follow-up. In the second phase (Study 2), a prospective study was performed to evaluate the adjunctive benefit of IPC for maintenance therapy in patients with stable, chronic, breast carcinoma-associated lymphedema. This study was conducted with a randomized, 2-month, cross-over design and included a 6-month follow-up.

Patients

Study 1 (initial therapy)

Patients with lymphedema of the upper extremity after surgical and/or radiotherapeutic interventions for breast carcinoma were eligible for enrollment. Recruitment was undertaken from the population of patients who presented to the Stanford Center for Lymphatic and Venous Disorders for prospective evaluation of upper extremity edema in the setting of therapy for breast carcinoma. The patient characteristics are shown in Table 1.

Inclusion and exclusion criteria for Study 1

Patients were eligible for inclusion if they presented with breast carcinoma-associated lymphedema, which was defined as the presence of an increase $\geq$ 20% in the volume of the swollen limb compared with the volume of the contralateral, normal arm. For this reason, patients with bilateral disease were excluded. Volume was assessed by water-displacement volumetry, as described below. Patients were required to have an interval of at least 12 weeks from the completion of breast carcinoma therapy (either surgery, or radiotherapy, or both) prior to enrollment in the trial. Evidence of bilateral lymphedema; breast carcinoma recurrence; active clinical infection; or clinically evident, concomitant venous occlusion constituted the exclusion criteria for Study 1.

TABLE 1
Demographics by Patient Group in Study 1

Variable	Group I	Group II
No. of patients	12	11
Age (yrs)		
Mean ± SD	68.8 ± 9.11	65 ± 10.8
Range	56–81	47–81
Duration of edema (mo)		
Mean ± SD	41.1 ± 62.3	35.6 ± 21.6
Range	3–180	3–72
Excess limb volume (%)		
Mean ± SD	41 ± 32.9	43.8 ± 24.3
Range	11–104	16.5–86
Axillary dissection alone (no.)	2	5
History of radiation therapy (no.)	10	6
History of recurrent cellulitis (no.)	4	3
History of hypertension (no.)	5	4
Reduced joint mobility (no.)	8	3

SD: standard deviation.

Study 2 (maintenance therapy)

Patients with stable, treated, breast carcinoma-associated lymphedema of the upper extremity were eligible for randomization into Study 2.

Inclusion and exclusion criteria for Study 2

Patients were eligible for inclusion in Study 2 if they demonstrated chronic lymphedema of a single extremity as a consequence of prior therapy for breast carcinoma and had completed the initial course of intensive DLT at least 1 month and less than 1 year prior to the time of enrollment in the study. Exclusion criteria included the presence of recurrent malignancy, active infection, clinical evidence of venous obstruction, or bilateral lymphedema of the upper extremity.

For both studies, informed consent was obtained from all participants. The study was performed under the auspices of the Institutional Review Board of Stanford University.

Treatment Methods

Decongestive lymphatic therapy (DLT) was performed as described previously.[10] In summary, DLT is a multidisciplinary, physiotherapeutic approach to improve lymphatic flow and reduce the excess limb volume of lymphedema. All patients received their outpatient therapy at the Stanford Center for Lymphatic and Venous Disorders. Each session of therapy included manual lymphatic drainage (MLD; from 30 minutes to 1 hour, as required), compressive wrapping of the limb with minimally elastic bandages, and decongestive exercises. MLD was performed according to the technique advocated by the Vodder School.[12] At each treatment session, massage was followed by decongestive exercises and multilayered, low-stretch compressive bandaging (Comprilan®; Beiersdorf, Germany). Bandages were left in place for the interval spanning successive daily manipulations. Each patient received 10 days of daily DLT.

When IPC was used, it was applied to the treated arm with a four-chamber pneumatic sleeve and a gradient-sequential pneumatic pump (Sequential Circulator 2004; BioCompression Systems Inc.). A standard pressure setting of 40–50 mmHg was used. In Study 1, for the patients who were randomized to this treatment arm, IPC was performed daily for 30 minutes at the designated pressure settings. In Study 2, IPC was prescribed as a daily, self-administered session of 60 minutes at the same pressure settings.

Treatment Regimens

Study 1

Patients were randomized to one of two treatment groups. In Group I, IPC (30 minutes at 40–50 mm Hg) was performed daily after MLD and before compression bandaging. Patients in Group II received standard, initial, decongestive therapy without the adjunctive IPC. After completion of the initial intervention, all patients were fitted with a Class II compression garment (MEDI USA) to be worn on a daily basis. Patients were instructed in the techniques of self-applied manual lymphatic massage, which was continued on a daily basis at home after completion of the initial decongestive intervention. Assessments of limb volume, tissue elasticity, and joint mobility were performed at the time of enrollment and subsequently on Days 10 and 40 (follow-up, Day 30) of the study.

Study 2

After an initial objective assessment of limb volume and skin tonometry, patients were randomized to one of two arms of the study. In the first arm of the study, the patients were instructed simply to continue maintenance measures for lymphedema (daily, self-administered, manual lymphatic massage and the Class II compression garment). In the second arm of the study, these maintenance techniques were supplemented with 1 hour of IPC. Each patient was supplied with a gradient-sequential pneumatic pump (Sequential Circulator 2004; BioCompression Systems Inc.) for their home use. All patients were reassessed after 1 month of therapy and, thereafter, cross-over to the alternate arm was undertaken during the second month, and this was followed by a complete, objective reevaluation.

Quantitative assessments were performed at the

time of enrollment and at the completion of each arm of the study. Upon completion of both arms of this study, each patient was given the opportunity to maintain the adjunctive home use of pneumatic compression therapy. All such patients were reassessed objectively after a period of 6–12 months of continuous therapy. Compliance with the therapy was assessed through an exit interview of the patient at the completion of the study.

Measurements and Assessments

Tank volumetry

Water-displacement volumetry was used to quantitate limb volume prior to randomization and at each subsequent clinical evaluation. Each limb was immersed sequentially in a water-filled tank. The displaced fluid was collected and measured. The patient rested the immersed hand on a plastic bar positioned within the tank to ensure consistency in the depth of immersion with repetitive, sequential volume determinations.

The response to the therapeutic intervention (DLT and IPC vs. DLT alone) was quantified as the percent reduction in limb volume (Study 1) or as the absolute reduction in limb volume (Study 2), as follows: $Vpre_A$: volume of the affected arm prior to treatment; $Vpre_N$: volume of the nonaffected arm prior to treatment; $Vpost_A$: volume of the affected arm after treatment; $Vpost_N$: volume of the nonaffected arm after treatment; Δpre arm volume difference prior to treatment ($Vpre_A - Vpre_N$); Δpost arm volume difference prior to treatment ($Vpost_A - Vpost_N$); absolute arm volume reduction: Δpre − Δpost and % volume reduction: [(Δpre − Δpost) / Δpre] × 100.

Skin tonometry

Skin tonometry measurements were performed as described previously.[13,14] We used a mechanical tonometer with a base diameter of 1 cm and a probe weight of 60 g. The probe was applied to the skin of the forearm for 1 minute before the quantitative recording of the depth of the probe descent as a measure of tissue elasticity.

Goniometry

The range of motion of the shoulder, elbow, and wrist joints was quantitated with the standard techniques of goniometry.[15] The quantitation of range of motion was performed prior to randomization. For all patients with impaired range of motion at baseline, the effect of therapeutic randomization on joint range of motion was reassessed at each subsequent clinical reevaluation.

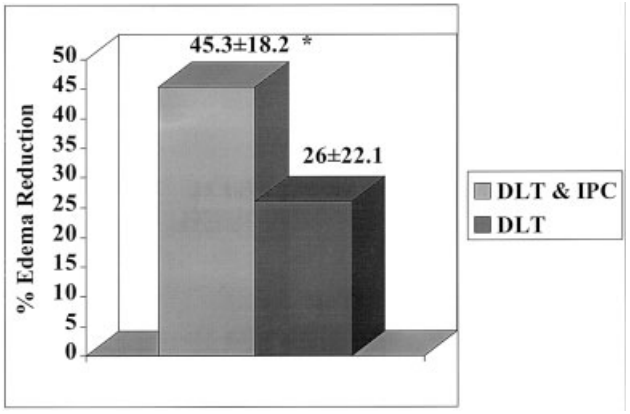

FIGURE 1. The effect of adjunctive, intermittent pneumatic compression (IPC) on initial decongestive lymphatic therapy (DLT) in patients with breast carcinoma-associated lymphedema. The data depict the percent reduction in volume of the limb attained after 10 days of daily therapy with either 1) DLT plus IPC or 2) DLT alone. The data are provided as the mean ± standard deviation for each group. The asterisk denotes a statistically significant difference ($P < 0.05$, unpaired *t*-test).

Data Analysis

Data were assessed using both paired and unpaired *t*-test and analyses of variance.

RESULTS

Study 1

Demographics

Twenty-three women with arm lymphedema were recruited into the study. The mean patient age was 66.9 years (range, 47–81 years), and the average duration of untreated arm lymphedema was 48.3 months (range, 3–180 months). For these patients, the average time elapsed from breast carcinoma therapy was 144.1 months (range, 11–408 months). Sixteen of 23 patients had undergone adjunctive radiation therapy. Seven patients had a history of recurrent cellulitis, and eight patients had a history of hypertension.

Clinical responses

Twelve patients were randomized to Group I (DLT plus IPC), and 11 patients were randomized to Group II (DLT alone). After 2 weeks of treatment, the mean percent reduction in volume of the edematous arm was 45.3% for Group I and 26% for Group II ($P < 0.05$, Fig. 1). The therapeutic benefits were durable: after the completion of intensive therapy, at Day 40, the mean % volume reduction was 30.3% (range, − 13% to 83%) for Group 1 and 27.1% (range, − 23% to 59.5%) for Group 2. These results were not significantly different compared with the outcomes noted at Day 10. For each treatment group, the serial tonometry mea-

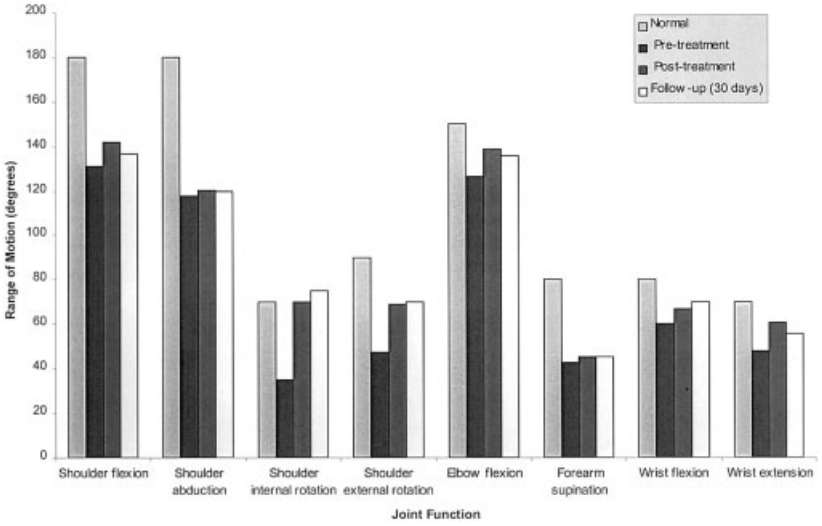

FIGURE 2. The effect of therapeutic choices on joint mobility after initial decongestive therapy and after 30 days of follow-up. All range-of-motion determinations were obtained by standard goniometry. The graph depicts the data derived from those patients who presented with an initial pretreatment impairment of joint mobility. Because the number of patients from Group II with preexisting mobility problems was small (see Table 1), the data represent the aggregate measurements from patients in both Group I and Group II. The patients who presented without an initial impairment of joint mobility did not change during or after therapy and are not shown.

surements of skin elasticity revealed no significant differences between the pretreatment values and posttreatment values (paired *t*-test). Furthermore, a comparison between DLT plus IPC (2.4 mm ± 0.7 mm) and DLT alone (2.3 mm ± 5.7 mm) revealed no significant difference (unpaired *t*-test).

Adverse effects

The addition of IPC to standard DLT techniques was well tolerated almost universally. In one instance, a patient from Group II repetitively experienced headache and modest increases blood pressure during pneumatic compression pump therapy.

Goniometry

To examine the potential for adverse consequences of IPC on joint mobility, we examined the effect of the adjunctive therapy on the subgroup of individuals who presented with impaired upper extremity range of motion at the time of randomization. Shoulders, elbows, and wrists were evaluated by goniometry along with forearm supination. Eleven of 23 patients in Study I (48%) had objective evidence of impaired range of motion at baseline. Of these, eight patients were randomized to receive DLT plus IPC therapy (Group I), and three patients received DLT only (Group II).

After patients received therapy for initial volume reduction, joint mobility improved uniformly ($P = 0.011$; baseline compared with posttreatment), without regard to treatment group (Fig. 2). There were no significant differences among the changes observed at the conclusion of treatment (Day 10) and at Day 40.

Study 2

Demographics

Twenty-seven patients were recruited for the study, with a mean age of 65.9 years (range, 43–81 years). The average duration of lymphedema was 60 months (range, 3–480 months), and the average time from surgery was 113.7 months. Twenty-five of 27 patients completed the study. Two patients voluntarily withdrew.

Clinical responses

During the month of self-administered maintenance therapy with DLT alone, there was a mean ± standard deviation increase in volume of the treated limb of 32.7 ± 115.2 mL. There was no apparent effect of treatment order. Conversely, during the month of therapy that included self-administered, adjunctive IPC, without a perceptible effect of treatment order, there was a mean volume reduction of 89.5 ±195.5 mL ($P < 0.05$; Fig. 3). Tonometry performed at the conclusion of Study II revealed no significant difference between the group that was randomized to receive IPC first (2.2 mm ± 0.6 mm) and the group that was randomized to receive DLT first (1.9 mm ± 0.8 mm; unpaired *t*-test). There were no adverse responses observed to maintenance IPC.

Follow-up study

Of 25 patients who completed Study 2, 20 patients elected to continue the use of the pump as an adjunct to their daily maintenance DLT. One patient died during the follow-up study; the remaining 24 patients were available for follow-up reassessment at 6 months. Nineteen of those 24 patients continued to

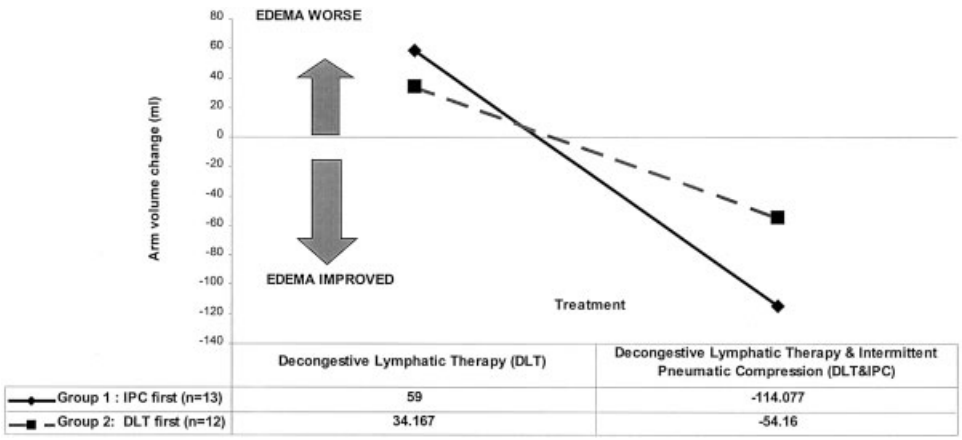

FIGURE 3. The effect of therapeutic choices on edema volume after chronic maintenance therapy in patients with breast carcinoma-associated lymphedema. The two therapeutic regimens were assessed in a 1-month, cross-over design. For decongestive lymphatic physiotherapy (DLT) alone, without an effect of treatment order, the patients in both randomized groups experienced a slight mean increase in edema volume, as detected by water displacement volumetry. in contrast, DLT combined with intermittent pneumatic compression, without regard to the treatment order, yielded a mean additional decrease in edema volume. The data are provided as the mean ± standard deviation for each group. The asterisk denotes a statistically significant difference ($P < 0.05$; paired *t*-test).

use the pump at the time of reevaluation, with an average reported frequency of 4 times per week.

In these 19 patients, there was a subsequent, additional average arm reduction of 29.1 mL compared with the documented limb volume at the conclusion of Study 2: In the 5 patients who elected to discontinue IPC, there was average increase in arm volume of 35 mL. No adverse consequences of IPC were reported.

Range of motion was evaluated at the beginning of the study and at follow-up. Seventeen patients with a pretreatment impairment were available for follow-up analysis. Fifteen of those 17 patients continued IPC at home. All 17 patients continued standard DLT, including self-administered massage and application of the compression garment. Joint mobility improved over time in all patients.

DISCUSSION

Lymphedema of the upper extremity is a common occurrence after patients receive therapeutic interventions for breast carcinoma. Current estimates suggest that secondary lymphedema affects approximately 26% of women who undergo treatment for breast carcinoma.[2] It has been estimated that, currently, approximately 400,000 patients in the United States are afflicted with lymphedema of the upper extremity.[2] This number may represent an underestimate: The definition of lymphedema in some studies often relies on either subjective criteria or objective documentation of lymphedema in the absence of well-defined or widely accepted criteria, and the majority of the available studies on patients with breast carcinoma-associated lymphedema are retrospective. In addition, current prognostic estimates predict an increase in the incidence of breast carcinoma in the United States, from 185,000 per year to 420,000 per year, over the next 20 years.[16] The increasing incidence of breast carcinoma may produce an increase in the incidence of secondary lymphedema despite the developments in breast-conserving surgery and sentinel lymph node biopsy. The increasingly popular approach of sentinel lymph node biopsy is intended to eliminate the necessity for axillary lymph node dissection. However, with 28–46% of eligible patients manifesting a positive sentinel lymph node,[16,17] this approach will not render lymphedema obsolete. Axillary lymph node dissection correlates positively with 10-year survival in breast carcinoma patients[18] and continues to be employed for the majority of patients with early-stage disease.[18]

DLT currently is the most popular treatment for patients with lymphedema. DLT includes MLD and compressive bandaging, which is intended to stimulate cutaneous lymphatic transport, along with decongestive exercises and meticulous skin care.

The physiologic basis for the accentuation of lymphatic flow with IPC has been well established.[19] Similarly, early studies demonstrated an ameliorative effect on lymphatic protein transport.[20] Historically, the pneumatic compression pump often was used as stand-alone therapy for patients with lymphedema and, in all likelihood, was the most frequently prescribed treatment modality for lymphedema in the

United States. The incorporation of IPC into a multidisciplinary, therapeutic approach long has been advocated empirically by some physiotherapeutic schools.[21,22] Numerous early studies purported to demonstrate the efficacy of pumps as a sole therapeutic intervention for patients with lymphedema;[23–27] nevertheless, individual reports of complications and lack of efficacy[28–30] have tended to dampen enthusiasm for the use of IPC. It was to address these unresolved questions that the current study was undertaken.

The results of our investigation suggest that IPC, when it is used as an adjunct to the other established elements of DLT, provides an enhancement of the therapeutic response both in the initial, decongestive phase of therapy as well as in the maintenance of volume reduction. The therapy is well tolerated and remarkably free of complications. The tolerability of this therapy is supported indirectly by the sustained, elective use of IPC among many of the patients who completed our study protocol.

It has been alleged that IPC may contribute both to inappropriate tissue retention of interstitial protein, leading to an excess of cutaneous fibrosis, and to a reduction in joint mobility. Thus, we elected to observe the patients in this investigation for changes in tissue elasticity (as detected by serial tonometry) and for range of motion (by serial goniometry of the large joints of the upper extremity). In neither case was there any evidence of deterioration that might be ascribed to the addition of IPC to the therapeutic regimen.

The results of this investigation support the observation, reported in previous studies,[23–27] that pneumatic compression pumps can be used safely and effectively for the treatment of patients with breast carcinoma-associated lymphedema. Conversely, we were unable to validate published claims that IPC has a deleterious effect on patients who receive prior treatment for lymphedema.[28,29]

The current investigation suggests that the use of IPC can be used effectively in the therapeutic approach to patients with breast carcinoma-associated lymphedema. In view of the important psychosocial ramifications of breast carcinoma-associated lymphedema,[4] the ease of application of IPC as a long-term therapeutic intervention suggests that it may warrant more widespread use in this patient population.

The apparent efficacy and tolerability of IPC warrants additional evaluation of its role in the therapeutic approach to chronic, secondary lymphedema. Certainly, it should be possible to extrapolate our observations obtained in patients with breast carcinoma-associated lymphedema to individuals with other iatrogenic types of acquired lymphedema, including lymphedema as a result of other neoplastic diseases, such as malignant melanoma, lymphoma, and urologic and gynecologic malignancies, among others. In addition, more formal evaluations of the impact on quality of life and the cost of care should be undertaken. Additional limitations of the current studies include the relatively small and clinically diverse sample population. Further study will permit correction for these features and, ideally, will serve to confirm the broader applicability of our observations.

The current study was not designed as a formal evaluation of the cost-effectiveness of IPC, although certain inferences can be drawn. In the initial phases of lymphedema therapy, the addition of IPC to the regimen can be expected to increase slightly the cost of the therapy (although the fixed utilization costs may be offset in part by reductions in the time spent by therapists with the patient). IPC may be expected to have its greatest economic impact in the chronic phase of therapy, during which the device may help to maintain the therapeutic effect in patients who no longer are receiving active interventions by therapists. This, in turn, may translate into a reduction in office visits and, plausibly, reduced use of resources for the evaluation and treatment of recurrent cellulitis. These benefits may be realized best by older or disabled patients who have difficulty with self-bandaging or application of gradient elastic garments. Most third-party payers, including Medicare, currently reimburse patients with breast carcinoma-related lymphedema for pneumatic compression pumps. Clearly, further investigation of the economic implications of this treatment is warranted.

The current study adds an important dimension to the existing literature on therapeutic approaches to the treatment of patients with breast carcinoma-associated lymphedema. Historically, to date, there has been a bias against the use of intermittent pneumatic therapy. The results of our study contradict this bias. In fact, given the availability and ease of use of the pneumatic devices, the documentation of a salutary therapeutic response constitutes a suitable stimulus for further study that may help to confirm the results of our investigation within a larger population of patients. Additional prospective observations may help to identify subpopulations of patients who may benefit most from combination physiotherapy. It will be important to study patient groups with both primary and secondary lymphedema, the latter in relation to a much broader array of malignant diseases.

REFERENCES

1. Segerstrom K, Bjerle P, Graffman S, Nystrom A. Factors that influence the incidence of brachial oedema after treatment of breast cancer. *Scand J Plast Reconstr Surg Hand Surg.* 1992;26:223–227.
2. Erickson V, Pearson M, Ganz P, Adams J, Kahn K. Arm edema in breast cancer patients. *J Natl Cancer Inst.* 2001;93: 96–111.
3. Pecking A, Lasry S, Boudinet A, Floiras J, Rambert P, Guérin P. Postsurgical physiotherapeutic treatment: interest in secondary upper limb lymphedemas prevention. In: Partsch H, editor. Progress in lymphology-proceedings of the XIth Congress in Vienna, 1987. Amsterdam: Elsevier Science, 1988: 561–564.
4. Velanovich V, Szymanski W. Quality of life of breast cancer patients with lymphedema [see discussion]. *Am J Surg.* 1999; 177:184–188.
5. Woods M, Tobin M, Mortimer P. The psychosocial morbidity of breast cancer patients with lymphoedema. *Cancer Nurs.* 1995;18:467–471.
6. Maunsell E, Brisson J, Deschenes L. Arm problems and psychological distress after surgery for breast cancer. *Can J Surg.* 1993;36:315–320.
7. Passik S, Newman M, Brennan M, Holland J. Psychiatric consultation for women undergoing rehabilitation for upper-extremity lymphedema following breast cancer treatment. *J Pain Symptom Manage.* 1993;8:226–233.
8. Rockson SG, Miller LT, Senie R, et al. American Cancer Society Lymphedema Workshop. Workgroup III: diagnosis and management of lymphedema. *Cancer.* 1998;83(Suppl): 2882–2885.
9. Badger CM, Peacock JL, Mortimer PS. A randomized, controlled, parallel-group clinical trial comparing multilayer bandaging followed by hosiery versus hosiery alone in the treatment of patients with lymphedema of the limb. *Cancer.* 2000;88:2832–8327.
10. Szuba A, Cooke JP, Yousuf S, Rockson SG. Decongestive lymphatic therapy for patients with cancer-related or primary lymphedema. *Am J Med.* 2000;109:296–300.
11. Dini D, Del Mastro L, Gozza A, et al. The role of pneumatic compression in the treatment of postmastectomy lymphedema. A randomized Phase III study. *Ann Oncol.* 1998;9:187–190.
12. Kasseroller RG. The Vodder School: the Vodder method. *Cancer.* 1998;83(Suppl):2840–2842.
13. Clodius L, Deak L, Piller NB. A new instrument for the evaluation of tissue tonicity in lymphoedema. *Lymphology.* 1976;9:1–5.
14. Liu NF, Olszewski W. Use of tonometry to assess lower extremity lymphedema. *Lymphology.* 1992;25:155–158.
15. Gajdosik RL, Bohannon RW. Clinical measurement of range of motion. Review of goniometry emphasizing reliability and validity. *Phys Ther.* 1987;67:1867–1872.
16. Cox C, Bass S, McCann C, et al. Lymphatic mapping and sentinel lymph node biopsy in patients with breast cancer. *Annu Rev Med.* 2000;51:525–542.
17. Giuliano AE, Haigh PI, Brennan MB, et al. Prospective observational study of sentinel lymphadenectomy without further axillary dissection in patients with sentinel node-negative breast cancer. *J Clin Oncol.* 2000;18:2553–2559.
18. Bland KI, Scott-Conner CE, Menck H, Winchester DP. Axillary dissection in breast-conserving surgery for Stage I and II breast cancer: a National Cancer data base study of patterns of omission and implications for survival [see discussion]. *J Am Coll Surg.* 1999;188:586–596.
19. McGeown JG, McHale NG, Thornbury KD. Effects of varying patterns of external compression on lymph flow in the hindlimb of the anaesthetized sheep. *J Physiol.* 1988;397:449–457.
20. Zelikovski A, Manoach M, Giler S, Urca I. Lympha-press A new pneumatic device for the treatment of lymphedema of the limbs. *Lymphology.* 1980;13:68–73.
21. Leduc O, Leduc A, Bourgeois P, Belgrado JP. The physical treatment of upper limb edema. *Cancer.* 1998;83(Suppl): 2835–2839.
22. Brennan MJ, Miller LT. Overview of treatment options and review of the current role and use of compression garments, intermittent pumps, and exercise in the management of lymphedema. *Cancer.* 1998;83(Suppl):2821–2827.
23. Zanolla R, Monzeglio C, Balzarini A, Martino G. Evaluation of the results of three different methods of postmastectomy lymphedema treatment. *J Surg Oncol.* 1984;26: 210–213.
24. Richmand DM, O'Donnell TF Jr., Zelikovski A. Sequential pneumatic compression for lymphedema. A controlled trial. *Arch Surg.* 1985;120:1116–1119.
25. Kim-Sing C, Basco VE. Postmastectomy lymphedema treated with the Wright linear pump. *Can J Surg.* 1987;30: 368–370.
26. Klein MJ, Alexander MA, Wright JM, Redmond CK, LeGasse AA. Treatment of adult lower extremity lymphedema with the Wright linear pump: statistical analysis of a clinical trial. *Arch Phys Med Rehabil.* 1988;69(3 Pt 1):202–206.
27. Pappas CJ, O'Donnell TF Jr. Long-term results of compression treatment for lymphedema [see discussion]. *J Vasc Surg.* 1992;16:555–556,562–564.
28. Foeldi E, Foeldi M, Clodius I. The lymphedema chaos: a lancet. *Ann Plast Surg.* 1989;22:505–515.
29. Casley-Smith JR. Modern treatment of lymphoedema. I. Complex physical therapy: the first 200 Australian limbs. *Australas J Dermatol.* 1992;33:61–68.
30. Boris M, Weindorf S, Lasinski BB. The risk of genital edema after external pump compression for lower limb lymphedema. *Lymphology.* 1998;31:15–20.