The efficacy of complex decongestive physiotherapy (CDP) and predictive factors of response to CDP in lower limb lymphedema (LLL) after pelvic cancer treatment

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Objective. The aim of this study was to estimate the efficacy of an intensive CDP program, as well as to identify the predictors associated with lymphedema severity and response to CDP in lower limb lymphedema (LLL) after pelvic cancer therapy.

Methods. We performed a retrospective review of post-pelvic cancer LLL patients that were treated with a CDP program between January 2004 and March 2011.

Results. Twenty-seven (61.4%) of the total 44 patients had cervical cancer, 9 (20.5%) had endometrial cancer, and 8 (18.2%) had ovarian cancer. The mean age was 62.2 years, 18 (40.9%) patients received radiotherapy and a mean of 12.6 sessions of daily CDP, and mean lymphedema duration was 34.8 months. The interval from pelvic cancer treatment to LLL development was 63.4 months. Lymphedema severity, baseline and post-CDP percentage of excess volume (PEV) were 32.9%±18.4% and 18.8%±16.7%. Baseline PEV was not correlated with duration of lymphedema, number of CDP sessions, age or radiotherapy, and was significantly different to post-CDP PEV (p<0.001). CDP efficacy, percentage reduction of excess volume (PREV), was −55.1%, and was correlated with baseline PEV, but not with the number of CDP sessions, duration of lymphedema, or age. PEV (p<0.001) was the only predictive factor for CDP efficacy.

Conclusions. The key to predicting successful lymphedema treatment of LLL is the initial PEV. The intensive CDP program was effective and successful. We should encourage and refer patients to undergo treatment for LLL, even when the LLL is mild.

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Introduction

Lymphedema can be defined as the abnormal accumulation of protein-rich interstitial fluid that occurs primarily as a consequence of malformation, dysplasia or acquired disruption of the lymphatic circulation [1]. Breast cancer-related lymphedema (BCRL) is the most common morbidity in women with breast cancer; it increases psychosocial maladjustment and physical morbidity, and affects the quality of life (QOL). Lower-limb lymphedema (LLL) is a common long-term complication that further decreases the QOL of gynecological cancer survivors [2,3], but it has received less attention than BCRL.

Several studies have reported the benefits of CDP in LLL, with a percentage reduction of excess volume between 31% and 73.4%, depending on the different severities of lymphedema and the number of CDP sessions, but some studies were of mixed LLL and BCRL [7–9]. Few studies have focused on the predictive factors of CDP efficacy and lymphedema severity in LLL. Only one study, by Yamamoto, reported that the degree of lymph node dissection tended to influence the rate of edema reduction and that no correlation was found between duration of lymphedema and the number of CDP sessions or CDP efficacy [7]. Our hospital, Changhua Christian Hospital in central Taiwan, established CDP therapy for lymphedema in 2002 in response to the needs of an increasing number of post-cancer lymphedema patients. The aim of this retrospective cohort study was to summarize our 8-year experience with LLL and estimate the efficacy of an intensive therapy, exercise, and skin care [5]. CDP is separated into the intensive phase and the maintenance phase. The intensive phase of treatment comprises a course of daily exercise and MLD to decongest the lymphedematous area of the body, followed by multiple-layer short stretch bandaging to prevent the reaccumulation of fluid and create a counter-force to muscle contraction in order to promote lymph flow [1,5,6], and skin care. The compression garment replaces bandaging in the maintenance phase.

The key to predicting successful lymphedema treatment of LLL is the initial PEV. The intensive CDP program was effective and successful. We should encourage and refer patients to undergo treatment for LLL, even when the LLL is mild.
CDP program, as well as to identify the predictors associated with lymphedema severity and response to CDP in LLL after pelvic cancer therapy.

**Materials and methods**

After obtaining institutional review board (IRB) approval, we performed a retrospective review of patients with LLL after pelvic cancer who were treated with a CDP program in the Department of Physical Medicine and Rehabilitation, Changhua Christian Hospital between January 2004 and March 2011, to indentify the efficacy of CDP therapy and the independent predictive factors of response to CDP and LLL severity.

The 66 female patients with LLL that were referred for CDP therapy were enrolled in this study. For the purpose of this study, lymphedema was defined as a percentage of excess volume (PEV) larger than 5% [10]. Of the 66 patients, 22 were excluded because they had bilateral lymphedema, cancer recurrence, active infection, concomitant venous occlusion, or PEV<5%. In the end, 44 female patients with unilateral LLL who underwent the CDP program were included in our review.

All patients underwent an intensive CDP program of 10–24 sessions depending on lymphedema severity. The CDP program included four components: 45 min of MLD, then compression therapy with a short stretch bandage for 23 h per day, remedial exercise to facilitate venous and lymphatic flow, and instructions for skin and nail care.

On initial assessment, both legs were measured. The affected leg was measured at the start and end of the intensive phase of CDP. Circumferential measurements were done at the metatarsophalangeal joint and the ankle, and repeated every 10 cm proximally from the heel pad to the maximum height. The volume of each limb was calculated from the circumference using with the truncated cone formula [11]. The reliability and specificity of the calculated volume has already been established [12].

The severity of lymphedema is defined as the PEV, the excess volume (the difference between lymphedema leg (VL) and healthy leg (VH)) relative to the healthy leg volume. PEV = (baseline VL-VL)/(VH×100%). The PEV is better for delineating the severity of lymphedema than the absolute difference volume [5,7,8]. The mean interval from pelvic cancer treatment to leg lymphedema was 176.4±1037 ml, and the lymphedema severity-PEV was 32.9%±18.4% (range 5.8–66.5%), which was moderate lymphedema based on the ISL definition (International Society of Lymphology, 2009) [13]. The baseline PEV was not reduced by half with 12 sessions of CDP therapy (Table 3). Lymphedema severity was improved to mild lymphedema after 24 sessions of CDP (Table 3).

Results

The baseline characteristics and lymphedema severity of 44 patients are listed in Table 1. Twenty-seven (61.4%) patients had cervical cancer, 9 (20.5%) had endometrial cancer, 8 (18.2%) had ovarian cancer, 18 (40.9%) patients received radiotherapy, and 43 (97.7%) patients receiving lymphectomy. The mean age was 62.2±11.8 (range 38–83) years, 12.6±3 sessions (range 10–24) of daily CDP, and the lymphedema duration when the patient was referred to CDP therapy was 34.8±50.3 (range 1–192) months. Because some patients received pelvic cancer therapy in other hospitals, the complete pathology reports were not available.

The mean interval from pelvic cancer treatment to leg lymphedema development was 63.4±64.9 (range 0–240) months, and the median interval was 36 months; 52% of lower limb lymphedema cases occurred within three years after surgery.

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In the post-CDP programs, lymphedema volume decreased 755±557 (range 2430–(−265)) ml. PEV was 18.8%±16.7% (range (−5)–69.8%), which was significantly different to baseline PEV (p<0.001) (Table 3). Lymphedema severity was improved to mild lymphedema post-CDP therapy [13]. The CDP efficacy, PREV, was −55.1%±39% (range (−188)–8%), meaning that the edema volume could be reduced by half with 12 sessions of CDP therapy (Table 3).

After univariate and multivariate analysis using Pearson Correlation, PREV was found to be correlated with PEV, but not with the number of CDP sessions, duration of lymphedema and age (Table 4). In linear regression, we found that PEV (p<0.001) was the only predictive factor of interest. The categorical variables were analyzed by independent T-test and one-way ANOVA. Continuous factors associated with PEV and PREV were initially identified by Pearson correlation. Factors, and a p value<0.05 was chosen to determine the final predictive factors in multivariate linear regression analysis.

All analyses were performed using SPSS Version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). A p value less than 0.05 was considered as statistically significant.

**Statistical analysis**

Descriptive statistics (including mean, range, frequency and percent) are presented for demographic and clinical/treatment factors.
The latency period from surgery to the onset of lymphedema was 63 months; 52% of lymphedema cases occurred within 3 years of surgery, and only 25% developed within 1 year. The latency period was longer than that in other reports. Both Ryan et al. [14] and Beesley et al. [4] confirmed that most lymphedema diagnoses occurred within the first year after gynecological cancer diagnosis (84% and 75%, respectively). Only Szuba et al. had findings similar to ours; the interval from surgery to lower limb lymphedema onset was 76 months, but there were only 12 patients in the study [8]. Since ours was a retrospective analysis, it was difficult to identify the exact time of occurrence of lymphedema due to patient recall errors. LLL occurs unconsciously and is not as noticeable as arm lymphedema, and different patients’ group because our patients were the most refractory cases of LLL referred to specialized centers.

We used PEV, not absolute excess volume, to calculate lymphedema severity, so as to exclude the confounding factors of individual body shape and weight [5]. The baseline PEV was 32.9%, which was moderate lymphedema according to the ISL definition [13]. Our patients’ lymphedema severity (PEV) improved from 32.9% to 18.8% after CDP therapy, or from moderate to mild lymphedema. The lymphedema reduction after 12.6 sessions of CDP was ~55.1%, so treatment was successful using Ramos’s definition [17]. This study showed the effectiveness of a limited intervention of 12 CDP sessions, as we reported before [18]. PEV was not correlated with the number of CDP sessions in this study, because most of the lymphedema volume reduction occurs in the first 10 days of CDP therapy and after this, much less reduction will be achieved [19]. The purpose of undergoing more than 12 sessions is to relieve the fibrotic tissue and maintain superficial lymphatic drainage, not further reduce edema volume [11], as in the 4-week intensive CDP program suggested by Földi M and Casley-Smith [11,20].

PEV was the only predictor of PREV in our study; in other words, a lower PEV would predict a better response to CDP. Ramos SM reported that edema volume, not timing, was the key to success in lymphedema treatment [17]. But he compared only the absolute excess volume of 3 groups (≤250 ml, 250–500, >500 ml), and did not conduct linear regression analysis of both factors. We found that PEV of LLL could predict CDP efficacy in linear regression analysis; Forner-Cordero I reached the same conclusion in treating BCRL [5]. Yamamoto R reported that the degree of lymph node dissection tended to influence PREV in patients with LLL, and that removing only the pelvic lymph nodes had better CDP efficacy than removing pelvic and para-aortic lymph nodes [7]. We did not record the lymph node dissection status because complete pathology reports were not available for some patients that received cancer therapy in other clinics.

We found no significant relationship between duration of lymphedema and PEV, or PREV, indicating that duration of LLL would affect neither lymphedema severity nor CDP efficacy. Yamamoto R [7], Vignes S et al. [21] and Ramos SM [17] also reached a similar conclusion, that duration of lymphedema was not associated with PREV. Yamamoto R thought that duration of lymphedema was not correlated with disease stage, or in other words, duration of LLL would not affect the skin, subcutaneous tissue or the fascia [7]. However, studies on BCRL reported the opposite conclusion: Bar AdV et al. [22] reported the progression rate of mild lymphedema to more severe lymphedema was 21% at 1 year and 34% at 3 years; and Casley-Smith JR reached a similar conclusion [16]. We think that the differences in conclusion are due to the large variation in duration of lymphedema in our patients (from 1 to 198 months), the mean duration not being able to act as a substitute for the whole study group, the differences pathological change between BCRL and LLL, and the small patient number; a prospective follow-up result for LLL of pelvic cancer is still needed.

Although radiation has been proved to increase the risk of LLL in gynecological cancer, radiation did not affect PEV or PREV in our study, as Ryan M and Tada H reported [14,15].

We know that bandage compliance is a major factor for CDP efficacy. Badger GM reported that multilayer bandaging achieves greater and more sustained limb volume reduction than hosiery alone [23]. Forner-Cordero I concluded that good bandage compliance improved PREV by 25%, compared with fair or bad compliance in BCRL patients [5]. However, there is no report on the effect of bandage compliance on CDP efficacy in LLL patients. The weather and temperature will affect patient compliance with compression therapy, so the seasons were substituted for bandaging compliance in our analysis. We found that there was no difference in CDP efficacy in different seasons.

Although body mass index (BMI) was not recorded in our analysis, BMI has been reported to be associated with CDP efficacy and lymphedema severity, and is a risk factor for developing BCRL [5,24]. However, there is no strong evidence linking BMI and post-cancer LLL [7]. Only Hinrichs CS [25] found that elevated BMI was associated with a decreased response to CDP, but they reported only 14 patients after groin dissection for melanoma and almost all patients were overweight; only one patient had a BMI <25.

The limitations of this study are (a) it was a retrospective cohort study, (b) bandage compliance, BMI and pelvic cancer treatment characteristics (radiation dose, and pathology results) were not recorded, and (c) QOL was not included.

Discussion

Among our lymphedema patients, 61% were cervical cancer patients; there was no vulvar cancer. Because the incidence of LLL in cervical cancer is the highest in pelvic cancer groups [14,15], and cervical cancer was the most predominant cancer in the past in Taiwan, the number of cervical cancer patients was 2-fold the number of endometrial-added ovarian cancer patients before 2000. Vulvar cancer is seldom seen in Taiwan, although the lymphedema incidence with vulvar cancer is nearly 50% [4].

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Conclusion

The key to predicting successful lymphedema treatment for LLL is the initial PEV. The intensive CDP program is effective and successful. The duration of LLL did not affect lymphedema severity and CDP
aggressive therapy. Although, by some criteria, a PEV may seem to be slight or not very significant, it is precisely these patients that can benefit the most from aggressive therapy.

**Conflict of interest statement**
The authors do not have any conflicts to disclose.

**References**


