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ORIGINAL ARTICLE

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Effectiveness of the treatment-phase of two-phase complex decongestive physiotherapy for the treatment of extremity lymphedema

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Abstract
Background. Complex decongestive physiotherapy (CDP) consists of a two-phase treatment program and is the international standard therapy for lymphedema. However, this therapy is not performed at most hospitals in Japan.
Methods. The subjects of the present study were 82 Japanese women with lymphedema of an extremity (median age, 64 years; range, 40–86 years). The volume of the affected extremity was compared before and after therapy, and the duration of the CDP treatment phase and rate of edema reduction were ascertained. The associations between the effect of CDP and duration of lymphedema, operative procedure, and radiotherapy were also investigated.
Results. For patients with upper-extremity lymphedema, the median duration of the CDP treatment phase was 6 treatment days (range, 3–26 days), median reduction of edema volume was 328.7 ml (range, 76.6–1258.0 ml; $P = 0.0014$), and median rate of edema reduction was 58.9% (range, 42.7%–97.1%). For patients with lower-extremity lymphedema, the median duration of the CDP treatment phase was 10 treatment days (range, 2–35 days), median reduction of edema volume was 1573.7 ml (range, 293.9–3471.1 ml; $P < 0.0001$), and median rate of edema reduction was 73.4% (range, 29.2%–117.3%). Although no correlation was seen between duration of lymphedema and duration of the CDP treatment phase or rate of edema reduction, the degree of lymph node dissection tended to influence rate of edema reduction in patients with lower-extremity lymphedema.
Conclusion. In a study of Japanese women with lymphedema, CDP comprising a two-phase treatment program was clearly effective.

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Introduction

In recent years, patients with malignancies have undergone surgery and/or radiotherapy that is intended not only to cure but also to conserve quality of life (QOL) and prevent complications.[1–3] Lymphadenectomy, performed during the resection of malignant tumors, is known to be a factor precipitating secondary lymphedema,[4] and studies have been actively conducted on sentinel lymph nodes to avoid broad lymphadenectomy in various malignancies.[5,6] However, except in certain countries, including Germany, little interest has been shown in lymphedema that has already occurred, and in many countries, conservative therapy for lymphedema is not covered by insurance.

The International Society of Lymphology has stated that "complex decongestive physiotherapy (CDP) is backed by longstanding experience and generally involves a two-phase treatment program that can be applied to both children and adults".[7] This indicates that CDP is effective for lymphedema, and unlike surgery, long-term efficacy can be expected without severe adverse effects. However, only a very small number of institutions in Japan currently perform two-phase CDP, as its effectiveness has not been well-known. In order to popularize this international therapeutic standard for lymphedema in Japan, we analyzed therapeutic data collected by the Földiklinik for Lymphology (Hamburg, Germany)[8,9] and Lerner Lymphedema Services (New York, USA)[10] and we opened an outpatient clinic for lymphedema in Sapporo, in September 2005.

At our clinic, only a small number of patients have been followed for more than 1 year after CDP, and reliable statistical analysis of long-term prognosis is not possible at this point in time. The present study therefore prospectively investigated the duration of the CDP treatment phase, the rate of edema reduction, and the adverse effects of two-

phase CDP, comprising treatment and maintenance phases for lymphedema, in Japanese women. As the duration of lymphedema, degree of lymph node dissection, and radiotherapy have been reported to affect the duration of the CDP treatment phase,[11] the effects of these factors on CDP response were therefore assessed.

Patients and methods

A total of 222 patients with extremity edema visited our clinic from September 1, 2005, to October 31, 2006, and all underwent complete medical evaluations. After the exclusion of those with edema caused by lymph node metastasis or recurrent malignancy and those with terminal cancer requiring palliative care, there were 82 patients with extremity edema in whom two-phase CDP was indicated. These patients were the subjects of the study (median age, 64 years; range, 40–86 years; median body mass index [BMI], 24.05; range, 14.3–35.5; Table 1). All 82 patients were Japanese women, with upper-extremity lymphedema in 27 patients and lower-extremity lymphedema in 55 patients. All patients with upper-extremity lymphedema displayed secondary lymphedema, whereas 3 patients with lower-extremity lymphedema had primary lymphedema and the other 52 had secondary lymphedema. One of the patients with secondary lower-extremity lymphedema underwent radiotherapy for pelvic bone metastases originating from breast cancer. The onset of lymphedema was determined by interviewing each patient, and the median duration from lymphedema onset to the start of CDP was 20.0 months (range, 1–444 months). The median duration from surgery to the start of CDP was 69.5 months (range, 2–588 months). The surgery date was ascertained from reports submitted by referring medical institutions. After the onset of lymphedema, many patients did not respond to gradient compression garments or pneumatic compression therapy. However, the present study did not take into account such pretreatments, as obtaining accurate information regarding pretreatments (size and pressure and duration of using gradient compression garments, and use of pneumatic pumps) at other facilities would have been difficult.

At our institution, CDP is performed based on a two-phase treatment program, consisting of treatment and maintenance phases, which has been reported as the Földi technique.[11–13] The treatment phase (phase 1) consists of the following four steps: meticulous skin care; manual lymph drainage; compression bandaging; and remedial exercises.[12] This treatment, intended to shrink an affected extremity, is performed on an outpatient basis, and as a general rule is performed daily for 60–90 min/day. However, because the treatment is performed on an outpatient basis, attending the clinic daily is not easy, and the clinic is not open 365 days a year. Hence, in the present study, patients who underwent therapy on3 or more days/week were enrolled.

As far as the adverse effects of CDP are concerned, therapy was immediately discontinued if there was fever or pain and dermal redness occurred in the affected extremity, and the presence or absence of cellulitis was then investigated. In the case of pruritus, rash, urticaria, or pain, thorough diagnostic interviews and observations were performed,

Table 1. Patient characteristics and causes of lymphedema[a]

Number of patients	82
Age (years)	64[b] (40–86)
BMI	24.05[b] (14.3–35.5)
Duration of lymphedema (months)	20[b] (1–444)
Primary lymphedema	3
Secondary lymphedema	79
Upper extremity lymphedema	27
Breast cancer treatment	27
Lumpectomy, axillary node sampling, and RT	4
Mastectomy and axillary dissection	11
Mastectomy, axillary dissection, and RT	12
Lower extremity lymphedema	52
Endometrial cancer treatment	25
mRH, BSO, and PLN + PAN dissection	22
Operation above and RT	3
Cervical cancer treatment	13
RH, BSO, and PLN dissection	8
Operation above and RT	5
Ovarian cancer treatment	8
mRH, BSO, and PLN + PAN dissection	8
Other cancers	6
Radical operation	3
Radical operation and RT	3

Numbers in parentheses are ranges
mRH, Modified radical hysterectomy; BSO, bilateral salpingoophorectomy; PLN, pelvic lymph node; PAN, paraaortic node; RH, radical hysterectomy; RT, radiotherapy
[a] Patients treated between September 1, 2005 and October 31, 2006
[b] Median values

and CDP was discontinued when there were events of grade 2 or higher in accordance with the National Cancer Institute Common Terminology Criteria for Adverse Events.

The volume of the affected limb was assessed by measuring the circumference at a total of seven locations for upper extremities (elbow: 10, 15, and 20 cm above the elbow, and 10, 15, and 20 cm below the elbow) and seven locations for lower extremities (knee: 10, 20, and 30 cm above the knee and 10, 20, and 30 cm below the knee). Extremity volume was calculated using a formula reported by Casley-Smith:.[14]

$$V = h(C^2 + Cc + c^2)/12\pi$$

where V is the volume of an extremity segment, C and c are circumferences at each end, and h is the distance between the ends. The rate of edema reduction (%) was calculated using the following formula

(Affected extremity volume after therapy–affected extremity volume before therapy)/(affected extremity volume before therapy–unaffected extremity volume) × 100

The Mann-Whitney *U*-test was used to statistically assess changes in volume of the affected extremity before and after therapy.

During the maintenance phase, the aim was to conserve and optimize the results obtained in the treatment phase. Patients were therefore quickly transitioned from the treatment phase to the maintenance phase when no further improvements in lymphedema were seen in terms of affected extremity volume or findings on ultrasonography. Figure 1 shows macroscopic findings for a patient with secondary lymphedema of the right leg on each day of the treatment phase and changes in ultrasound findings at 10 cm below the

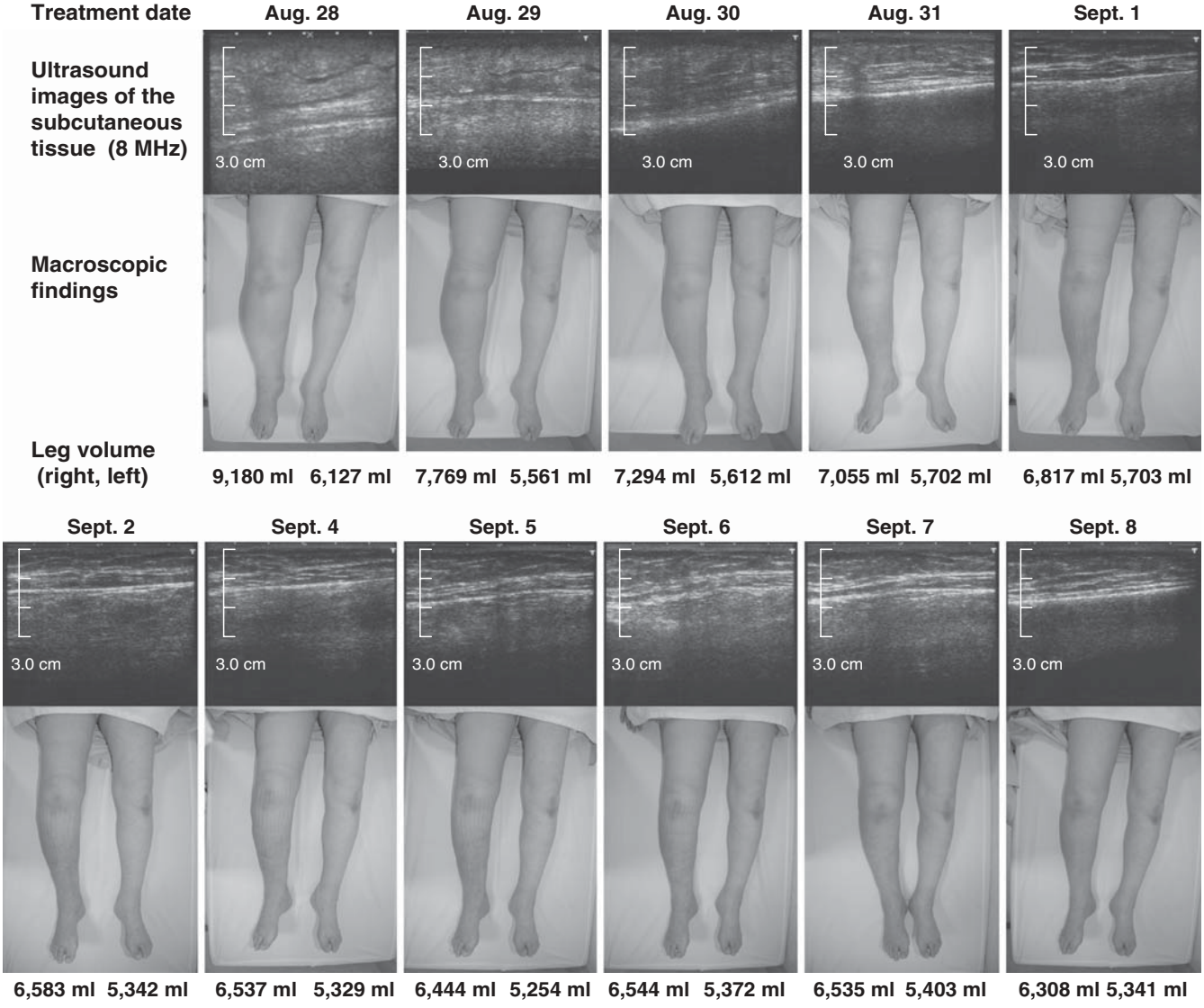

Fig. 1. Changes in volume of the left and right legs and changes in ultrasound images of subcutaneous tissue 10 cm below the right knee on each day of the complex decongestive physiotherapy (CDP) treatment phase in a patient with secondary lymphedema of the right leg who displayed a typical clinical course

knee, and changes in the volume of the left and right legs. Written informed consent was obtained from the patient whose photographs are included.

We then investigated relationships between duration of lymphedema and length of time following surgery. Also, relationships between duration of lymphedema and both the duration of the CDP treatment phase and the rate of edema reduction during the treatment phase were investigated in the 27 patients with upper-extremity lymphedema and the 55 patients with lower-extremity lymphedema. Due to the small number of subjects, distribution analysis was not possible, but Pearson product-moment correlation coefficients were used to assess statistically significant correlations.

In the present study, treatments that caused secondary lymphedema were classified from the perspective of degree of lymph node dissection and radiotherapy, and the effects of these two factors on CDP response, i.e., duration of the CDP treatment phase and rate of edema reduction, were investigated. Among the breast cancer patients, treatments were classified into three groups: axillary node sampling and radiotherapy; axillary dissection alone; and axillary dissection and radiotherapy. Among patients with endometrial cancer, cervical cancer, ovarian cancer, and other cancers, lymph node surgeries were classified into three groups: pelvic lymph node dissection; pelvic lymph node and paraaortic node dissection; and groin dissection. Each of the three groups was then subdivided into two groups with respect to radiotherapy, and data were compared among the six groups.

Statistical analyses were conducted using StatView J-5.0 PPC software (SAS Institute, Cary, NC, USA). The level of significance was set at $P < 0.05$.

Results

For patients with upper-extremity lymphedema, the volume of the affected extremity decreased significantly during the treatment phase, with a median of 6 treatment days (range, 3–26 days), from 2118.8 ml (range, 1359.0–3777.3 ml) to 1745.8 ml (range, 1030.3–2837.8 ml; $P = 0.0014$). Hence, the volume change was 328.7 ml (range, 76.6–1258.0 ml) and the rate of edema reduction was 58.9% (42.7–97.1%; Table 2). For patients with lower-extremity lymphedema, the volume of the affected extremity decreased significantly during the treatment phase, with a median of 10 treatment days (range, 2–35 days), from 8221.6 ml (range, 4387.5–12 451.0 ml) to 6578.3 ml (range, 4093.7–9585.3 ml; $P < 0.0001$). Volume change was thus 1573.7 ml (range, 293.9–3471.1 ml) and the rate of edema reduction was 73.4% (range, 29.2%–117.3%; Table 3).

None of the patients developed cellulitis during the therapy. Regarding grade 1 adverse effects, pruritus was seen on the lower extremity in three patients and on the upper extremity in one patient; rash was seen on the leg in one patient; urticaria was seen on the lower extremity in one patient; and pain occurred in the lower extremity in one patient. However, CDP was not discontinued because of adverse effects of grade 2 or above in any of the patients.

Figure 1 shows results in a patient with lymphedema of the right leg. During an 11-day treatment phase, the patient underwent ten treatments, achieving a reduction rate of 74.8%. Hence, based on the above statistical analysis, this patient displayed a typical clinical course. For this patient, the volume of edema reduction throughout the treatment phase was 2872 ml, and the reduction rate was 49.1% after

Table 2. Therapeutic results during the treatment phase (upper extremity)

Number of patients, 27	Median	Range
Duration of the CDP treatment phase (days)	6	(3–26)
Affected extremity volume before therapy (ml)	2118.8[a]	(1359.0–3777.3)
Unaffected extremity volume before therapy (ml)	1596.7	(996.4–2992.9)
Affected extremity volume after therapy (ml)	1745.8[b]	(1030.3–2837.8)
Unaffected extremity volume after therapy (ml)	1511.7	(968.4–2777.8)
Reduction in volume (ml)	328.7	(76.6–1258.0)
Rate of edema reduction (%)	58.9	(42.7–97.1)

a vs b, $P = 0.0014$ (Mann Whitney *U*-test)
CDP, Complex decongestive physiotherapy

Table 3. Therapeutic results during the treatment phase (lower extremity)

Number of patients, 55	Median	Range
Duration of the CDP treatment phase (days)	10	(2–35)
Affected extremity volume before therapy (ml)	8221.6[a]	(4387.5–12 451.0)
Unaffected extremity volume before therapy (ml)	6188.1	(3408.7–10 577.3)
Affected extremity volume after therapy (ml)	6578.3[b]	(4093.7–9585.3)
Unaffected extremity volume after therapy (ml)	6022.4	(3382.3–9248.9)
Reduction in volume (ml)	1573.7	(293.9–3471.1)
Rate of edema reduction (%)	73.4	(29.2–117.3)

a vs b, $P < 0.0001$ (Mann-Whitney *U*-test)
CDP, Complex decongestive physiotherapy

Table 4. Analysis of the association between the effect of CDP, degree of lymph node dissection, and radiotherapy

Treatment	No. of patients	Median age in years (range)	Duration of CDP treatment phase (days)	Rate of edema reduction (%)
Axillary node Sampling and RT	4	52 (43–56)	5.5 (3–26)	63.3 (45.8–96.5)
Axillary dissection	11	66 (47–84)	7 (4–23)	59.1 (43.3–91)
Axillary dissection and RT	12	67.5 (45–86)	5.5 (3–18)	57.2 (42.7–97.1)
PLN dissection	9	58 (41–79)	10 (3–26)	88.3 (60.8–112.2)[a]
PLN + PAN dissection	31	63 (40–78)	10 (2–35)	70.4 (29.2–97.1)[b]
Groin dissection	1	45	16	98.1
PLN dissection and RT	6	52.5 (43–68)	12 (4–16)	77.4 (35–85.6)
PLN + PAN dissection and RT	3	66 (66–67)	8 (5–10)	72.7 (64.8–73.4)
Groin dissection and RT	1	51	5	67.2

a vs b, $P = 0.0501$ (Mann-Whitney *U*-test)
RT, Radiotherapy; PLN, pelvic lymph node; PAN, paraaortic node

treatment day 1 and 90.4% after treatment day 5. Moreover, as shown on ultrasonography, tissue fluid retention at 10 cm below the knee had disappeared by treatment day 3, and the volume of hyperechoic subcutaneous tissue had improved markedly by treatment day 5. No clear changes were seen thereafter.

Among patients with secondary lymphedema, the duration of lymphedema exhibited a positive correlation with length of time after surgery (upper extremity, $r = 0.500$, $P = 0.0085$; lower extremity, $r = 0.849$, $P < 0.0001$). However, no correlation was seen between duration of lymphedema and duration of the CDP treatment phase. Furthermore, no correlation was evident between duration of lymphedema and rate of edema reduction during the treatment phase.

The median rate of edema reduction for patients who had had pelvic lymph node dissection was 88.3% (range, 60.8%–112.2%), and the rate for those with pelvic lymph node and paraaortic node dissection was 70.4% (range, 29.2%–97.1%; $P = 0.0501$) (Table 4).

Discussion

Many treatments for lymphedema have been reported, both operative and nonoperative.[7,10,15–17] The International Society of Lymphology has published a consensus document listing common treatments for peripheral lymphedema.[7] However, in Japan, treatments with a low evidence base that are not listed in this consensus document or in the United States National Library of Medicine are still being performed in a large percentage of lymphedema patients.

Gradient compression garments are essential to maintain edema reduction and compensate for elastic insufficiency of the skin after volume reduction.[17] In a randomized, controlled, parallel-group clinical trial, Badger et al.[18] demonstrated that multilayer bandaging as an initial phase of treatment for lymphedema patients, followed by hosiery, achieved greater and more sustained limb volume reduction than hosiery alone. Many physicians in the field of lymphology are opposed to the use of pneumatic compression devices.[10,11,19] Furthermore, a randomized clinical trial has demonstrated that intermittent pneumatic compression has a limited clinical role in the treatment of postmastectomy lymphedema.[20] In Japan, oncologists occasionally recommend the use of gradient compression garments or self-administered therapy using a pneumatic compression device. However, according to past studies of the treatment of lymphedema,[7–13,15–17,21,22] CDP involving the two-phase treatment program exhibits the highest level of efficacy, with established improvements in long-term prognosis. The use of this treatment in Japan is greatly anticipated.

The results, shown in the present study, are comparable to those obtained in studies conducted in Western countries,[11,13–15] but the duration of the treatment phase appeared to be slightly shorter in the present study. Hinrichs et al.[13] reported that BMI was found to be negatively associated with reduction in edema. The median BMI of the subjects in the present study was 24.05. Thus, compared to the BMI of subjects in previous studies in Western countries,[11,13,21] the subjects in the present study were less obese. This suggests the importance of conducting a large-scale study in Japanese female patients with lymphedema, to establish a standard duration for the CDP treatment phase in Japan.

As the onset of lymphedema after surgery is unpredictable, we anticipated no correlation between duration of lymphedema and length of time after surgery, but a positive correlation existed for both patients with upper-extremity lymphedema and those with lower-extremity lymphedema. However, the duration of lymphedema exhibited no correlation with the duration of the CDP treatment phase or the rate of edema reduction during the treatment phase. This suggests that the duration of lymphedema is not correlated with disease stage,[7] or, in other words, the duration of lymphedema is not correlated with pathological changes in the skin, subcutaneous tissue, or fascia.

As to the effects of the degree of lymph node dissection on CDP response, the rate of volume reduction tended to be greater for patients with lower-extremity lymphedema with narrow lymphadenectomy compared to that in patients with broad lymphadenectomy ($P = 0.0501$), but in order to validate the results, further investigations involving more patients are needed. The present study also included insufficient patients to investigate differences in CDP response with respect to radiotherapy for each treatment, and more patients are needed to assess this issue.

In Japan, some institutions perform manual lymph drainage and/or compression bandaging only once a week.

However, this frequency of therapy is inappropriate, based on the changes in affected extremities shown in Fig. 1. In fact, based on our experience, the affected extremities reverted back to their former condition after 1 week, and no clear reduction in edema could be obtained (data not shown). Moreover, in Japan, to promote self-care by lymphedema patients, guidance on manual lymph drainage and compression bandaging is provided once every 1–3 months. This is similar to the maintenance method for patients in the maintenance phase as reported by the Földiklinik for Lymphology,[12] and is useful for managing treated extremities and in preventing recurrence of lymphedema. However, expecting clear therapeutic effects after instructing patients to self-administer lymphedema therapy during the treatment phase, with limited training, will be difficult.

The reason for the lack of interest in lymphedema therapy at public institutions in Japan is that CDP is not covered by the national healthcare insurance. As CDP involving the two-phase treatment program is covered by insurance in some countries, including Germany, where CDP was developed, some physicians and patients in Japan believe that this is an administrative problem. However, physicians involved with lymphedema therapy should publish details of the treatment programs, numbers of patients treated, and the duration of treatments at their institutions, to establish effective treatments for lymphedema using an evidence-based approach. Such hard work will surely benefit lymphedema patients in Japan.

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