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EFFICACY OF MANUAL LYMPHATIC DRAINAGE IN PREVENTING SECONDARY LYMPHEDEMA AFTER BREAST CANCER SURGERY

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ABSTRACT

This study evaluated the effectiveness of manual lymphatic drainage (MLD) in the prevention of secondary lymphedema after treatment of breast cancer. The study consisted of 67 women, who underwent breast surgery for primary breast cancer. From the second day of surgery, 33 randomly chosen women were given MLD. The control group consisted of 34 women who did not receive MLD. Measurements of the volumes of both the arms were taken before surgery and on days 2, 7, 14, and at 3 and 6 months after surgery. At 6 months after breast cancer surgery, among the women who did not undergo MLD, a significant increase in the arm volume on the operated side was observed (p=0.0033) when compared with the arm volume before surgery. At this time, there was no statistically significant increase in the volume of the upper limb on the operated side in women who underwent MLD. This study demonstrates that regardless of the surgery type and the number of the lymph nodes removed, MLD effectively prevented lymphedema of the arm on the operated side. Even in high risk breast cancer treatments (operation plus irradiation), MLD was demonstrated to be effective against arm volume increase. Even though confirmatory studies are needed, this study demonstrates that MLD administered early after operation for breast cancer should be considered for the prevention of lymphedema.

Keywords: breast cancer, lymphedema, manual lymphatic drainage, prevention

Secondary arm lymphedema is a chronic and distressing condition that affects a significant number of women who undergo breast cancer treatment. It can cause disfigurement, physical discomfort, and functional impairment. Anxiety, depression, and emotional distress are more common in women with secondary lymphedema than those without it. This can affect social relationships, undermining body image and self-esteem. The condition may also precipitate cellulitis, erysipelas, lymphangitis, and occasionally lymphangiosarcoma (1).

A number of health professional- and patient-instigated conservative therapies, including complex physical therapy, manual lymphatic drainage (MLD), pneumatic pumps, oral pharmaceuticals, low-level laser therapy, compression bandaging and garments, limb exercises, and limb elevation aimed to decrease limb swelling and its associated problems, have been developed (2).

It was found that the more intensive and health professional-based therapies such as complex physical therapy, MLD, pneumatic

pump, and laser therapy generally yielded greater volume reductions; while self-instigated therapies such as compression garment wear, exercises, and limb elevation yielded smaller reductions. MLD is a recognized treatment for secondary lymphedema following treatment of breast cancer. Its application can frequently produce a 25% reduction in lymphedema volume. When supplemented with compression bandaging and garments, it is the most effective method of lymphedema treatment, which results in about 45% reduction in lymphedema volume (2).

However, prophylactic use of MLD has caused much discussion and controversy. Some authors consider that its application is unnecessary, pointing to the lack of its effectiveness in preventing lymphedema. Instead, they recommend the use of MLD after the occurrence of edema (3). Still others recommend its implementation as a good method to support the compensation of the damaged lymphatic system (4).

Although efforts have been made to reduce the risk of secondary lymphedema and early physiotherapy is now increasingly used to prevent lymphedema after treatment of breast cancer, serious scientific studies that prove its effectiveness and benefits, which are not clearly known, are lacking (1,5).

A randomized clinical trial on the prevention of secondary lymphedema through early physiotherapy, especially MLD, lacked sufficient evidence (1). Most studies have been concerned with the effectiveness of a comprehensive physiotherapy, including numerous different components. These studies could not distinguish the effects of each component of the intervention, namely, manual lymph drainage, intermittent pneumatic compression, massage of the scar, exercises, and education. Hence, further research is needed to clarify the relative contributions of each of these components for the prevention of lymphedema, and large-scale, high-level clinical trials are needed in this area (5).

This study was designed to evaluate the effectiveness of MLD in the prevention of secondary lymphedema of the upper limb in women after treatment of breast cancer. Its hypothesis is that use of MLD immediately after breast cancer surgery significantly reduces the risk of lymphatic edema of the upper limb.

MATERIALS AND METHODS

The study consisted of 67 women in the age range of 34-81 years, who underwent breast surgery for primary breast cancer in DRK-Kliniken Westend in Berlin. The subjects were fully informed about the study, gave their consent for participation, and this research was performed with the approval of the Ethics Committee. According to the type and the size of the tumor, 40 women were classified for breast-conserving therapy (BCT) and 27 were subjected to modified mastectomy (ME). A total of 32 women received sentinel lymph node dissection (SLND) and 35 received axillary lymph node dissection (ALND). The median number of the removed lymph nodes was 2 (1-10) in the SLND women and 17 (8-29) in the ALND women. As adjuvant therapies, radiation therapy, chemotherapy, or endocrine therapy was used. Forty-seven women (41 individuals in breast field, 1 in axillary field, and 5 in breast and axillary fields) received postoperative external radiation therapy in standard dosage (1.8-2 Gy daily, 5 days a week, 5 weeks + boost 10 Gy). Twenty-eight women received an adjuvant treatment consisting of four series of chemotherapy of CE (cyclophosphamide 600 mg/m^2 + epirubicin 90 mg) or six series of CEF (cyclophosphamide 600 mg/m^2+ epirubicin 60 mg/m^2 + 5-fluorouracil 600 mg/m^2). Treatment with tamoxifen was administered to 33 women. Radiotherapy was planned to be administered 4-6 weeks after surgery, followed by eventual chemotherapy.

From the second day of surgery, a standard program of physiotherapy (exercises

of limb and chest physical therapy) was administered for all the subjects. As an additional treatment, among the 33 randomly chosen women, MLD was applied five times a week during the first 2 weeks, and twice a week from day 14 to 6 months after surgery. The control group comprised 34 women without MLD, but with applied self-drainage.

MLD was performed using a modification of the method described by Földi and Strößenreuther (6). Massage strokes were applied to the side of the edematous limb, starting at the base of the neck and then progressing to the affected limb. The massage was always directed proximally from the upper arm to the axilla, and then from the hand to the elbow. Finally, the whole limb was massaged from the distal to the proximal extremity.

Characteristics of the subjects in both groups are shown in *Table 1.* Information on demographic data such as age, marital status, educational background, and employment status was obtained using a self-report at the time of diagnosis. Medical data such as type of surgery, lymph node dissection, lymph node involvement, and adjuvant therapy (radiotherapy, chemotherapy, or endocrine therapy) were collected from the women's medical reports after surgery. Before surgery and 6 months after surgery, anthropometric traits were measured. Height and weight were used to calculate the body mass index (BMI, weight/height^2), and waist and hip circumferences were used to calculate the waist-to-hip ratio (WHR).

The volumes of both the arms were measured with water displacement, using a glass cylinder with water, before surgery and on days 2, 7, 14, and at 3 and 6 months after surgery, following the procedures described by King (7). All physical examinations were performed by the same physiotherapist.

The volume of the lymphedema (Vol%) is the ratio of the difference between the arm volumes on the operated and the nonoperated sides, and the arm volume of the nonoperated side at particular times of treatment assessment expressed in percentages.

$$Vol\% = \frac{(V_o - V_n)_t}{(V_n)_t} \, x100\%$$

where V_o is the volume of the arm on the operated side

V_n is the volume of the arm on the nonoperated side

t is the time of treatment assessment

The volume difference between the upper limbs from 5% to 10% was recognized as mild lymphedema, from 10% to 20% as moderate lymphedema, and above 20% as substantial lymphedema. Values below 5% were defined as the absence of edema (3).

Statistics

Comparisons of arm volumes on the operated side before and 6 months after surgery were made using Student's t-test. Values of $p \leq 0.05$ were regarded as significant. To evaluate the relative effect of MLD on the volume of lymphedema, two three-factor analyses of variance (ANOVA) with MLD (Yes/No), the number of removed lymph nodes (SLND/ALND), and radiotherapy (Yes/No) as independent variables, were carried out 3 and 6 months after surgery. Statistical analyses were carried out with Statistica 7.0 PL software (Statsoft Inc. Tulsa, OK, USA).

RESULTS

Women in both groups were of similar ages; the mean age in the MLD and the control groups was 60.3 and 58.6 years, respectively. Those with MLD and the controls revealed no statistically significant differences in adiposity measured by BMI and fat distribution measured by WHR, both prior to the surgery and 6 months after it. In both groups, postmenopausal women formed the majority ($n1 = n2 = 22$), followed by those living with a partner ($n1 = 26$ vs. $n2 = 23$)

TABLE 1
Comparison Between Randomized Groups at Baseline

Variables	Sample (n=67)	1 Women with MLD (n=33)	2 Women without MLD (n=34)	Two-sided test 1 vs 2 P
Mean (SD) age (years)	59.4 (10.4)	60.3 (8.2)	58.6 (12.2)	0.46
Mean (SD) BMI (kg/m2) before surgery	24.9 (4.7)	25.6 (5.4)	24.3 (3.9)	0.28
Mean (SD) BMI (kg/m2) 6 months after surgery	24.9 (4.8)	25.7 (5.4)	24.2 (4.0)	0.18
Mean (SD) WHR before surgery	0.80 (0.07)	0.81 (0.07)	0.83 (0.07)	0.18
Mean (SD) WHR 6 months after surgery	0.80 (0.08)	0.82 (0.08)	0.82 (0.07)	0.70
Surgery type (No. of women):				
Breast-conserving therapy (BCT)	40 (60%)	20 (61%)	20 (59%)	
Modified mastectomy (ME)	27 (40%)	13 (39%)	14 (41%)	
Excision of lymphatic nodes (No. of women):				
Sentinel lymph node dissection (SLND)	32 (48%)	14 (42%)	18 (53%)	
Axillary lymph node dissection (ALND)	35 (52%)	19 (58%)	16 (47%)	
Median of removed nodes (range)	6 (1-29)	9 (1-25)	3 (1-29)	
Positive lymph nodes (No. of women)	27 (40%)	14 (42%)	13 (38%)	
Stages of breast cancer (No. of women):				
I	23 (34%)	12 (36%)	11 (32%)	
II	31 (46%)	15 (46%)	16 (47%)	
III	13 (20%)	6 (18%)	7 (21%)	
Endocrine therapy (No. of women)	33 (49%)	14 (42%)	19 (56%)	
Chemotherapy (No. of women)	28 (42%)	13 (39%)	15 (44%)	
Radiotherapy (No. of women)	47 (70%)	22 (67%)	25 (74%)	

MLD - Manual lymphatic drainage

and those having one or two children ($n1$ = 18 vs. $n2$ = 15). Furthermore, the majority of them had secondary or vocational education. Chemotherapy, radiotherapy, and endocrine therapy were applied to 39, 67, and 42% of the breast cancer women with MLD, respectively, and to 44, 73, and 56% of the controls, respectively (*Table 1*).

Table 2 shows the mean values of the arm volume measurements on the operated side in women with MLD and the controls at consecutive examinations, as well as the significance of differences between the arm volume measurements before surgery (0 day) and 6 months after surgery. In the controls, mean values of the arm volume measurements on the operated side increased continually from the second day of surgery. In the MLD subjects, mean values increased on day 2 after surgery and started to resolve by day 7. At 6 months after treatment, among women *without* MLD, a significant increase in the arm volume on the operated side was observed (p=0.0033) when compared with the arm volume before surgery. On the other hand, among women *with* MLD, the increase was not evident (*Table 2*).

Figure 1 presents the percent volume increased due to lymphedema (%) in women with and without MLD during the study.

TABLE 2
Mean Values of Arm Volume in Women with MLD and Controls at Consecutive Examinations, and Significance of Differences Between V_0 Before Surgery (0 Day) and V_0 6 Months after Surgery

Time of examination	Women with MLD V_0 (ml)				Women without MLD V_0 (ml)			
	Non operated side		Operated side		Non operated side		Operated side	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
0 day -Before surgery	2113	482	2122	488	1914	348	1908	365
2 days after surgery	2103	487	2130	502	1904	337	1927	365
7 days after surgery	2112	482	2119	497	1922	342	1970	363
14 days after surgery	2109	483	2118	497	1938	367	1989	369
3 months after surgery	2127	500	2115	506	1932	374	2036	391
6 months after surgery	2130	489	2108	502	1932	367	2124	470
Significance of differences 0 day - 6 months			p=0.9089				**p=0.0033**	

p values were computed from two-sided tests

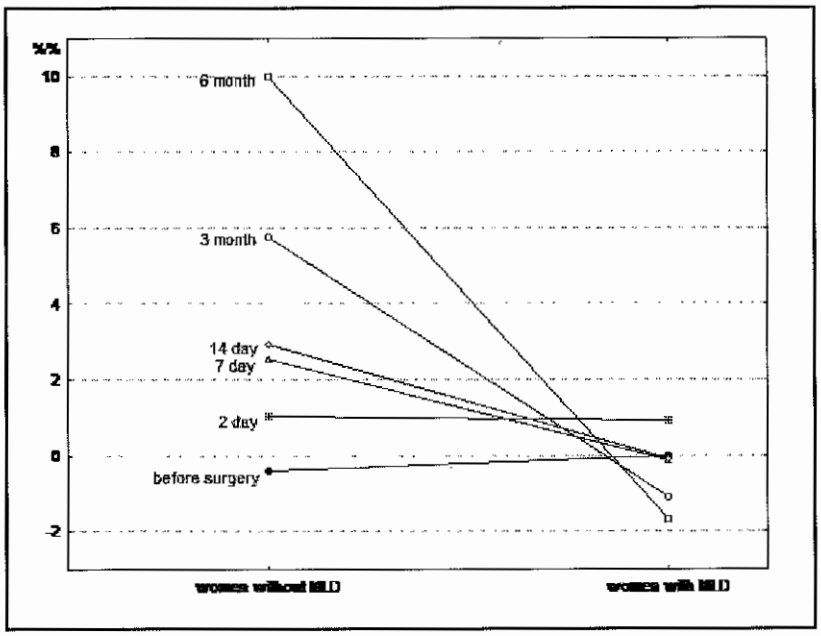

Fig. 1. The percent increase in volume due to lymphedema in women after breast cancer treatment during the study with and without MLD treatment.

Intergroup differences in the mean values of the volume of lymphedema were noticeable beginning day 7 after surgery and were still evident at the end of the study. At 3 months post-surgery, controls demonstrated 6% volume increase which increased to 10% at

TABLE 3
Results of the Three-factor ANOVA of the Effect of MLD, the Number of the Excised Lymph Nodes, and Radiotherapy on the Edema Volume at 3 and 6 Months after Surgery

Factors	df	F	*p*
Three months after surgery			
Main effects:			
A. MLD (Yes/No)	1	10.04	**0.0024****
B. Excised lymph nodes (SLND/ALND)	1	0.21	0.6481
C. Radiotherapy (Yes/No)	1	3.22	0.0779
Interactions:			
A × B	1	1.57	0.2146
A × C	1	2.04	0.1580
B × C	1	0.04	0.8407
A × B × C	1	0.01	0.9554
Six months after surgery			
Main effects:			
A. MLD (Yes/No)	1	18.25	**0.0001*****
B. Excised lymph nodes (SLND/ALND)	1	1.84	0.1801
C. Radiotherapy (Yes/No)	1	3.69	**0.0499***
Interactions:			
A × B	1	1.78	0.1876
A × C	1	3.23	0.0775
B × C	1	0.12	0.7268
A × B × C	1	0.32	0.5712

* $p<0.05$; ** $p<0.01$; *** $p<0.001$ level of significance

6 months. In women treated with MLD, lymphedema of the upper limb on the operated side did not occur (*Fig. 1*).

The results of the three-factor ANOVA (*Table 3*) indicated that a highly significant relationship between MLD and arm lymphedema existed at 3 and 6 months after surgery irrespective of the number of the removed lymph nodes (SLND/ALND) and the applied radiotherapy.

Among women with ALND and SLND, the MLD significantly prevented lymphedema of the npper limb. The essential influence of massage on edema prevention was also observed in women after radiotherapy (*Fig. 2*).

DISCUSSION

Treatment of breast cancer is associated with the risk of upper-limb lymphedema, which occurs on average in about 30% of women. Acquired interruption or damage to the axillary lymphatic system after surgery or radiotherapy for breast cancer can lead to regional or generalized accumulation of lymph fluid in the interstitial space, known as secondary lymphedema (1,8-10).

Lymphedema may arise immediately after surgery, as a temporary edema, 7-10 days after treatment as postsurgery trauma, or 2-3 weeks later or after several months or even 30 years after treatment (11, 12).

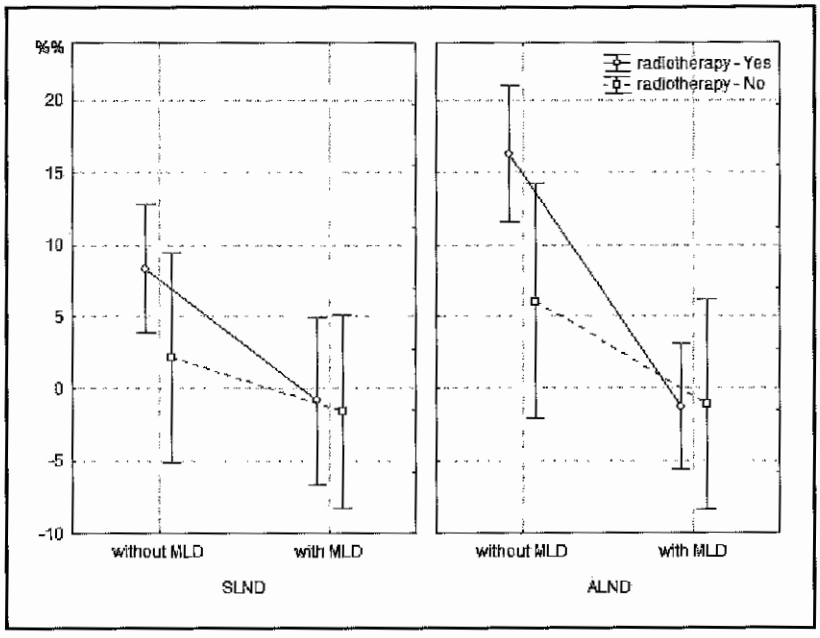

Fig. 2. The percent increase in volume due to lymphedema in women with either SNLD or ALND for breast cancer treatment with and without MLD treatment.

Additionally, many trials have reported that lymphedema has a significant tendency to increase with time (13).

The main factors responsible for the development of lymphedema are treatment and disease-related factors such as surgery, irradiation, systemic treatment (chemotherapy, tamoxifen), and the number of removed lymph nodes (14). Authors evaluating the degree of lymphedema with respect to the number of the removed lymph nodes (ALND and SLND) demonstrate that ALND causes a larger amount of secondary lymphedema with volumes ranging from 6 to 56% on average (15) than SLND – on average from 1.1 to 17.1% (16). Rönkä et al (9) found a statistically significant higher frequency of breast edema among women with axillary clearance (35-48%) when compared with those after sentinel node biopsy (23%). In addition, Clarke et al (17) observed a higher frequency of breast edema in women after axillary clearance (25%), whereas among women without any axillary surgery, the prevalence of lymphedema was clearly lower (about 6%). Excision of more lymph nodes causes more damage to lymphatic vessels, and therefore disturbs a free flow of lymph. The absence of regional lymph nodes collecting lymph from their area enhances the risk for lymphedema and arm morbidity. In the population-based cohort of breast cancer women, arm morbidity was significantly related to the number of lymph nodes dissected, and 20% of the women evidenced considerable impairment in arm functioning 1 year after ALND (18).

The risk of breast edema significantly increases after radiotherapy. Numerous authors have mentioned side effects of radiotherapy such as breast edema and secondary lymphedema of the arm, tissue fibrosis, and acute radiation-induced dermatitis (19,20). It has been estimated that after radiotherapy, edema occurred in 21-51% of the cases, and in those without radiotherapy, in 6-39% (15). Radiotherapy increased the frequency of edema from 25

to 38% in women with ALND (21). Højris et al (22) analyzed women after mastectomy and demonstrated that 14% of the irradiated women versus 3% of the nonirradiated women had lymphedema. Furthermore, irradiated women noticed significantly more periodic or even constant swelling of their arms (22).

Treatment of secondary lymphedema after breast cancer surgery is difficult, lengthy, and not always successful. Application of nonpharmacological methods of treatment can reduce swelling by an average of 50%. Therefore, it is particularly important to search for effective methods of lymphedema prevention after treatment of breast cancer.

The literature on prevention of lymphedema primarily focuses on specific surgical techniques to reduce damage to the axillary lymphatic system. No randomized controlled trials or cohort studies addressing interventions designed specifically to prevent lymphedema after treatment with surgery or radiation therapy could be identified. Although a number of recommendations for preventing lymphedema could be found in review articles and literature, no evidence base exists that demonstrates the efficacy of one mode of prevention over another or even the efficacy of preventive measures versus no preventive measures (15).

Four categories of prevention interventions have been repeatedly mentioned across the breast cancer literature: 1) avoidance of trauma/injury, 2) prevention of infection, 3) avoidance of arm constriction, and 4) use and exercise of the limb. However, no scientific evidence exists to show that any of these strategies is more effective than any other or even that preventive measures have any effect (15). Among these strategies, there are no such methods as MLD or intermittent pneumatic compression.

MLD is a special method involving gentle massage to improve lymphatic circulation, especially subcutaneous circulation, to stimulate the initial lymphatics and to stretch the lymph vessels, consequently improving the removal of interstitial fluid. Manual lymph drainage encourages and improves resorption without increasing filtration. It has been shown to be effective in the treatment of lymphedema because it improves the removal of fluid from interstitial space (1).

Despite the increasing amount of scientific evidence, the effectiveness of manual lymph drainage is still discussed and needs further evaluation (23-26). Földi (27) recommended immediate MLD to regenerate damaged lymphatic vessels promptly and create lymphatic and venous-lymphatic connections. SBU-Alert (a system for identification and early assessment concerning new methods in health care) has listed trials that have studied the therapeutic effects of MLD combined with compression treatment for arm lymphedema. Two of the studies showed a statistically significant greater reduction of edema in a group that underwent compression treatment than that observed in a group that underwent MLD (28,29), and the study by Andersen et al (11) showed that MLD did not contribute significantly to the reduction of edema volume. According to the authors of the present study, lack of therapeutic benefits of MLD in this trial resulted from very short duration of treatment (for 2 weeks only, followed by a self-lymphatic drainage). The results also demonstrated that the application of self-performed lymphatic drainage by controls was insufficient to restore the balance of lymph circulation in the lymphedema arm in the majority of them. Additionally, their therapy began a few months after surgery when they had already developed a considerably lymphedematous arm.

In the present study, all women who had received MLD on day 2 after surgery and continued receiving it for the 6 ensuing months did not develop secondary lymphedema of the arm on the operated side. In the group of women without MLD, 6 months after surgery, 70.6% of the subjects suffered from lymphedema.

The results confirm the few studies on edema prevention after treatment of breast cancer published by other authors. Lacomba

et al (1) reported a randomized controlled trial that assessed the effectiveness of the early physiotherapy (MLD, progressive massage of the scar, stretching exercises for trunk and shoulder muscles, and PNF exercises) to prevent lymphedema in women after surgery for breast cancer (including axillary lymph node dissection). The authors found that significantly fewer women receiving physiotherapy developed clinically important lymphedema at 1 year when compared with the controls. Lacomba et al's study included numerous different components and did not separate the effects of each component of the intervention, while in the present study, only the influence of MLD on lymphedema prevention was assessed.

Box et al (30) evaluated an intervention to minimize postoperative lymphedema in women after the removal of axillary lymph nodes due to breast cancer and stated that a physiotherapy program, including exercises, and progressive educational strategies may reduce the occurrence of secondary lymphedema 2 years after surgery.

The results presented in this study emphasize the significant influence of MLD in preventing secondary lymphedema of the arm on the operated side irrespective of the number of excised lymph nodes (ALND/SLND) and applied radiotherapy. The results showed that although radiotherapy is one of the highest risk factors for lymphedema of the arm after breast cancer surgery, prophylactic application of MLD helped the women escape or considerably alleviate this negative effect. This result is much stronger when the higher number of the removed lymph nodes in the group with MLD was taken into consideration.

The initial post-surgery weeks and months are of utmost importance for women who should be given the best medical control and physiotherapy to counteract the ensuing consequences such as secondary lymphedema and reduction in the mobility of the shoulder girdle and the arm (25,31). The results discussed earlier indicate unequivocally that irrespective of the surgery type and the adjuvant therapy, prophylactic MLD diminishes the risk of arm lymphedema.

Although the present study showed evidence of the positive effect of MLD in the prevention of secondary lymphedema, it is limited by the duration of follow-up (6 months after surgery). The observation did not exceed 6 months, while lymphedema after breast cancer surgery usually develops within the first year after treatment, although the risk of its occurrence decreases with time after surgery for breast cancer.

In conclusion, MLD applied immediately after breast cancer surgery prevented secondary lymphedema of the arm irrespective of the method of breast cancer treatment. Regardless of the surgery type (ME or BCT) and the number of lymph nodes removed (ALND or SLND), MLD effectively prevented lymphedema of the arm on the operated side after surgery for breast cancer. This study shows that MLD administered early after operation for breast cancer and continuing over time should be considered for the prevention of lymphedema.

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