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ORIGINAL ARTICLE

Factors Influencing Efficacy of Complete Decongestive Treatment in Patients with Breast Cancer-Linked Arm Lymphoedema

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Abstract

Background/Aim: The most recommended form of lymphoedema therapy is complete decongestive treatment (CDT). Efficacy of CDT in patients with arm lymph-oedema related to malignant breast tumour has reported in many studies, but the predictive factors of outcome of this therapy have not been yet sufficiently investi-gated. The purpose of this research was to identify predictive factors of efficacy of CDT in patients with breast cancer-linked arm lymphoedema throughout the inten-sive phase of therapy.
Methods: The prospective study included 51 patients with breast cancer-linked arm lymphoedema who were subjected to a 3-week program of CDT. Patients' clini-cal and demographic features, breast cancer treatment characteristics, lymph-oede-ma and CDT characteristics were collected and assessed for their prognostic value. The influence of certain predictors on the degree of lymphoedema reduction was evaluated by multivariate linear regression analysis.
Results: Mean age was 58.1 ± 8.0 (95 % CI: 55.8 - 60.3), median of BMI was 28.4 kg/m^2 (95 % CI: 27.2 - 29.6). The average duration of lymphoedema was 36.5 ± 43.9 months (95 % CI: 24.1 - 48.8). The mean size of lymphoedema before CDT was 6.99 ± 5.36 %, and the mean degree of lymphoedema reduction was 63.7 ± 28.6 %. The mean compliance to bandages was 217.5 ± 97.8 hours (95 % CI: 190.0 - 245.0) and 7 (13.7 %) patients had a history of erysipelas of the ipsilateral arm. When observ-ing each individual predictor, statistically most significant contribution showed the size of lymphoedema before the therapy ($p < 0.001$), then history of erysipelas ($p < 0.01$), and patients' age ($p < 0.05$).
Conclusion: Size of lymphoedema before treatment is the most crucial prognostic factor of the efficacy of CDT in the patients with breast cancer-linked arm lymph-oedema. The present study also identified history of erysipelas and patients age as independent predictors of the CDT efficacy.

Key words: Breast cancer; Lymphoedema; Physical therapy modalities; Compression bandages; Drainage; Treatment outcome.

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Introduction

Breast cancer-linked arm lymphoedema is ab-normal accumulation of interstitial fluid due to mechanical failure of the lymphatic system of the upper limb, usually because of the breast cancer surgery, radiotherapy, infection, or trauma. In the available literature, the average incidence of breast cancer-linked arm lymphoedema caused by axillary dissection is greater than 20 %, and

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after sentinel lymph node biopsy is less than 10 %.[1-4] The overall goal of lymphoedema treat-ment is to reduce swelling, mobilise congestive interstitial fluid, reduce connective and fat tissue proliferation, control symptoms, and minimise the consequences.[5]

The most effective and most common form of lymphoedema therapy is complete decongestive treatment (CDT), which represents the gold standard in the conservative treatment.[6-9] Efficacy of CDT in patients with arm lymphoedema related to malignant breast tumour has reported in many studies,[10-14] but the predictive factors of outcome of this therapy have not been yet sufficiently in-vestigated. The purpose of this research was to identify independent predictive factors of effica-cy of CDT in patients with breast cancer-linked arm lymphoedema throughout the intensive phase of therapy.

Methods

Study design

This prospective study was carried out at the In-stitute for Physical Medicine and Rehabilitation "Dr Miroslav Zotović" in Banja Luka, and included patients with arm lymphoedema who underwent malignant breast tumour surgical procedure. The research was permitted by the Ethics Committee of the facility.

Participants

The inclusion criteria for the study were: unilateral axillary dissection, clinically verified lymphoede-ma (difference in circumference between affected and healthy arm was larger than 2 cm at minimum 1 measurement level), more than 3 months from the breast cancer surgery and radiotherapy and patient-signed informed consent form, with prior knowledge of the trial purpose.

The elimination criteria were: metastatic breast disease, clinically verified acute erysipelas; un-treated and poorly controlled hypertension, heart failure, deep venous thrombosis and anticoagulant therapy, shoulder and upper limb damage caused by neurological, orthopaedic or rheumatic diseas-es diagnosed prior to breast cancer surgery, diag-nosed and medically treated psychiatric disorders, liver cirrhosis and nephrotic syndrome. For each patients following data were collected and assessed for their prognostic value: clinical and de-mographic features (age, body mass index-BMI, co-morbidity), breast cancer treatment characteristics (time from surgery, type of breast surgery, number of lymph nodes removed and involved, therapy before and/or after surgery), lymphoedema char-acteristics (duration of lymphoedema, time until lymphoedema onset, size of lymphoedema, report-ing pain and other symptoms in the arm, history of erysipelas) and CDT characteristics (compliance to bandages).

Intervention

Patients were taken to a 3-week program of CDT, once a day, 5 days a week. The CDT protocol con-sisted of manual lymphatic drainage (MLD), short-stretch multilayer compression bandages (Rosidal® K Lymphset, Lohmann & Rauscher, Vienna, Austria) and exercises provided by therapists. Exercises were performed with compression bandages as an essential part of the decongestive phase of lymph-oedema therapy. The exercises consisted of: exer-cises of diaphragmatic breathing, remedial exercis-es, flexibility (stretching) exercises and resistance (weight-lifting) exercises of the affected arm.

Lymphoedema size

Lymphoedema was assessed by the arm circum-ference. It was measured at 7 symmetrical levels (metacarpophalangeal joints, radial styloid process, at 10, 20, 30 and 40 cm from the radial styloid pro-cess and over olecranon) of the affected and contra-lateral arm. The lymphoedema size was expressed as the ratio of the total circumference of the affect-ed and unaffected arm, and calculated according to the following formula: [(total circumference of the affected arm - total circumference of the unaffected arm) / - total circumference of the unaffected arm] x 100, where 0 % indicates the same total circum-ferences of two arms. The degree of lymphoedema reduction was calculated by the following formu-la: (total circumference of the affected arm before treatment - total circumference of the affected arm after treatment/ total circumference of the affected arm before treatment - total circumference of the unaffected arm) x 100.[14-16]

Bandage compliance

All patients received instructions for wearing the bandages as long as possible ie, until the next treat-ment day. The bandage-carrying compliance was evaluated through the so-called "bandage log" in which all patients registered the exact time of ap-plication and removal of bandages daily, based on which the total number of hours under the ban-dage was calculated.

Statistics

Descriptive statistics methods were used to describe all data in the study. Numerical data associated with the percentage of lymphoedema reduction were identified by Pearson correlation. Categorical data were analysed by the independent samples t-test. Factors with $p < 0.05$ in the stated analyses were selected as final predictors for multivariate linear regression analysis. All analyses were carried out using SPSS Version 21.0 for Windows. The result was significant if the p-value was less than 0.05.

Results

The prospective study included 51 female patients with secondary arm lymphoedema after breast cancer treatment. Mean age was 58.1 ± 8.0 (95 % CI: 55.8 - 60.3), median of BMI was 28.4 kg/m^2 (95 % CI: 27.2 - 29.6). The largest number of patients (47.1 %) were in the category of overweight, 29.4 % were obese patients, 21.5 % were in normal range and only 1 patient (2.0 %) was in the category of underweight. The average duration of lymphoedema was 36.5 ± 43.9 months (95 % CI: 24.1 - 48.8). The mean degree of lymphoedema reduction was 63.7 ± 28.6 %. The mean compliance to bandages was 217.5 ± 97.8 hours (95 % CI: 190.0 - 245.0) and 7 (13.7 %) patients had a history of erysipelas of the ipsilateral arm. Table 1 shows characteristics of the patients.

Table 1: Patients' characteristics

Characteristics	N (%)	Mean ± SD	Range (min-max)
Patients' age (years)		58.1±8.0	41.0-77.0
Time from surgery (months)		53.4±50.0	3.0-185.0
Type of breast surgery			
Rradical mastectomy	30 (58.8)		
Breast conserving surgery	21 (41.2)		
Number of lymph nodes removed		14.2±6.6	3.0-42.0
Number of lymph nodes involved		2.8±6.1	0.0-32.0
Therapy			
Chemotherapy	37 (72.5)		
Radiotherapy	38 (74.5)		
Hormonal	37 (72.5)		
Duration of lymphoedema (months)		36.5±43.9	0.5-170.0
Time until lymphoedema onset (months)		17.0±22.9	0.0-124.0
Size of lymphoedema before CDT (%)		6.99±5.36	1.99-25.0
Degree of lymphoedema reduction (%)		63.7±28.6	13.8-100
Reporting pain and other symptoms in the arm			
Yes	44 (86.3)		
No	7 (13.7)		
Hystory of erysipelas			
Yes	7(13.7)		
No	44 (86.3)		
Body mass index - BMI (kg/m^2)		28.4±4.3	17.9-37.9
Underweight (< 18.5)	1 (2.0)		
Normal range (18.50-24.99)	11 (21.5)		
Underweight (25.00-29.99)	24 (47.1)		
Obese (> 30)	15 (29.4)		
Comorbidity (medication for)			
Hypertension	23 (45.1)		
Heart disease	9 (17.6)		
Thyroid problems	12 (23.5)		
Diabetes	4 (7.8)		
Venous insufficiency in the lower limbs	5 (9.8)		
Osteoporosis	8 (15.7)		
Others	5 (9.8)		

The size of lymphoedema before therapy was statistically significantly negatively correlated with degree of lymphoedema reduction ($p < 0.001$). Also, there was statistically significant negative correlation between patients' age and percentage of lymphoedema reduction ($p < 0.05$). The degree of lymphoedema reduction in patients with history of erysipelas, was statistically significantly lower than in those who did not have erysipelas ($p < 0.01$) (Table 2).

Table 2: Factors accociated with efficacy of CDT

Variable	Pearson correlation		Independent samples T-test	
	R	p	T	p
Patients' age (years)	-0.280	**0.047**		
Time from surgery (months)	-0.129	0.367		
Type of breast surgery				
Number of lymph nodes removed	-0.186	0.191	-0.608	0.546
Number of lymph nodes involved	-0.016	0.914		
Chemotherapy				
Radiotherapy			-0.508	0.614
Hormonal therapy			0.109	0.914
Duration of lymphoedema (months)	-0.082	0.569	0.142	0.888
Time until lymphoedema onset (months)	-0.124	0.386		
Size of lymphoedema before CDT	-0.710	**0.000**		
Reporting pain and other symptoms in the arm			-0.406	0.687
Hystory of erysipelas	-0.129	0.367	-3.808	**0.002**
Body mass index - BMI (kg/m^2)				
Comorbidity (yes/no)			0.516	0.608
Number of comorbidities	0.076	0.598		
Compliance to bandages (hours)	0.008	0.956		

Table 3: Predictors of complete decongestive treatment (CDT) efficacy after multivariate analysis

Factors	β coefficient of linear regression	t-value	p
Size of lymphoedema before the CDT	-0.553	-6.207	0.000
Hystory of erysipelas	0.273	3.078	0.004
Patients' age (years)	-0.200	-2.354	0.023

Influence of certain predictors on the degree of lymphoedema reduction was evaluated by multi-variate linear regression analysis. The results showed that the model explained 65.4 % of the total variance, ($F = 24.579$, $p = 0.000$). When ob-serving each individual predictor, statistically most significant contribution showed the size of lymphoedema before the therapy ($p < 0.001$), then history of erysipelas ($p < 0.01$), and patients' age ($p < 0.05$). Table 3 shows predictors of CDT efficacy after multivariate analysis with the per-centage of lymphoedema reduction as dependent variable.

Discussion

In this study, the influence of independent predictors on the success of decongestive therapy of reast cancer-related arm lymphoedema was investigated. Younger age and lower size of lymphoedema before CDT were identified as predictors associated with better response to treatment. The history of erysipelas was associated with a poor outcome of CDT.

The most important predictor of the degree of reduction of lymphoedema was the size of lymphoedema before the therapy: the lower the size of lymphoedema before the treatment was, the greater the degree of reduction achieved. Efficacy of CDT is better, if the therapy starts as earlier as possible, when lymphoedema is less pronounced. Similar results were obtained by other authors.[14, 15, 17]

The younger age was also a predictor of better therapy response. Lia SF et al also reported that younger age would predict CDT efficacy, believing that older patients have poor compliance with bandages.14 That could not be concluded in the present study. In the study of predictors of lower limb lymphoedema, Vignes et al reported that older patients had better treatment outcomes. The average age of patients in this study (45.8; range 32-60.4) was considerably less than in mentioned study (58.1; range 41-77).[18]

The most common lymphoedema complication is erysipelas. It is an infection that involves the superficial layer of the skin with primarily affects-the lymphatic vessels (lymphangitis). Upper limb erysipelas occurs in up to 24 % of women aftersurgical treatment for breast cancer follow-inglymphatic system damage. Lymphoedema is considerable risk factor for reappearance of erysipelas.[19-21]

The only study that identified previous erysipelas as predictor of the efficacy of CDT was a study of primary lower extremity lymphoedema. But, in that study patients with previous episode(s) of erysipelas obtained higher lymphoedema volume reduction.18 History of earlier erysipelas has proved to be an individually negative significant predictor in the present research. Considering total of patients who had erysipelas in this study was 7 (13.7 %), this clinical feature requires further research.

Erysipelas may have negative impact on CDT efficacy. Every episode od erysipelas affects the lymphatic vessels, aggravating of pre-existing lymphatic impairment and worsening lymphoedema.

A surprising finding in these results is that bandage-carrying compliance was not associated with better treatment response. Bandage compliance is generally considered a factor influencing-CDT outcomes. According to the findings of some authors, bandage-carrying compliance is a dominant predictive factor of CDT effectiveness, not only after the intensive phase of treatment, but also during the maintenance phase.[15, 22]

Forner-Cordero et al concluded that good bandage
compliance improved the percent reduction of lymphoedema by 25 % compared with fair or bad bandage compliance in breast cancer-linked lymphoedema.[15]

The present study is, to authors' knowledge, the only study that evaluated bandage-carrying compliance using a "bandage log" and compared the total number of hours of wearing a bandage with the degree of lymphoedema reduction. The average number of hours of bandage wearing in this study was 217.5 ± 97.8 hours (range 81-471). If the criteria from the Forner-Cordero' study were used, 72.5 % of patients in this study would have bad bandage-carrying compliance, 25.5 % fair compliance, and only 1 patient (2 %) good bandage-carrying compliance. Since most patients

had poor bandage-carrying compliance, this factor requires further examination in a larger number of patients.

BMI and duration of lymphoedema also were not associated with better response to CDT. The results of other studies are contradictory. Vignes et al demonstrated that duration of lymphoedema and BMI were correlated with a greater absolute reduction, but not a relative decrease in lymphoedema volume.[23] Forner-Cordero at al found that the duration of lymphoedema does not affect the outcome of the therapy and that patients may benefit from treatment long time after symptoms appear.[15]

The authors consider that the most important factor in keeping lymphoedema under control is the
regular administration of CDT to reduce swelling and that the largest lymphoedemas are not the oldest.

It is well known that overweight or obesity, expressed as a BMI greater than 25.0 and 30.0 respectively, is important risk factor for secondary lymphoedema.24-26 The effect of BMI on CDT outcome has been described in some studies,[18, 22, 23] but in this one, such a result was not obtained. The
reason could be that most of the patients in this study were in the pre-obese or obese category, and only 21.5 % were in the normal range.

The breast cancer treatment characteristics (time from surgery, type of breast surgery, number of lymph nodes removed and involved, treatment before and/or after surgery) did not affect CDT efficacy in present study.

Study strengths and limitations

The present study was conducted at an institution specialised in the treatment of patients with lymphoedema and only included patients with arm lymphoedema linked to breast cancer. The study was prospective and monocentric. All patients received homogenous CDT protocol and MLD was carried out by two trained physiotherapists and under the supervision of the researcher. The main restriction of this study is little sample size. Forthcoming research with greater number of patients is necessary.

Conclusion

Size of lymphoedema before treatment is the most crucial prognostic factor of the efficacy of CDT in the patients with breast cancer-linked arm lymphoedema. The present study also identified history of erysipelas and patients age as independent predictors of the CDT efficacy.

Although this study did not show statistical significance for the bandage-carrying compliance, BMI and duration of lymphoedema, these factors should be paid attention in the further prospective studies with a larger number of patients.

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Conflict of interest

None.

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