Breast Cancer Research and Treatment (2019) 175:191–201
https://doi.org/10.1007/s10549-019-05136-9

CLINICAL TRIAL

Efficacy of self-administered complex decongestive therapy on breast cancer-related lymphedema: a single-blind randomized controlled trial

M. B. Ligabue[1] · I. Campanini[2,3] · P. Veroni[1] · A. Cepelli[1] · M. Lusuardi[4] · A. Merlo[2]

Received: 20 November 2018 / Accepted: 11 January 2019 / Published online: 2 February 2019

Abstract

Purpose After surgery, breast cancer-related lymphedema (BCRL) is a frequent chronic condition. The complex decongestive therapy (CDT) delivered by physiotherapists at hospitals is the state-of-the-art treatment choice. As lymphedema requires continuous management, we designed a 1-month-long course to train women to professionally carry out a self-administered CDT (saCDT) and tested its efficacy while keeping the benefits of CDT.

Methods Consecutive patients treated with CDT over a 1-year period at an Italian facility were randomly assigned to either experimental (EXP, saCDT course) or control (CTRL, usual care) group. Women were assessed before, at 1, and 6 months from enrolment. Pain assessed by the numerical pain rating scale (NPRS) was the primary outcome. Arm asymmetry assessed by the excess limb volume (ELV) was the secondary outcome. Outcome variations were compared to their MCID to classify women as improved, stable, or worsened.

Results Forty-one women were included. The proportion of stable or improved women was significantly different between EXP and CTRL groups at 6 months after enrolment for both arm pain ($p=0.01$) and asymmetry ($p<0.01$). Noteworthy, only one EXP woman had worsened after 6 months. NPRS significantly decreased in the EXP group only, with a median variation of 2 points. Arm ELV significantly decreased with respect to the baseline value in the EXP group only, with a median reduction of 8%.

Conclusions Teaching saCDT to women with BCRL is effective in maintaining or improving the benefits of CDT and can be used as a self-care tool in the management of BCRL.

Keywords Lymphedema · Breast cancer · Self-care · Complex decongestive therapy

Background

Breast cancer-related lymphedema (BCRL) is a common complication following breast cancer surgery, and is characterized by arm swelling due to the accumulation in the interstitial spaces of lymphatic fluids that do not drain back into the bloodstream [1–3]. Affected women may

M. B. Ligabue and I. Campanini contributed equally to this manuscript.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10549-019-05136-9) contains supplementary material, which is available to authorized users.

✉ I. Campanini
isabella.campanini@ausl.re.it

[1] Functional Rehabilitation and Recovery Service, San Sebastiano Hospital, Correggio, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy

[2] LAM-Motion Analysis Laboratory, San Sebastiano Hospital, Correggio, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy

[3] Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy

[4] Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy

experience body image issues, pain, impaired arm range of motion, and loss in strength, with an overall worsening in their quality of life [4–6].

The true incidence of lymphedema is still being debated, as different definitions and assessment methods have been used in the literature [3, 7]. Incidence values ranging between 20% and 30% have been considered realistic by several authors [3, 8], while a 5-year cumulative incidence of 42 out of 100 women has been found in a population-based prospective study [9].

Lymphedema cannot be completely cured, and requires continuous management [5, 8, 10]. The state-of-the-art treatment of BCRL is a fourfold conservative treatment referred to as Complex Decongestive Therapy (CDT), consisting of manual lymphatic drainage (MLD) carried out by physiotherapists. This is the primary intervention which allows for the reduction of lymphedema [2, 11]. It is followed by a maintenance phase based on compression therapy with the aid of bandages or sleeves, skin care, and a targeted work out [8]. The efficacy of MLD and CDT delivered by health professionals has been addressed in a large number of randomized controlled trials [4, 11, 12] and synthesized in three recent systematic reviews [1, 2, 8, 10, 13].

Lymphedema is a chronic condition and when untreated, the risk of worsening over time in terms of volume and stage of tissue fibrosis increases [14]. Hence, alongside the treatments that patients receive from professionals in hospitals and institutions, the management of lymphedema should also rely on continuous self-care activities performed by the affected women themselves [15, 16]. Self-care typically relies on the use of compressive garments during the night, skin care products, tailored-made exercises, and fitness programs [15, 17].

While the efficacy of professionally delivered MLD and CDT has been investigated by several studies, the efficacy of self-treatments has only been addressed in a few studies, which primarily focused on tailored-made physical activities [5]. The possibility of assigning women the ability of self-performing both MLD and arm bandage has not yet been investigated in the literature, even if these two treatments provide the largest benefits in lymphedema reduction.

We therefore designed a randomized controlled trial to assess both short-term and long-term effects on arm pain and swelling of a month-long standardized training routine of self-administered Complex Decongestive Therapy (saCDT). This included self-drainage, self-bandaging, and physical exercises in a sample of women with chronic arm lymphedema. Our hypothesis is that such training program can provide women with the proper tools to immediately counteract any arm swelling, hence prolonging the positive effects of the hospital-delivered treatments. A positive result of such approach would provide benefits for women's health and could reduce the costs associated with the management of arm lymphedema.

Materials and methods

Trial design

The study is a randomized, single blinded, parallel group trial. A prospective evaluation was undertaken focusing on the effects of a course on lymphedema self-treatment, also referred as saCDT protocol (the intervention) and its subsequent self-administration in patients with breast carcinoma-associated lymphedema.

Women, after receiving CDT at the hospital, were enrolled by the research manager (Fig. 1). When 10 women were successfully enrolled, a teaching course was duly set up. Women were randomly assigned to either the experimental or the control group, as detailed below. The women of both groups were separately summoned and assessed in the week preceding the beginning of the course (T0), then after 1 month (T1), and again at 6 months (T2). The saCDT course was imparted to the women in the treatment group between T0 and T1. The self-treatment courses were made up of small groups of 4–6 women (with the same number of women for the control group). In order to teach all patients, the same trained physiotherapist repeated the course five times. Due to the nature of the study, participants were not blinded to the treatment; however, the one physiotherapist who assessed all outcomes and all other professionals of the hospital were. Random group labels were used in order to keep the statistician who performed the data analysis blind to the allocation.

Participants

All the women with lymphedema secondary to breast cancer who received CDT treatment at our facility over a 1-year period, and satisfied the inclusion criteria are reported in Table 1.

Intervention and control treatments

The randomization sequences were created by the biostatistician using the Randomizer software [18] and were kept concealed until interventions were assigned. Block randomization was used (e.g., BA AB). Over the phone, the research manager told each woman if they were assigned to either the experimental (EXP) or the control (CTRL) group.

The control group received only the usual care provided at discharge after CDT. This consists of a point-by-point briefing and discussion of the leaflet. It includes the description of specifically tuned exercises, behavioral and hygienic

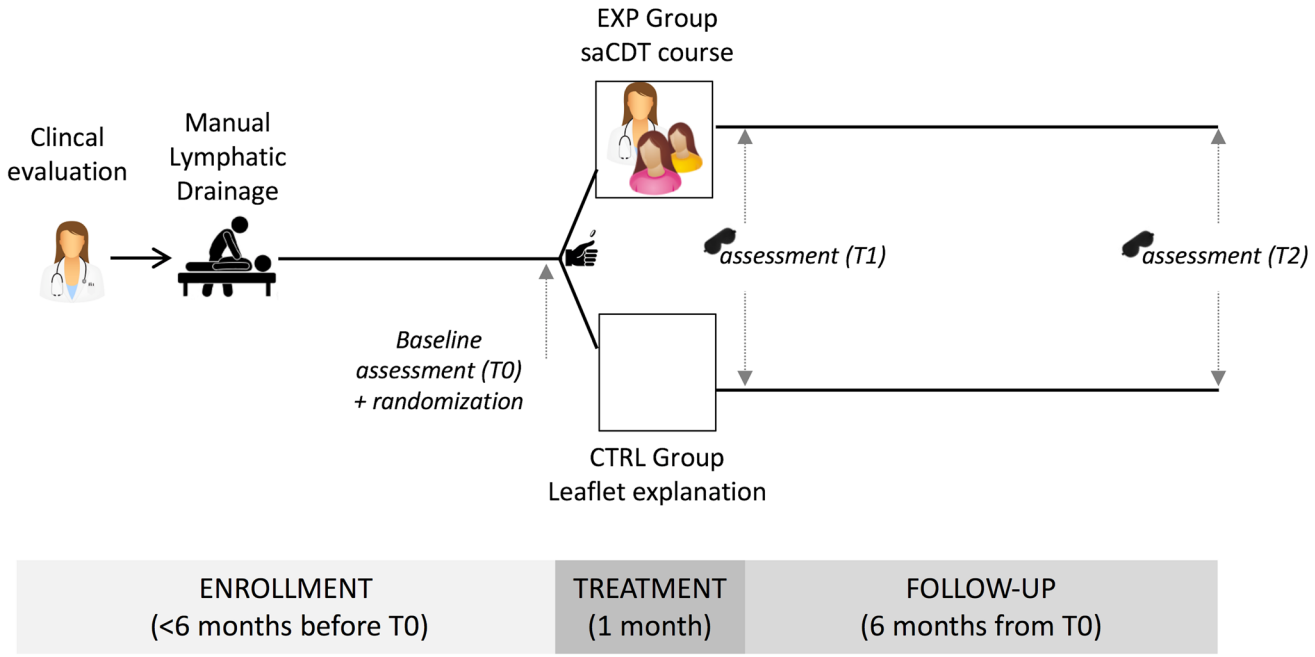

Fig. 1 Study design, phases of the study, and assessment times (T0, T1, T2). Women were randomly allocated to either the experimental (EXP) or the control (CTRL) group. The treatment consisted of a thorough course on self-administered Complex Decongestive Therapy (saCDT) delivered by a trained physiotherapist over a period of 4 weeks

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Breast cancer diagnosis	Recurrent cancer
Mastectomy or quadrantectomy	Active infections
Removal of at least two axillary lymph nodes	Vascular damages (e.g., phlebitis)
Concluded chemotherapy and radiotherapy	Known impossibility to participate in at least 80% of saCDT course
Superior arm lymphedema	
CDT concluded within 6 months	
At least 4 cm of difference between affected and unaffected arm total circumference	

standards and is given to all patients after breast surgery (Italian version, http://www.asmn.re.it/allegati/RiabilitazioneinterventosenoOttobre2013.pdf). Women were strongly encouraged to follow the recommendations contained in the pamphlet.

The experimental group received the saCDT course. A trained physiotherapist held a ten-session course over a period of 4 weeks. Each meeting lasted about one and half hours. The program of each of the 10 meetings was standardized in terms of topics, practical demonstrations, trials, and discussion time with patients. The women were taught: manual lymphatic self-drainage, self-bandage, breathing exercises, mobilization exercises, muscle reinforcement exercises, muscle contracture management, and the understanding of the changes occurring after suffering from lymphedema. The physiotherapist taught women until they were able to manage the whole treatment autonomously at home. Problems and difficulties that arose were collected and discussed within the group. The institution provided for all the equipment and consumables. A copy of the course manual was given to all women during the first meeting. This is available on the website of our institution in both Italian and English (https://www.ausl.re.it/comunicazione/opuscoli-informativi/linfedema-auto-trattamento). During the last lesson, women were strongly encouraged to carry out all the saCDT protocol 6 days out of seven. Subsequently, the study physician offered medical expertise including lifestyle and nutritional recommendations aiming at preventing weight gain and promoting self-care activities. Finally, all patients including those in the control group were asked to use the arm-guard.

Objectives

The aim of this study was to test the efficacy of the saCDT protocol compared to the usual care in the management of lymphedema-related arm pain, volume, and asymmetry at 6 months after enrolment. The short-term efficacy at 1 month after enrolment has also been assessed.

Primary outcome

In this study, lymphedema-related arm pain was selected as the primary outcome. Pain was assessed by the Numerical Pain Rating Scale (NPRS), and executed according to Williamson and colleagues [19]. NPRS is a validated and worldwide used scale for pain assessment, with excellent metric characteristics. It scores between 0 (no pain) and 10 (worst pain imaginable) with one-step increments [19]. In the assessment of pain of oncological patients, a MCID of 2 is suggested [20]. Pain reduction greater than MCID was reported in intervention studies published in the literature, with Effect Sizes (ES) varying between 1.6 and 5 [21–23]. NPRS was preferred over other multidimensional scales for pain assessment because it allowed for the a priori design of the sample size, considering that both MCID and ES are available in the literature.

Secondary outcome

Asymmetry was selected as the secondary outcome in this study. This was computed by means of the Excess Limb Volume (ELV) indicator, also referred to as interlimb discrepancy [24], being a standard outcome in the literature on lymphedema [13, 15, 16, 24, 25]. In this study, ELV was computed for both hand (handELV) and arm (armELV), as follows: ELV = (Affected Side Volume−Unaffected Side Volume)/Unaffected Side Volume × 100. Volume measurement procedures and computations to obtain arm and hand ELVs are reported in Online Resource 1.

Longitudinal variations in arm volume and asymmetry were computed as the difference between the baseline value and T1 and T2 values. ELV variations greater than 5% were considered clinically significant in this study [24, 26].

Sample size

Sample size was determined according to the following design criteria: two tailed Mann–Withney test, $\alpha = 0.05$; $1-\beta = 80\%$, Effect Size = 1 ($\Delta\mu = \text{MCID} = 2$ and $\sigma = 2$), allocation rate N1/N2 = 1, and dropout rate = 10%. A sample of at least 40 women was necessary to match these requirements.

The effect of the treatment was analyzed by intention to treat.

Statistical analysis

Descriptive statistic was used to summarize data during each stage of the study.

In line with the main aim of this study, the number of women that either showed an Improvement (I), were Stable (S), or showed a Worsening (W) in the outcome variables at the follow-up assessments (T1 and T2) was determined for both groups. For each variable (e.g., pain level), a reduction greater than MCID was required to classify a woman in group I. Similarly, an increase greater than MCID was required to classify a woman in the group W. Women were otherwise classified in the group S. This allowed to fulfill a 2×3 contingency table that summarized the variations (W, S, I) for the two groups (EXP and CTRL). At each follow-up assessment, three contingency tables were created, to assess pain, hand asymmetry, and arm asymmetry variations. The Freeman–Halton extension of the Fisher exact probability test for a 2×3 contingency table was used to analyze the differences between the treated women and the control patients.

The Mann–Whitney test was used to verify the presence of group differences at each stage of the study. The Wilcoxon test was used to analyze variations with respect to the baseline values. Non-parametric tests were selected, based on a preliminary analysis of data (Lilliefors test). Data analysis was performed using Matlab and its statistical toolbox (The Mathworks inc., Thorofare, USA). Statistical significance was set at 5%.

Results

Forty-one women were enrolled throughout the 1-year study period. The overall attendance of individual participants through each stage of the trial is reported in Fig. 2.

The women from both groups did not meet during the study period thanks to the allocation and timing when administering the procedures. No unforeseen difficulty arose while replicating the courses, and these were comparable for execution and content.

Baseline data

Demographic and clinical characteristics of both EXP and CTRL groups are reported in Table 2. For all of the reported variables, no significant group differences were found at the baseline evaluation. As expected from published literature, a large between-subject variability was found in both groups, both in terms of pain and of arm asymmetry. Due to the randomization, the level of impairment at enrollment was

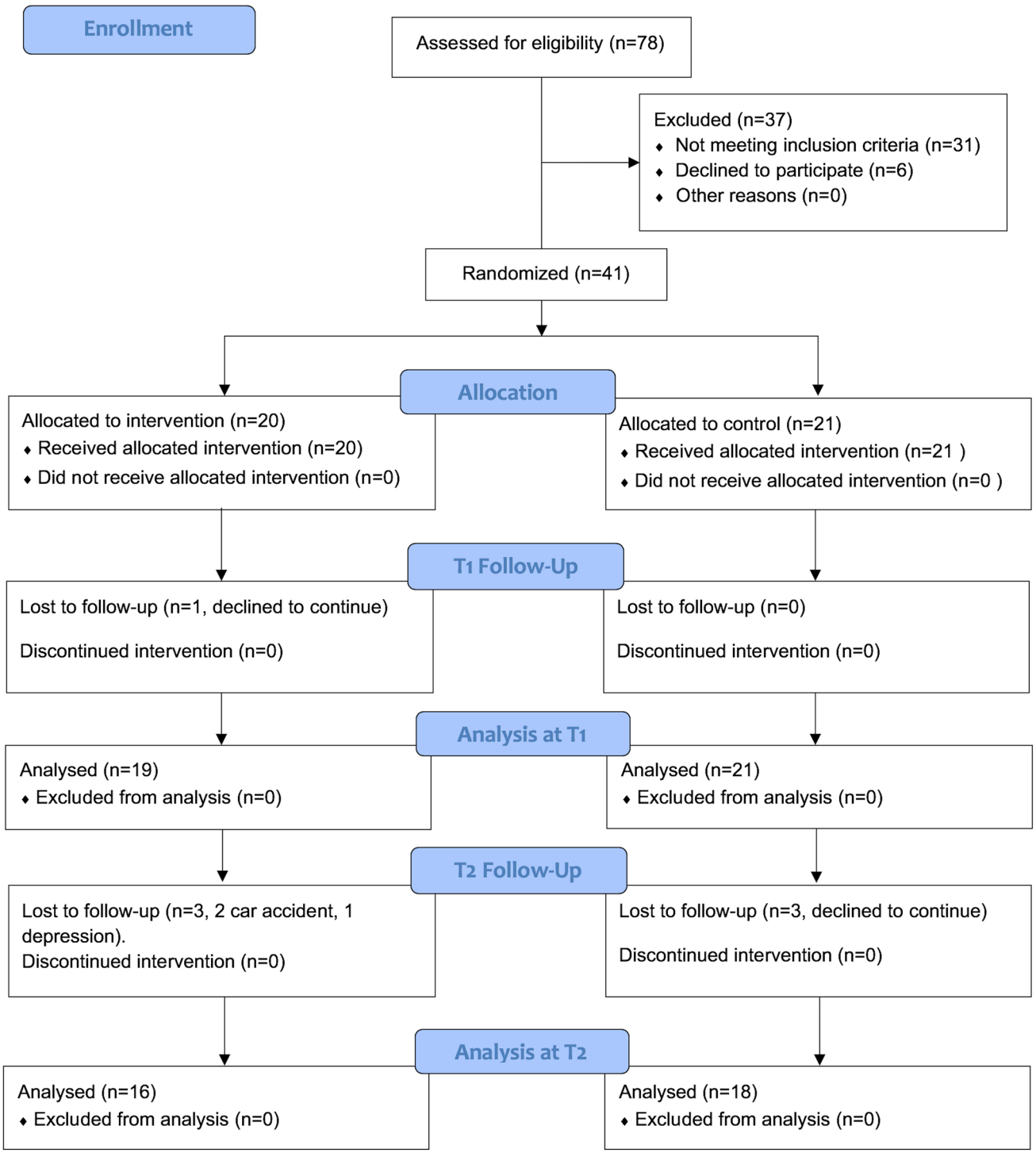

Fig. 2 Consort-like flow diagram of participants through the phases (enrolment, intervention allocation, follow-up, and data analysis) of the parallel randomized trial

slightly higher in the EXP group compared to that of the CTRLs.

At baseline evaluation, the complete dataset was available for 20/20 subjects of EXP and for 21/21 subjects of CTRL. At T1, NPRS was available for 19/20 subjects of EXP and

Table 2 Sample characteristics

Characteristic	Experimental group ($n=20$)	Control group ($n=21$)	p value
Age (years)	56. 8 (8.8); 45–76	57.1 (9.8); 40–71	0.784
Years since breast cancer surgery	6 (6.8; 0–30)	7.5 (6.5; 1–26)	0.288
Years since lymphedema diagnosis	2.7 (2.9; 0–10)	2.8 (2.9; 0–11)	0.978
Type of surgery mastectomy/quadrantectomy	8/12	3/18	
Lymph node removal/axillary cavity emptying	11/9	13/8	
Affected side (L/R)	12/8	8/13	

Table 3 Values of the outcome variables at the baseline assessment (T0), after 1 month from the enrolment (T1) and after 6 months from the enrolment (T2)

	Baseline	After 1 month	After 6 months
Outcome variables			
NPRS			
Experimental group	4.3 (2.6); 0–10	2.9 (2.4); 0–10[a,b]	2.1 (2.5); 0–10[a,b]
Control group	3.8 (2.8); 0–10	4.8 (3.0); 0–10	3.8 (3.3); 0–10
Hand volume, ml			
Experimental group	603 (143); 425–1050	551(120); 400–850	535 (84); 400–675
Control group	571 (146); 400–1050	583(156); 400–1100	579 (151); 400–1000
handELV, %			
Experimental group	15 (13); 0–50	10 (10); − 6–31[b]	8 (9); − 10–24[b]
Control group	10 (11); − 9–33	11 (12); − 6–40	13 (16); − 9–50
Total arm girth, cm			
Experimental group	314 (35); 256–399	303 (37); 252–390	299 (40); 254–403
Control group	306 (51); 210–427	309 (52); 213–430	308 (53); 222–432
Arm volume, ml			
Experimental group	2727 (636); 1775–4465	2543 (647); 1726–4240	2495 (734); 1746–4561
Control group	2624 (902); 1184–5052	2668 (934); 1214–5117	2665 (977); 1317–5168
armELV, %			
Experimental group	25 (16); 8–68	24 (16); 2–62[b]	20 (16); 4–63[b]
Control group	17 (10); 2–41	18 (11); 3–39	18 (11); 2–37

Values are reported as mean (standard deviation); range

[a]Between-group difference, Mann–Whitney test, $p<0.05$

[b]Different from baseline, Wilcoxon test, $p<0.05$

for 21/21 subjects of CTRL. At T2, NPRS was available for 16/20 subjects of EXP and for 18/21 subjects of CTRL.

Intervention efficacy

For all study stages NPRS, HandELV and armELV values are presented in Table 3.

Primary outcome

By considering a MCID of 2 in the assessment of pain variation by NPRS, the following 2×3 contingency table was obtained (Table 4). The null hypothesis of equivalence between treatment and control groups was rejected both at T1 ($p=0.0005$) and at T2 ($p=0.011$).

Table 4 NPRS variation at 1 month (T1) and 6 months (T2) from the enrolment. MCID of 2 was used in the assessment of pain variation by NPRS

NPRS variation with respect to the baseline			
	Worsened	Stable	Improved
T1			
EXP ($n=19$)	0	7	12
CTRL ($n=21$)	5	14	2
T2			
EXP ($n=16$)	0	3	13
CTRL ($n=18$)	4	8	6

The null hypothesis of equivalence between experimental (EXP) and control (CTRL) groups was rejected both at T1 ($p=0.0005$) and at T2 ($p=0.011$)

The pain level significantly decreased in the EXP group, with a median variation of 2 points at T1, and remained consistently lower than in the CTRL group until T2 (see Table 3). The reduction in pain was reached at T1 ($p=0.019$) and was maintained until T2 ($p=0.007$). Focusing on women who did have pain at the baseline evaluation, the difference between groups resulted significant both at T1 (nC = 17, nT = 17, Mann U test, $p=0.015$) and at T2 (nC = 15, nT = 14, Mann U test, $p=0.059$).

Secondary outcome

By considering a MCID of 5% in the assessment of asymmetry variation by ELV, the following 2 × 3 contingency tables were obtained (Table 5). The null hypothesis of equivalence between treatment and control groups at 6 months from enrollment was rejected for both arm and hand asymmetry ($p=0.007$ and $p=0.044$, respectively). A significant asymmetry variation was reached at T1 for the arm ($p=0.019$) but not for the hand ($p=0.278$). Similar results were obtained when considering a MCID as high as 10%.

Arm asymmetry significantly decreased with respect to the baseline value in the EXP group only, both at T1 (median reduction: 5%, $p=0.015$) and at T2 (median reduction: 8%, $p=0.001$). Similarly, hand asymmetry significantly decreased with respect to the baseline value in the EXP group only, both at T1 (median reduction: 3%, $p=0.030$) and at T2 (median reduction: 8%, $p=0.015$).

Due to the very large within-subject variability and the relatively small sample size, the between-group comparison was not significant. However, the statistical power of this test was merely 10%. To be of statistical significance, this comparison would require two groups of at least 120 women.

The variability in lymphedema characteristics—either distributed all over the upper limb or localized at specific areas along the arm—includes the change of the whole arm size over time. Figure 3 shows an example from two women of the EXP group and two from the CTRL group.

Table 5 armELV and handELV variation at 1 month (T1) and 6 months (T2) from enrolment

ELV variations with respect to the baseline			
	Worsened	Stable	Improved
armELV			
T1			
EXP ($n=17$)	1	9	7
CTRL ($n=21$)	2	18	1
T2			
EXP ($n=15$)	1	6	8
CTRL ($n=18$)	4	13	1
handELV			
T1			
EXP ($n=17$)	2	7	8
CTRL ($n=21$)	6	10	5
T2			
EXP ($n=15$)	3	3	9
CTRL ($n=18$)	8	7	3

MCID of 5% was used in the assessment of arm asymmetry variation. For armELV, the null hypothesis of equivalence between experimental (EXP) and control (CTRL) groups was rejected both at T1 ($p=0.019$) and at T2 ($p=0.007$). For handELV, the null hypothesis of equivalence between experimental (EXP) and control (CTRL) groups was not rejected at T1 ($p=0.278$) and was rejected at T2 ($p=0.044$)

Discussions

Our goal was to determine the long-term effects on arm pain and lymphedema of self-administered complex decongestive therapy, when taught to women by trained physiotherapists. Results show the efficacy of saCDT in reducing pain and arm swelling.

Efficacy of pain management

At the 6-month mark, treated women were either stable or showed an improvement, while control women were either stable or had worsened. The terms "improved" and "worsened" refer to variations greater than MCID.

In women, arm pain is known to decrease when MLD or CDT is delivered by professionals. Pain decrease can be significant when the baseline pain value is high [2, 17, 21]. In this trial, self-taught treatment following professionally delivered CDT allowed for further reduction of the pain from 4 to 2 in nearly 70% of EXP women, and without any support from the health professionals. Even when the baseline value was relatively low, this progressive reduction in arm pain in the EXP group was significant all throughout the follow-up period (see Table 3).

The effect of self-care on arm pain in women with BCRL is scarcely discussed in the literature. According to a recent review from Douglass and Colleagues, only two studies are available debating this topic [5]. These studies report self-care activities, yoga, or gentle self-massage, having a general positive effect on women's well-being. Recently, a protocol for lymphedema prevention after breast surgery has been proposed by Dönmez and Colleagues [23]. This included both professionally delivered and self-administered MLD, along with a steady increase in physical activity. Effects were tested in a randomized controlled trial lasting 6 weeks, and compared against the usual care given for CDT (information on lymphedema). In this study, arm pain assessed with the visual analogue scale decreased from 5 to 1 in the experimental group, thus advocating for the inclusion of

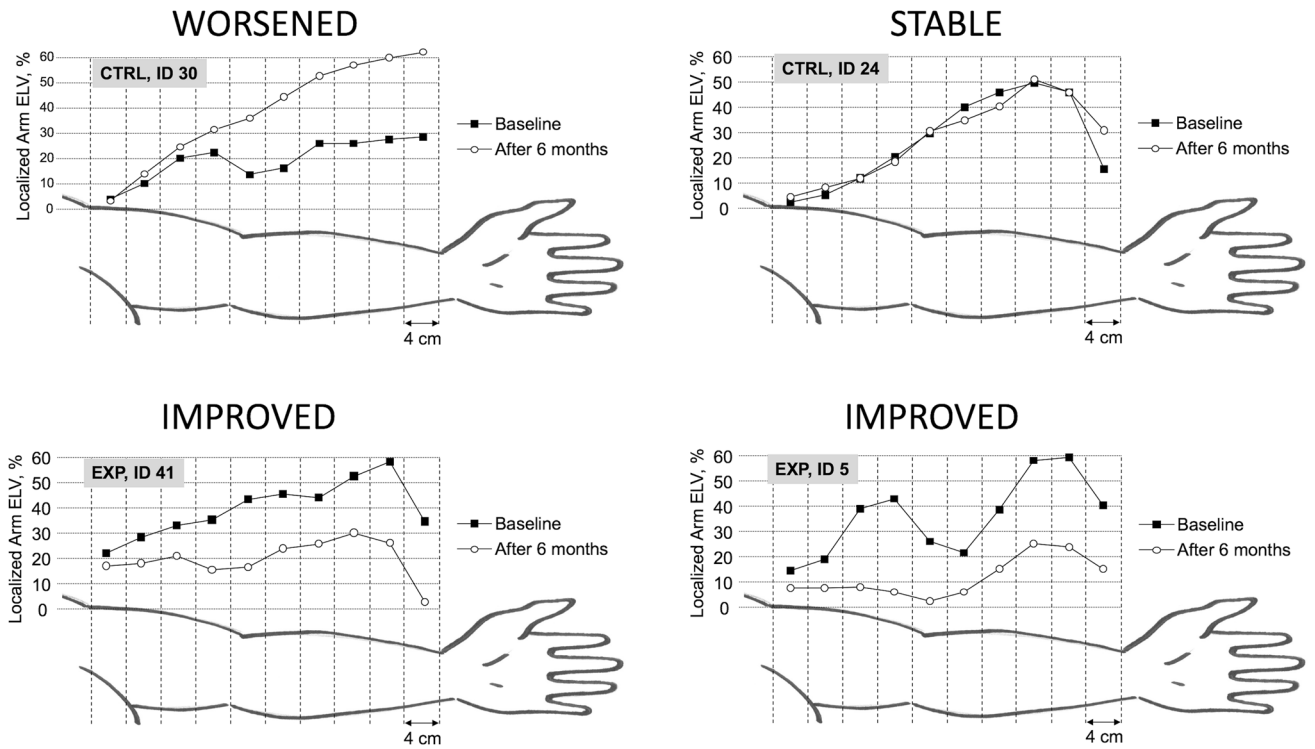

Fig. 3 Localized arm asymmetry at the beginning (T0) and the end (T2) of the study in four subjects. Two subjects belonged to the control group (CTRL) and two to the experimental (EXP) group

preventive activities comprehensive of MLD teaching in the early stages of lymphedema management. Teaching women to incorporate short periods of moderate activity into their daily routines (lifestyle intervention) can improve their overall well-being, as measured by the Short Form-36 Questionnaire, which includes bodily pain assessment [27]. However, multimodal physical activity programs did not result in a particularly economically efficient means for improving the overall women's health-related quality of life [28].

Efficacy on arm swelling

At 6 months after the end of the saCDT training period, more than 50% of treated women presented a clinically significant reduction in arm and/or hand swelling. Also noteworthy of this study is the average reduction in arm volume of 230 ml obtained by saCDT (see Table 3) which is comparable to that obtained through MLD and CDT, when provided by professionals [7, 11, 12]. This result was nearly doubled compared to the average one obtained by Hwang and Colleagues in a similar study, even though it introduced a different self-treatment protocol [29].

Moreover, the self-treatment proposed in this study exceeded the exercise-based self-care protocols in terms of ELV reduction. Jeffs and Colleagues compared the effect of compressive garments at night-time (usual care) to that of daily physical activity and usual care [15]. The sampled women were similar in age and clinical characteristics to those of our study. Physical activity reduced arm asymmetry by about 1 point only, from %ELV = 15.80 to %ELV = 14.66 (median values).

Chronicity, self-care, and health-care system sustainability

Better screening and improved treatments allowed for a progressive decrease in the breast cancer mortality rate [30]. As survival rates improve, the sustainability of chronicity management has to be handled by the health-care systems. This encouraged the development of low-cost protocols for self-care, aiming at supporting the patients' quality of life [31, 32]. Our work targets this area. It is based on an intense academic, theoretical, and practical activity, which allows women to recognize symptoms of lymphedema worsening, to intervene in a semi-professional manner from the onset of the symptoms, and to be able to manage this chronicity in their daily life, without falling back into becoming a patient once again.

The implementation of effective and standardized primary interventions for BCRL, delivered by professionals, has shown to decrease BRCL-related costs by about 20% [33]. Instead, self-care programs based on physical exercises

resulted in questionable economic effectiveness, as shown by the study by Haines and Colleagues [28]. In our study, women were given a 15-h course treatment by a physiotherapist. This is much cheaper compared to individual sessions of professionally delivered MLD, typically consisting of 10 h of physiotherapy per woman.

Sample

In published intervention studies dealing with the treatment of lymphedema, the baseline mean volume of the affected arm ranges between 2000 and 3000 ml, with a standard deviation of about 500 ml and overall range of 1500–6000 ml. Data in this study are homogeneous with the values available in the literature [5, 7, 12, 16, 21, 34]. This supports the external validity of our results.

Methodological aspects

Over the years, the scientific community has come to a mutual consensus where the excess in limb volume (ELV) is viewed as the outcome to be used in the assessment of lymphedema and treatment efficacy [2]. However, the profound differences in data presentation, normalization, and interpretation make it difficult to compare the results among the different studies. Some authors normalized the ELV variation with respect to the ELV initial value, thus presenting the rate of ELV variation [7, 11, 15]. In this case, for example, a variation in ELV from 10 to 7% would result in a 30% reduction and could overemphasize the treatment's positive effects. In our study, a woman with such an ELV variation would be classified as stable, the variation (3%) being lower than MCID. The choice of using a threshold set at MCID to discuss asymmetry variations is a novelty of this study and provides robustness to the results. The strength of this approach is that it allows, when present, to highlight the clinical evidence of treatment efficacy.

We applied the same criterion to the assessment in pain variation, with MCID set at 2 [20]. In this study, pain was selected as the primary outcome because of its direct impact on a woman's quality of life [35]. It is noteworthy to mention that the rate of women with persistent pain, reduced health, and overall well-being, even 5 years after breast surgery, can be as high as 80% [36].

Finally, the technique used to assess arm lymphedema is worth discussing. Centimetric measurement allows for volume and asymmetry computation along the whole length of the arm. Through centimetric measurement, we monitored the evolution of localized lymphedemas over time, e.g., at the wrist or at the elbow, as shown in Fig. 3. Such a result cannot be achieved by the direct volumetric assessment only performed via arm immersion. For professionals in the field, this element and its graphical presentation are a further novelty of this study.

Limits

The main limitation of this study was the small sample size ($N=41$), which may limit the generalizability of the results. This was a consequence of the monocentric design of the study and of the inclusion/exclusion criteria. In fact, 31 out of 78 women assessed for eligibility were excluded from the study (see Fig. 2). As a countermeasure, to limit the effects of uncontrolled confounding factors and in order to provide reliable results with such a small sample, we only discussed very large variations (> MCID) in the study variables.

Another limitation in this study is the assessment of pain only by the NPRS. A multidimensional approach to pain assessment and to the women's quality of life by means of specific tools should be addressed in future studies.

A further limit was that we did not directly measure whether the women followed the recommendations provided by the professionals. Future studies should consider using a diary to track women self-treatment, any noticeable change, and the potential use of medication, including analgesics and antidepressant, that may affect the perception of pain and of the quality of life.

Finally, we did not perform a direct measurement of the reduction of the costs determined by the self-treatment protocol. A thorough cost-effective analysis of our protocol for saCDT should be performed in a future study, e.g., by inspecting the institutional file records of the two groups in the year following the end of the trial.

Conclusions

Our work reveals that saCDT can be used for the management of upper limb BCRL. After 6 months, we found significant statistical evidence in the efficacy of teaching saCDT to women in terms of maintaining or improving the benefits of the professionally delivered CTD.

With the aim of promoting its use, the full protocol for saCDT teaching has been made available in English on the website of our institution.

Acknowledgements The authors would like to acknowledge Dr. Franca Coppadoro and her team at the Fatebenefratelli Hospital, Milan, Italy, for their kind and fruitful suggestions on the use of self-treatment in the management of lymphedema.

Author contributions MBL, IC, AM: *Conceptualization*—Ideas; formulation or evolution of overarching research goals and aims. IC, AM: *Data Curation*—Management activities to annotate (produce metadata), scrub data, and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later reuse. AM: *Formal Analysis*—Application of statistical,

mathematical, computational, or other formal techniques to analyze or synthesize study data. ML: *Funding Acquisition*—Acquisition of the financial support for the project leading to this publication. IC, AC, PV, MBL: *Investigation*—Conducting a research and investigation process, specifically performing the experiments, or data/evidence collection. IC: *Methodology*—Development or design of methodology; creation of models. IC: *Project Administration*—Management and coordination responsibility for the research activity planning and execution. n.a.: Resources—Provision of study materials, reagents, materials, patients, laboratory samples, animals, instrumentation, computing resources, or other analysis tools. AM: *Software*—Programming, software development; designing computer programs; implementation of the computer code and supporting algorithms; testing of existing code components. IC: *Supervision*—Oversight and leadership responsibility for the research activity planning and execution, including mentorship external to the core team. n.a.: *Validation*—Verification, whether as a part of the activity or separate, of the overall replication/reproducibility of results/experiments and other research outputs. AM, IC: *Visualization*—Preparation, creation and/or presentation of the published work, specifically visualization/data presentation. AM, IC: *Writing—Original Draft Preparation*—Creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation). n.a.: *Writing—Review & Editing*—Preparation, creation, and/or presentation of the published work by those from the original research group, specifically critical review, commentary, or revision—including pre- or post-publication stages.

Data availability The dataset analyzed during the current study can be made available by the corresponding author upon request.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed during studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and comply to the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the local Ethics Committee (2017/0123714). All women signed an informed consent to data treatment.

References

1. Badger C, Preston N, Seers K, Mortimer P (2004) Physical therapies for reducing and controlling lymphoedema of the limbs. Cochrane Database Syst Rev. https://doi.org/10.1002/14651858.CD003141.pub2
2. Ezzo J, Manheimer E, McNeely ML, Howell DM, Weiss R, Johansson KI, Bao T, Bily L, Tuppo CM, Williams AF, Karadibak D (2015) Manual lymphatic drainage for lymphedema following breast cancer treatment. Cochrane Database Syst Rev 5:CD003475. https://doi.org/10.1002/14651858.CD003475.pub2
3. McNeely ML, Campbell K, Ospina M, Rowe BH, Dabbs K, Klassen TP, Mackey J, Courneya K (2010) Exercise interventions for upper-limb dysfunction due to breast cancer treatment. Cochrane Database Syst Rev 6–8. https://doi.org/10.1002/14651858.CD005211.pub2
4. Mondry TE, Riffenburgh RH, Johnstone P, a S (2004) Prospective trial of complete decongestive therapy for upper extremity lymphedema after breast cancer therapy. Cancer J 10:42–48; discussion 17–19. https://doi.org/10.1097/00130404-200401000-00005
5. Douglass J, Graves P, Gordon S (2016) Self-care for management of secondary lymphedema: a systematic review. PLoS Negl Trop Dis 10:1–20. https://doi.org/10.1371/journal.pntd.0004740
6. Taghian NR, Miller CL, Jammallo LS, O'Toole J, Skolny MN (2014) Lymphedema following breast cancer treatment and impact on quality of life: a review. Crit Rev Oncol Hematol 92:227–234
7. Koul R, Dufan T, Russell C, Guenther W, Nugent Z, Sun X, Cooke AL (2007) Efficacy of complete decongestive therapy and manual lymphatic drainage on treatment-related lymphedema in breast cancer. Int J Radiat Oncol Biol Phys 67:841–846. https://doi.org/10.1016/j.ijrobp.2006.09.024
8. Stuiver MM, ten Tusscher MR, McNeely ML (2017) Which are the best conservative interventions for lymphoedema after breast cancer surgery? BMJ 2330:j2330. https://doi.org/10.1136/bmj.j2330
9. Norman SA, Localio AR, Potashnik SL, Torpey HAS, Kallan MJ, Weber AL, Miller LT, Demichele A, Solin LJ (2009) Lymphedema in breast cancer survivors: incidence, degree, time course, treatment, and symptoms. J Clin Oncol 27:390–397. https://doi.org/10.1200/JCO.2008.17.9291
10. Finnane A, Janda M, Hayes SC (2015) Review of the evidence of lymphedema treatment effect. Am J Phys Med Rehabil 94:483–498. https://doi.org/10.1097/PHM.0000000000000246
11. McNeely ML, Magee DJ, Lees AW, Bagnall KM, Haykowsky M, Hanson J (2004) The addition of manual lymph drainage to compression therapy for breast cancer related lymphedema: a randomized controlled trial. Breast Cancer Res Treat 86:95–106. https://doi.org/10.1023/B:BREA.0000032978.67677.9f
12. Andersen L, Højris I, Erlandsen M, Andersen J (2000) Treatment of breast-cancer-related lymphedema with or without manual lymphatic drainage: a randomized study. Acta Oncol (Madr) 39:399–405. https://doi.org/10.1080/028418600750013186
13. Rogan S, Taeymans J, Luginbuehl H, Aebi M, Mahnig S, Gebruers N (2016) Therapy modalities to reduce lymphoedema in female breast cancer patients: a systematic review and meta-analysis. Breast Cancer Res Treat 159:1–14. https://doi.org/10.1007/s10549-016-3919-4
14. Casley-Smith JR (1995) Alterations of untreated lymphedema and it's grades over time. Lymphology 28:174–185
15. Jeffs E, Wiseman T (2013) Randomised controlled trial to determine the benefit of daily home-based exercise in addition to self-care in the management of breast cancer-related lymphoedema: a feasibility study. Support Care Cancer 21:1013–1023. https://doi.org/10.1007/s00520-012-1621-6
16. Sagen Å, Kåresen R, Risberg MA (2009) Physical activity for the affected limb and arm lymphedema after breast cancer surgery. A prospective, randomized controlled trial with two years follow-up. Acta Oncol (Madr) 48:1102–1110. https://doi.org/10.3109/02841860903061683
17. Van Dijck S, Nelissen P, Verbelen H, Tjalma W, Gebruers N (2016) The effects of physical self-management on quality of life in breast cancer patients: a systematic review. Breast 28:20–28. https://doi.org/10.1016/j.breast.2016.04.010
18. Urbaniak GC, Plous S (2013) Research randomizer (version 4.0) [Computer Software]
19. Williamson A, Hoggart B (2005) Pain: a review of three commonly used pain rating scales. J Clin Nurs 14:798–804. https://doi.org/10.1111/j.1365-2702.2005.01121.x
20. Farrar JT, Young JP, LaMoreaux L, Werth JL, Poole RM (2001) Clinical importance of changes in chronic pain intensity measured on an 11-point numerical rating scale. Pain 94:149–158. https://doi.org/10.1016/S0304-3959(01)00349-9
21. Cho Y, Do J, Jung S, Kwon O, Jeon JY (2016) Effects of a physical therapy program combined with manual lymphatic drainage on

shoulder function, quality of life, lymphedema incidence, and pain in breast cancer patients with axillary web syndrome following axillary dissection. Support Care Cancer 24:2047–2057. https://doi.org/10.1007/s00520-015-3005-1
22. Moseley AL, Piller NB, Carati CJ (2005) The effect of gentle arm exercise and deep breathing on secondary arm lymphedema. Lymphology 38:136–145
23. Dönmez AA, Kapucu S (2017) The effectiveness of a clinical and home-based physical activity program and simple lymphatic drainage in the prevention of breast cancer-related lymphedema: a prospective randomized controlled study. Eur J Oncol Nurs 31:12–21. https://doi.org/10.1016/j.ejon.2017.09.004
24. Hayes SC, Speck RM, Reimet E, Stark A, Schmitz KH (2011) Does the effect of weight lifting on lymphedema following breast cancer differ by diagnostic method: results from a randomized controlled trial. Breast Cancer Res Treat 130:227–234. https://doi.org/10.1007/s10549-011-1547-6
25. Leduc O, Leduc A, Bourgeois P, Belgrado JP (1998) The physical treatment of upper limb edema. Cancer 83:2835–2839
26. Buchan J, Janda M, Box R, Schmitz K, Hayes S (2016) A randomized trial on the effect of exercise mode on breast cancer-related lymphedema. Med Sci Sports Exerc 48:. https://doi.org/10.1249/MSS.0000000000000988
27. Basen-Engquist K, Taylor CLC, Rosenblum C, Smith MA, Shinn EH, Greisinger A, Gregg X, Massey P, Valero V, Rivera E (2006) Randomized pilot test of a lifestyle physical activity intervention for breast cancer survivors. Patient Educ Couns 64:225–234. https://doi.org/10.1016/j.pec.2006.02.006
28. Haines TP, Sinnamon P, Wetzig NG, Lehman M, Walpole E, Pratt T, Smith A (2010) Multimodal exercise improves quality of life of women being treated for breast cancer, but at what cost? Randomized trial with economic evaluation. Breast Cancer Res Treat 124:163–175. https://doi.org/10.1007/s10549-010-1126-2
29. Hwang JM, Hwang JH, Kim TW, Lee SY, Chang HJ, Chu IH (2013) Long-term effects of complex decongestive therapy in breast cancer patients with arm lymphedema after axillary dissection. Ann Rehabil Med 37:690–697. https://doi.org/10.5535/arm.2013.37.5.690
30. Allemani C, Weir HK, Carreira H, Harewood R, Spika D, Wang XS et al (2015) Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet 385:977–1010. https://doi.org/10.1016/S0140-6736(14)62038-9
31. Bartholomay M, Mannix C, Barton-Burke M, ML B, Delaney R, Doherty C, Lewis M (2008) A feasibility study of low-cost patient-administered skin care intervention among head and neck cancer patients receiving chemo-radiation. Oncol Nurs Forum 35:494
32. Jansen F, Cnossen IC, Eerenstein SEJ, Coupé VMH, Witte BI, van Uden-Kraan CF, Doornaert P, Braunius WW, De Bree R, Hardillo JAU, Honings J, Halmos GB, Leemans CR, Verdonck-de Leeuw IM (2016) Effectiveness and cost-utility of a guided self-help exercise program for patients treated with total laryngectomy: protocol of a multi-center randomized controlled trial. BMC Cancer 16:580. https://doi.org/10.1186/s12885-016-2613-6
33. Humphreys I, Thomas MJ, Morgan KM (2017) Managing chronic oedema in community settings. Wounds UK
34. Do JH, Kim W, Cho YK, Lee J, Song EJ, Chun YM, Jeon JY (2015) Effects of resistance exercises and complex decongestive therapy on arm function and muscular strength in breast cancer related lymphedema. Lymphology 48:184–196
35. Caffo O, Amichetti M, Ferro A, Lucenti A, Valduga F, Galligioni E (2003) Pain and quality of life after surgery for breast cancer. Breast Cancer Res Treat 80:39–48. https://doi.org/10.1023/A:1024435101619
36. Bell RJ, Robinson PJ, Nazeem F, Panjari M, Fradkin P, Schwarz M, Davis SR (2014) Persistent breast pain 5 years after treatment of invasive breast cancer is largely unexplained by factors associated with treatment. J Cancer Surviv 8:1–8. https://doi.org/10.1007/s11764-013-0306-6