

# Effects of early Manual Lymphatic Drainage in the prevention of secondary lymphoedema in breast cancer patients. A literature Review

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## Abstract:

**Background:** Secondary lymphoedema is a significant and life-changing complication following breast cancer treatment. Numerous studies have investigated its management following its occurrence, but very few have focused on its prevention. Manual Lymphatic Drainage (MLD) is part of the gold standard management regime for lymphoedema. The purpose of this review is to gather and present the most contemporary available evidence in an attempt to find out whether MLD aids in the prevention of lymphoedema, or delays its occurrence, if initiated shortly after the medical management (surgery, chemo- or radiotherapy).

**Methods:** A literature review was conducted using PubMed, PEDro (Physiotherapy Evidence Database), Cochrane Central Register of Controlled Trials and Google Scholar, searching for randomised controlled trials published from 2010 onwards.

**Results:** In total 7 RCTs with 622 patients were identified. Most of the studies showed favourable results for the preventive effect of MLD.

**Conclusions:** Our results showed that MLD might have a positive effect preventing the development of secondary lymphoedema, however, the quality of the studies was average and did not address its usefulness in specific patient sub-populations. Thus, necessitating further studies for more robust conclusions to be made.

**Keywords:** Manual Lymphatic Drainage, MLD, lymphoedema, prevention, breast cancer

## INTRODUCTION

Breast cancer is one of the leading cancers in the female population with 2.3 million new cases worldwide in 2020<sup>1,2</sup>. With advances in the field of cancer therapeutics, increasingly more people survive cancer<sup>1</sup>, however their quality of life post treatment may be severely compromised. Emphasis is therefore placed on the quality of life, focusing on the prevention of unwanted side effects and minimisation of associated functional and psychosocial morbidities<sup>3,4</sup>. Secondary lymphoedema constitutes an example of such a side effect<sup>2,5,6</sup>.

Secondary lymphoedema can be defined as the failure of the lymphatic system to drain lymph (a protein-rich fluid) following injury. This results to its accumulation in the interstitial space, leading to swelling of the affected limb<sup>7-10</sup>. It can occur in up to 1 in 4 women after breast cancer treatment. Secondary lymphoedema can occur at any time after the operation or

even years later<sup>5,15</sup>.

A 'swollen' limb can have a significant impact on one's quality of life. Pain, disfigurement, functional impairment, psychological (depression, low self-esteem) and socio-economic (loss of employment, social withdrawal) problems are just a few<sup>4,6,9,10,12,17,18</sup>.

Typically, the treatment for breast cancer includes surgery with removal of lymph nodes, radiotherapy and/or chemotherapy and/or hormonal therapy which may damage the lymphatic system, disturb the transport capacity of lymph and the lymph flow<sup>23,24</sup>. Overtime this could lead to accumulation of lymph in the interstitial space, resulting in an increase in protein stagnation, an increase in limb volume and the risk of lymphoedema formation.

Current management options include pharmacological therapy, surgery and Complete Decongestive Therapy (CDT). The limited number and the retrospective nature of trials on pharmacological regimes makes it difficult to ascertain their effectiveness for reducing lymphoedema<sup>10</sup>. Surgical treatments include debulking resection, liposuction and lymphatic-venous anastomoses (LVA), but these are offered in carefully selected patients, and the literature is currently inconclusive regarding the effectiveness of LVA on the permanent reduction of lymphoedema<sup>10,19</sup>. Therefore, most cancer survivors choose CDT as their management option<sup>10</sup>. This includes manual lymphatic drainage (MLD), compression garments/bandaging, ex-

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ercise and skin care.

It is believed that MLD offers several benefits such as enhancement of the immune system's response by accelerating the removal of waste products from tissues<sup>28,30-32</sup>, reduction of muscle spasm and pain<sup>28,32,35-37</sup> and aims in the formation of alternative routes for lymph removal<sup>3,11,14,26,27,29,36,37</sup>. Lastly, MLD's special techniques stretch the lymph collectors' walls, increasing their activity, causing a peristaltic wave which pumps lymph through the lymphatic system faster<sup>11,25-32</sup>.

Unfortunately, no cure currently exists for an established lymphedema<sup>3,9,10,12</sup>. Therefore, focusing on how to prevent it is worth investigating.

We herein present the current literature on the efficacy of Manual Lymphatic Drainage (MLD) at preventing the incidence of lymphoedema in breast cancer survivors.

## METHOD

A literature search was conducted using PubMed, PEDro (Physiotherapy Evidence Database), Cochrane Central Register of Controlled Trials and Google Scholar. The keywords used were "lymphedema OR lymphoedema", "prevent" "physiotherapy", "Manual lymphatic drainage" and "breast cancer". Studies that investigated the management of established lymphedema were excluded. Studies in which MLD was used to prevent the incidence of lymphoedema following breast cancer treatment were included. Titles and abstracts were screened and duplicates were eliminated. Only relevant randomised controlled trials (RCT) published after 2010 were selected to ensure the most recent evidence was reviewed. Any relevant references from the original articles were included in the review. The methodological quality of the included RCTs was taken from PEDro, as it is a reliable and valid source<sup>20,21</sup>.

## RESULTS

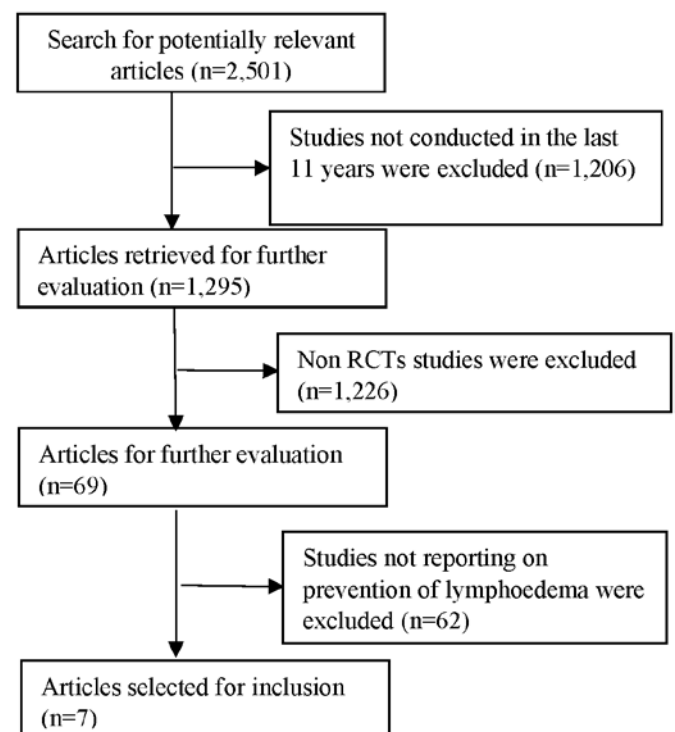
The literature search resulted in a total of 2,501 articles. The majority of the studies comprised either reviews or non-randomised studies. Seven randomised clinical trials conducted were deemed to meet the inclusion criteria (see flow chart 1). The participants in all included RCTs had undergone a form of surgery with or without adjuvant therapies for breast cancer. The results are presented in Table 1. Their main findings are presented below.

Sarri et al<sup>3</sup>, Donmez & Kapucu<sup>7</sup>, Lacomba et al<sup>8</sup>, Zimmerman et al<sup>17</sup> and Cho et al<sup>14</sup> all showed that MLD contributes in the prevention of lymphoedema. Sarri et al<sup>3</sup> with 22 cancer survivors post radical/quadractectomy with ipsilateral axillary lymph node dissection showed that MLD increases significantly the number of lymph nodes and the velocity of lymphatic flow. Donmez & Kapucu<sup>7</sup> with a sample of 52 cancer survivors post modified radical mastectomy and breast protective surgery with axillary lymph node dissection showed that the group with MLD had no change in the mean metacarpophalangeal joint circumference whereas the control group had a significant increase. Also, they found that MLD reduced the lymphoedema related symptom severity scores. Lacom-

ba et al<sup>8</sup> with a sample size of 120 post surgery with axillary node dissection found that the number of women who developed lymphoedema and the average increase in limb volume, 1 year post surgery, were significantly higher in the control group compared to the MLD group. Zimmerman et al<sup>17</sup> with 67 people post breast conserving and modified mastectomy with lymph node dissection found that in the group without MLD the limb volume increase at 6 months post-surgery and no lymphoedema developed in the MLD group. Lastly, Cho et al<sup>14</sup> with 41 cancer survivors post breast surgery found that no lymphoedema developed in the MLD group compared to the control group (6 people).

In contrast Devoogdt et al<sup>4,38</sup> in both studies found that MLD doesn't add any benefits to the prevention of lymphoedema. 160 cancer survivors post unilateral axillary lymph node dissection showed that from one year<sup>38</sup> to 5 years<sup>4</sup> post-surgery the incidence of lymphoedema, quality of life, arm circumference and arm volume were comparable in MLD and control groups.

Only four out of seven studies have a quality of 5 and above as per PEDro checklist (see table 1). Therefore, the results from these studies should be interpreted with caution.



Flow chart 1: Literature Search

Study (year)	Sample Size (n)	Breast Cancer Treatment	Intervention	Duration of intervention	Outcome Measures	Results	Quality
Sarri et al. (2010)	22	Radical or quadrantectomy with ipsilateral axillary lymph node dissection	MLD using Foldi technique	1 session, 5 minutes in length	First measurement performed between 15 and 60 days post-surgery and second 7±3 after first measurement using lymphoscintigraphy	There was an association present between MLD and the positive progression of lymphatic flow in all of the phases of the lymphoscintigraphy. A significant increase in the number of lymph nodes and velocity of lymphatic flow was detected in the intervention group ( $p=0.007$ ) when compared to the control group ( $p=0.014$ ).	4/10
Donmez & Kapucu (2017)	52	Modified radical mastectomy, breast protective surgery with axillary lymph node dissection	Patient information on lymphoedema prevention and management, physical activity and simple lymphatic drainage message	-20 mins of physical activity (hand exercises, aerobic exercises and stretching exercises) -Simple lymphatic massage commenced after the axillary drains were removed and lasted for 6 weeks for approximately 40 mins, twice a week.	-Arm circumference (using a tape measure), -Disability of the arm, shoulder and hand questionnaire (DASH) -Lymphoedema related symptoms (visual analogue scale)  Measurements were taken at the baseline, beginning and end of the 2nd, 4th, and 6th week of the trial.	Mean metacarpophalangeal joint circumference in the intervention group did not show a significant change. It was found to gradually increase in the control group ( $p>0.05$ ). At the 6 <sup>th</sup> week there was no significant change in the circumference measurements in the intervention group but there was a statistically significant increase in the control group compared to those in the intervention group ( $p>0.05$ ).  Lymphoedema-related symptom severity scores significantly decrease in the intervention group from baseline by the end of treatment ( $p<0.05$ ). Both groups showed a decrease in their DASH scores however the scores in the control group remained significantly higher than the scores in the intervention group.	5/10
Devoogdt et al. (2018)	160	Unilateral axillary dissection for breast cancer levels I-III	MLD (using Leduc and Vodder methods)	-30 mins exercise session -MLD commenced on week 5 post surgery for a period of 20 weeks (30mins sessions x 40 sessions) Frequency of MLD was increased from one to three times a week and then decreased to once a week	-Arm volume with water displacement -Arm circumference with a fixed tapeline -SF-36 questionnaire -Shoulder range of motion (tape measure) -function (Lymph-ICF)  Assessment was done before the operation and at 6,12,24 and 60 months after surgery.	The incidence rate of lymphoedema was comparable between the groups at all follow up measurements.  Five years post-surgery, the cumulative incidence rate was 35% in the intervention group versus 29% in the control group (RR0.89, $p=0.45$ ) for the arm volume, 35% vs 38% (RR 0.93 $p=0.73$ ) for the arm circumference, for the $\geq 5\%$ definition 68% versus 53% (RR1.28 $p=0.08$ ) and for the $\geq 10\%$ definition 28% versus 24% (RR 1.18, $p=0.57$ ).  No significant differences were found for the shoulder range of motion and function between the groups except at 5 year follow up were the household, mobility and life/social activity domains of the Lymph-ICF showed a statistically significant difference favouring the intervention group.	8/10
Lacomba et al. (2010)	120	Breast surgery with axillary node dissection	MLD using Leduc technique, scar massage, education and exercises	3 times per week for 3 weeks	Arm circumference (using a tape measure) measured at 4 weeks, 3-, 6- and 12 months post surgery	After 1 year, 18 (16%) women developed lymphoedema; 14 were in the control group and 4 in the intervention group, with a significant difference of $p=0.01$ .  The control group had an average of 5.1% increase in the volume of the affected arm compared to the unaffected. However, the intervention group had an average increase of 1.6% between the arms. The difference between the two groups was statistically significant ( $p=0.0065$ ).  Developing lymphoedema was four times faster in the control group (intervention group/control group, hazard ratio = 0.26, 95% CI = 0.09-0.79; $p=0.010$ ).	5/10

Zimmermann et al. (2012)	67	Breast-conserving and modified mastectomy for primary breast cancer with sentinel or axillary lymph node dissection with or without adjuvant treatment	Manual Lymph Drainage (using Foldi and Strobenreuther techniques)	MLD was applied 5 times per week during the first 2 weeks, and 2 times per week from day 14 to 6 months post surgery Arm and chest exercises commenced from day 2 post-surgery	Arm volume using water displacement before the operation, on days 2,7,14 and at 3 and 6 months.	At 3 months the control group had a 6% increase in arm volume which further increased to 10% at 6 months post-surgery ( $p=0.0033$ ). In the intervention group lymphoedema did not occur.	4/10
Cho et al (2016)	41	Any breast surgery with cording (axillary web syndrome) with or without adjuvant therapy and a pain score >3 in a numeric scale at least 4 weeks post-surgery	Exercises, manual therapy, Manual lymph drainage using Vodder's method	3 times per week for 4 weeks for 40mins physical therapy Additional 30mins MLD five times a week for 1 week by a therapist. Weeks 2-4 patients performed self -MLD	-Arm volume (circumferential measurement using an established formula) -Shoulder function and strength (hand-held dynamometer) -Active range of motion (using a digital inclinometer) -Disabilities of the arm, shoulder and hand (DASH questionnaire), -Quality of life (using EORTC questionnaire), -Visible /palpable cording in the axilla Pain (Numeric Rating Scale- NRS)  Measured at baseline and after 4 weeks of treatment	After 4 weeks, their results showed that the quality of life, shoulder strength, DASH and NRS scores were significantly improved in both groups ( $p<0.05$ ).  Cording was not significantly different between the groups with 28.5% in the intervention group versus 35% of patients in the control group.  Pain and arm volume were significantly reduced in the intervention group ( $p<0.05$ ) compared to the control group. Lymphoedema was observed in the control group (6 patients) and none in the intervention group ( $p<0.05$ ).	6/10
Devoogdt et al (2011)	160	Unilateral axillary lymph node dissection	Guidelines for lymphoedema prevention, exercise therapy, manual lymph drainage using Vodder method	Commenced one week post removal of axillary drains (approx. 5 weeks post- op) Duration of 20 weeks with 30 mins exercise session twice a week, then once a week and then once every two weeks 30 mins MLD with an increased frequency from once a week to 3 times a week and then decrease to once a week	-Arm volume with water displacement -Arm circumference with a fixed tapeline -SF-36 questionnaire  Assessment was done before the operation, 1,3,6, and 12 months after surgery.	12 months after surgery, the cumulative incidence rate for lymphoedema was comparable between the intervention group (18 subjects) and the control group (15 subjects); $p=0.045$ . The results for the mental and physical health related quality of life, arm circumference and arm volume were comparable between the groups at all follow up points.	8/10

**Table 1.** Studies Identifying the Efficacy of MLD at Reducing the Incidence of Lymphoedema in Breast Cancer Patients

## DISCUSSION

Manual Lymphatic Drainage is part of the Complete Decongestive Therapy which is currently recognized as the standard management for lymphoedema<sup>9,22</sup>. However, its effectiveness in preventing the development of lymphoedema following breast cancer treatment has yet to be firmly established.

The onset of administration of MLD can play a significant

role in the prevention of lymphoedema. Devoogdt et al<sup>4,38</sup> started one week after the removal of axillary drains (i.e. approximately 5 weeks post-operation). This might account for the negative results as they might have started too late for any preventive effects. All other authors commenced their studies before 5 weeks post-operation and had positive results. This suggests that starting MLD early in the post-operative period, could potentially aid in the flow of lymph fluid, the

formation of alternative routes such as lympho-lymphatic and lympho-venous anastomoses and thus prevention of lymph accumulation in the arm.

The authors in the included studies used different definitions for diagnosing lymphoedema. This might have resulted in mis-diagnosing lymphoedema in some patients and thus accounting for the difference in their results. Devoogdt et al<sup>38</sup> diagnosed lymphoedema when the difference in measurement was 200ml or more in the volume between the affected and unaffected arms compared with the difference before the operation. They have also used a difference in arm circumference of 2cm or more between the affected and unaffected side at two or more measurement points compared with the difference before the operation. The same authors in a later study<sup>4</sup> used a difference of  $\geq 200$ ml increase in volume or  $\geq 2$ cm increase in arm circumference or  $\geq 5\%$  or a  $\geq 10\%$  increase in relative arm volume compared to the pre-operation measurement. Cho et al<sup>14</sup> used  $\geq 3\%$  volume increase from baseline in the affected limb. Donmez & Kapucu<sup>7</sup> and Lacomba et al<sup>8</sup> defined lymphoedema by the difference in arm circumference of 2cm or more between the affected and unaffected arms in any 2 adjacent points. Sarri et al<sup>3</sup> used lymphoscintigraphy and assessed lymphatic function by measuring lymph flow in the affected arm. Zimmermann et al<sup>17</sup> defined lymphoedema as a difference in the volume between the affected and unaffected arm of 5% or more. It is therefore apparent that by using different definitions the authors in some studies might have missed participants with lymphoedema, or they may have included patients with transient lymphoedema.

The included studies had differences in their included populations. For instance, Lacomba et al<sup>8</sup> did not include people with axillary node dissection and Cho et al<sup>14</sup> did not specify, whereas all the other trials included people with axillary node dissection. With more lymph nodes resected, potentially more damage is done to the lymphatic system and thus the risk for developing lymphoedema is higher. Except Zimmermann et al<sup>17</sup> who excluded participants with adjuvant treatments and Donmez & Kapucu<sup>7</sup>, who don't specify if the patients had received adjuvant treatments, all other trials have included participants who had chemotherapy, radiotherapy and hormone therapy treatments. Unfortunately, the specifics of the aforementioned treatments were not presented in any of the included studies. Since current literature suggests that MLD may be ineffective in patients with transient post-operative lymphoedema following taxane-based chemotherapy<sup>4,39-41</sup>, this might account for some of the reported negative results in this review (Table 1).

Different outcome measures such as arm circumference, water displacement and lymphoscintigraphy were used to measure arm volume and the presence of lymphoedema. However, using different outcome measures may lead to different results and this might be one reason for the dissimilar conclusions in the studies included. Water displacement is considered the gold standard as it is the most accurate method of measuring arm volume, whereas arm circumference is more often used in clinical practice due to its simplicity. Although both are reliable and valid techniques, both are

susceptible to error and neither provides information about lymphatic function. It is not easy to ensure that arms are submerged to the same level and circumferential measurements could be affected by the positions on the arm chosen by different assessors<sup>9,10,13,42,43</sup>. There are other methods of lymphoedema assessment such as arm compressibility (tonometry), Magnetic Resonance Imaging (MRI), radionuclide scintigraphy and bioimpedance which may provide more accurate assessment on lymphatic function however they are expensive and not easy to use in everyday clinical practice<sup>13,44</sup>.

The included studies had different duration from a single session to 5 years. Maybe the effects of MLD have short-lasting duration and this might account for the results in Devoogdt et al studies<sup>4,38</sup>.

## FURTHER STUDIES AND LIMITATIONS

Most of the studies have investigated MLD in combination with other techniques, such as manual therapy, therefore more studies are needed to isolate the use of prophylactic MLD in preventing secondary lymphoedema. In addition, further studies should investigate the efficacy of self-massage at home in preventing lymphoedema incidence. Finally, a cost-benefit study would be beneficial as MLD is a time consuming and expensive treatment.

This analysis has three major limitations. Firstly, only studies presented in English and Greek and available online were used. Secondly, although most included studies have an average quality, they were the only recent ones available. Lastly, a meta-analysis was not appropriate as the trials had different outcome measures, different treatment duration, techniques used and onset of MLD treatment as well as the involvement of other interventions (eg. Exercises, guidelines, manual therapy). Despite their heterogeneity, an attempt was made to explain the disparity of the results.

## CONCLUSION

Most trials included in this study suggest that Manual Lymphatic Drainage has a preventing effect in secondary lymphoedema incidence among breast cancer survivors. However, more homogenous studies are needed to clarify the treatment onset, duration and the subpopulations of breast cancer survivors whom Manual Lymphatic Drainage can provide the maximal benefit.

## REFERENCES

- 1 Sung H, Ferlay J, Siegel RL, Lavaranne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of incidence and mortality worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021;71:209-249
- 2 Disipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol* 2013;14:500-15
- 3 Sarri AJ, Moriguchi SM, Dias R, Peres SV, Da Silva ET, Koga KH, Matthes AGZ, Dos Santos MJ, Da Rocha ET, Haikel RL. Physiotherapeutic stimulation: Early prevention of

- lymphedema following axillary lymph node dissection for breast cancer treatment. *Exp Ther Med* 2010; doi: 10.3892/etm\_00000024
- 4 Devoogdt N, Geraerts I, Kampen MV, Vrieze TD, Vos L, Neven P, Vergote I, Christiaens MR, Thomis S, Groef AD. Manual lymph drainage may not have a preventive effect on the development of breast cancer-related lymphoedema in the long term : a randomised trial. *J Physiother* 2018;64:245-254.
  - 5 De Oliveira MMF, Gurgel MSC, Amorim BJ, Ramos CD, Derchain S, Furlan-Santos N, dos Santos CC, Sarian LO. Long term effects of manual lymphatic drainage and active exercises on physical morbidities, lymphoscintigraphy parameters and lymphedema formation in patients operated due to breast cancer: a clinical trial. *PLoS One* 2018; doi: 10.1371/journal.pone.0189176.
  - 6 Pusic AL, Cemal Y, Albornoz C, Klassen A, Cano S, Sulimanoff I, Hernandez M, Massey M, Cordeiro P, Morrow M, Mehrara B. Quality of life among breast cancer patients with lymphedema: a systematic review of patient-reported outcome instruments and outcomes. *J Cancer Surviv* 2013; doi: 10.1007/s11764-012-0247-5.
  - 7 Donmez AA, Kapucu S. 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 randomised controlled study. *Eur J Oncol Nurs* 2017;31:12-21.
  - 8 Lacomba MT, Sanchez MJY, Goni AZ, Merino DP, del Moral OM, Tellez EC, Mogollon EM, 2010, 'Effectiveness of early physiotherapy to prevent lymphoedema after surgery for breast cancer: randomised, single blinded, clinical trial. *BMJ* 2010; 340:1-8.
  - 9 Lopera C, Worsley PR, Bader DL, Fenion D. Investigating the short-term effects of manual lymphatic drainage and compression garment therapies on lymphatic function using near-infrared imaging. *Lymphat Res Biol* 2017;15:235-240.
  - 10 Fu MR. Breast cancer-related Lymphoedema: Symptoms, diagnosis, risk reduction and management. *World J Clin Oncol*. 2014; doi: 10.5306/wjco.v5.i3.241
  - 11 Williams AF, Vadgama A, Franks PJ, Mortimer PS. A randomised controlled crossover study of manual lymphatic drainage therapy in women with breast cancer-related lymphoedema. *Eur J Cancer Care (Engl)* 2002;11:254-61.
  - 12 Shih YCT, Xu Y, Cormier JN, Giordano S, Ridner S, Buchholz TA, Perkins GH, Elting LS. Incidence, Treatment Costs and complications of lymphedema after breast cancer among women of working age: a 2 year follow-up study. *J Clin Oncol* 2009; doi: 10.1200/JCO.2008.18.3517.
  - 13 Armer JM, Stewart BR. A comparison of four diagnostic criteria for lymphedema in a post-breast cancer population. *Lymphat Res Biol* 2005;3:208-17.
  - 14 Cho Y, Do J, Jung S, Kwon O, Jeon JY. 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* 2016;24:2047-2057.
  - 15 Rebegea L, Firescu D, Dumitru M, Anghel R. The incidence and Risk factors for occurrence of arm lymphedema after treatment of breast cancer. *Chirurgia (Bucur)* 2015;110:33-7.
  - 16 Monleon S, Murta-Nascimento C, Bascuas I, Macià F, Duarte E, Belmonte R. Lymphedema predictor factors after breast cancer surgery: a survival analysis. *Lymphat Res Biol* 2015; doi: 10.1089/lrb.2013.0042.
  - 17 Zimmermann A, Wozniowski M, Szklarska A, Lipowicz A, Szuba A. Efficacy of manual lymphatic drainage in preventing secondary lymphedema after breast cancer surgery. *Lymphology* 2012;45:103- 12.
  - 18 Kärki A, Simonen R, Mälkiä E, Selve J. Impairments, activity limitations and participation restrictions 6 and 12 months after breast cancer operation. *J Rehabil Med* 2005;37:180-8
  - 19 Damstra RJ, Voesten HGJ, van Schelven WD, van der Lei B. Lymphatic venous anastomosis (LVA) for treatment of secondary arm lymphedema. A prospective study of 11 LVA procedures in 10 patients with breast cancer related lymphedema and a critical review of the literature. *Breast Cancer Res Treat* 2009;113:199-206.
  - 20 Macedo LG, Elkins MR, Maher CG, Moseley AM, Herbert RD, Sherrington C. There was evidence of convergent and construct validity of Physiotherapy Evidence Database quality scale for physiotherapy trials. *J Clin Epidemiol* 2010;63:920-5
  - 21 Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomised controlled trials. *Phys Ther* 2003;83:713-21
  - 22 Ko DS, Lerner R, Klose G, Cosimi AB. Effective treatment of lymphedema of the extremities. *Arch Surg* 1998;133:452-8
  - 23 Shenkier T, Weir L, Levine M, Olivotto I, Whelan T, Reyno L. Clinical practice guidelines for the care and treatment of breast cancer: 15 Treatment for women with stage III or locally advanced breast cancer. *CMAJ* 2004; doi: 10.1503/cmaj.1030944
  - 24 Truong PT, Olivotto IA, Whelan TJ, Levine M. Clinical practice guidelines for the care and treatment of breast cancer: 16. Locoregional post-mastectomy radiotherapy. *CMAJ* 2004; doi: 10.1503/cmaj.1031000
  - 25 Batavia M. *Contraindications in Physical Rehabilitation: Doing no harm*. 1st ed. Philadelphia: Saunders; 2006
  - 26 Ezzo J, Manheimer E, McNeely M, Howell DH, Weiss R, Johansson KI, Bao T, Bily L, Tuppo CM, Williams AF, Karadibak D. Manual Lymphatic drainage for lymphedema following breast cancer treatment. *Cochrane Database Syst Rev* 2015; doi: 10.1002/14651858.CD003475.pub2.
  - 27 Ferrandez JC, Laroche JP, Serin D, Felix-Faure C, Vinot JM. Lymphoscintigraphic aspects of the effects of manual

- lymphatic drainage. *J Mal Vasc* 1996;21:283-9.
- 28 Vairo GL, Miller SJ, McBrier NM, Buckley WE. Systematic review of efficacy for manual lymphatic drainage techniques in sports medicine and rehabilitation: an evidence-based practice approach. *J Man Manip Ther* 2009;17:e80-9
- 29 Stuiver MM, ten Tusscher MR, Agasi-Idenburg CS, Lucas C, Aaronson NK, Bossuyt PMM. Conservative interventions for preventing clinically detectable upper-limb lymphoedema in patients who are at risk of developing lymphoedema after breast cancer therapy (review). *Cochrane Database Syst Rev* 2015; doi: 10.1002/14651858.CD009765.pub2.
- 30 Chikly B. *Silent waves: Theory and practice of lymph drainage therapy with applications for lymphedema, chronic pain, and inflammation*. Scottsdale, AZ: International Health and Healing Inc. Publishing; 2001
- 31 Korosec B, 2004. *Manual Lymphatic Drainage therapy*. Home Health Care Manag Pract 2004; doi:10.1177/1084822304264618
- 32 Wittlinger H, Wittlinger D, Wittlinger A, Wittlinger M. Dr. Vodder's Manual Lymph Drainage: A Practical Guide. 1st ed. New York: Thieme Stuttgart; 2011
- 33 Moseley AL, Carati CJ, Piller NB. A Systematic review of common conservative therapies for arm lymphoedema secondary to breast cancer treatment. *Ann Oncol* 2007; doi: 10.1093/annonc/mdl182.
- 34 Andersen L, Hojris I, Erlandsen M, Andersen J. Treatment of Breast-cancer-related lymphedema with or without manual lymphatic drainage: a randomised study. *Acta Oncol* 2000;39:399-405
- 35 Goats GC. Massage- the scientific basis of an ancient art: part 2. Physiological and therapeutic effects. *Br J Sports Med*. 1994; 28: 153-156.
- 36 Harris R, Piller N. Three case studies indicating the effectiveness of manual lymph drainage on patients with primary and secondary lymphedema using objective measuring tools. *J Bodyw Mov Ther* 2003; 7: 213-221.
- 37 Foldi E. The treatment of lymphoedema. *Cancer* 1998; doi: 10.1002/(sici)1097-0142(19981215)83:12b+<2833::aid-cnrcr35>3.0.co;2-3.
- 38 Devoogdt N, Christiaens MR, Geraerts I, Truijten S, Smeets A, Neven P, Kampen MV. Effect of manual lymph drainage in addition to guidelines and exercise therapy on arm lymphoedema related to breast cancer: randomised controlled trial. *BMJ* 2011; doi: 10.1136/bmj.d5326
- 39 Cariati M, Bains SK, Grootendorst MR, Suyoi A, Peters AM, Mortimer P. Adjuvant taxanes and the development of breast cancer-related arm lymphoedema. *Br J Surg* 2015;102:1071-8.
- 40 Hugenholtz-Wamsteker W, Robbeson C, Nijs J, Hoelen W, Meeus M. The effect of docetaxel on developing oedema in patients with breast cancer: a systematic review. *Eur J Cancer Care* 2016;25:269-79
- 41 Lee MJ, Beith J, Ward I, Kilbreath S. Lymphoedema following taxane-based chemotherapy in women with early breast cancer. *Lymphat Res Biol* 2014; 12:282-288.
- 42 Chen YW, Tsai HJ, Hung HC, Tsao JY. Reliability study of measurements for lymphedema in breast cancer patients. *Am J Phys Med Rehabil* 2008;87:33-8.
- 43 Taylor R, Jayasinghe UW, Koelmeyer L, Ung O, Boyages J. Reliability and Validity of arm volume measurements for assessment of lymphedema. *Phys Ther* 2006;86:205-14
- 44 Ancukiewicz M, Miller CL, Skolny MN, O'Toole J, Warren LE, Jammallo LS, Specht MC, Taghian AG. Comparison of relative versus absolute arm size change as criteria for quantifying breast cancer-related lymphedema: the flaws in current studies and need for universal methodology. *Breast Cancer Res Treat* 2012;135:145-52.