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Manual Lymphatic Drainage vs. Photobiomodulation Therapy for Breast Cancer-Related Lymphedema

Vaishvik Vidavalapati

Academy for Health and Medical Sciences, USA

ABSTRACT

In this literature review, I compared the effects of manual lymphatic drainage (MLD) and photobiomodulation therapy (PBMT) in treating breast cancer-related lymphedema (BCRL). I focused on determining which treatment of the two optimized BCRL limb swelling reduction, symptom management, and QOL of patients the most, as well as comparing their minor side effects and potential major risks. There is limited information on the effects of the two treatments on BCRL, but from the information and studies I analyzed, I found that PBMT seems to be a slightly more effective treatment than MLD in the determiners I researched. However, more in-depth research in the future would certainly allow for a more accurate and significant comparison between the two treatments' efficacy in treating BCRL.

Introduction

A very common treatment for breast cancer is radiation therapy. However, radiotherapy can also cause some conditions to arise in those treated, a significant one being breast cancer-related lymphedema (BCRL). BCRL can occur when radiation damages lymph nodes and vessels in an area, disrupting the lymphatic system and causing lymph fluids to accumulate in tissues. This results in swelling, discomfort, and fatigue in the area. A typical therapy for BCRL is manual lymphatic drainage (MLD), a type of massage therapy that works to drain out the lymph fluids in the affected area. A promising treatment for BCRL currently being tested is photobiomodulation therapy (PBMT), also called low-level laser therapy, in which light of wavelengths ranging from 650 - 1000 nm is applied to the affected area to lessen inflammation and stimulate lymph flow.

Research Focus

In this literature review, I will focus on how PBMT, compared to MLD, optimizes treatment for breast cancer survivors with BCRL. In other words, I aim to determine whether MLD or PBMT is a more effective treatment for BCRL.

Methods

My method for this review included researching information on MLD and PBMT based on three primary determiners: impact on limb swelling, impact on symptoms (physical and emotional), and potential risks. As I planned to compare the two types of treatments, I figured these three factors and their subfactors would be optimal, simply arranged as such:

- Impact on limb swelling

- Impact on symptoms
    - Impact on number of symptoms
    - Impact on specific symptoms
    - Impact on quality of life (QOL)
- Potential risks
    - Potential minor side effects
    - Impact on tumor growth and recurrence

Results

Impact on Limb Swelling

In a randomized controlled trial (RCT), Ridner et al. (2013) compared MLD and PBMT as treatments for BCRL. As shown in Table 1, for circumferential arm volume, with a p-value of 0.42, the median arm volume for patients treated with MLD for 40 minutes decreased by 4.9 units, and the effect size (ES) was -0.42. The median arm volume for patients treated with PBMT for 20 minutes decreased by 8.2 units and the ES was -0.64 (Figure 1).

Table 1. Summaries of Impendance and Arm Volume (N=46)

	Study Group		
	MLD (N=16)	**LLLT (N=15)**	**Combined MLT & LLLT (N=15)**
	Median [IQR] (Min,Max)	**Median [IQR] (Min,Max)**	**Median [IQR] (Min,Max)**
Extracellular Fluid (LDEX)[a](p = .984)			
Baseline	27.7 [6,53] (−3,77)	39.3 [22,48] (3,104)	35.0 [15,56] (−14,93)
End of Study	17.8 [3,38] (−39,50)	28.0 [17,35] (0,47)	22.2 [11,37] (−3,44)
Effect Size	**−0.54**	**−0.55**	**−0.53**
Arm Volume[a](p = .422) (% Difference)			
Baseline	11.7 [3,28] (−2,45)	23.2 [12,40] (3,66)	20.4 [10,35] (6,70)
End of Study	6.8 [0,17] (−4,33)	15.0 [3,23] (−2,39)	13.4 [2,24] (−4,43)
Effect size	**−0.42**	**−0.64**	**−0.64**

Note: The specific p-values report the results from the primary hypotheses of differences in the changes among the three study groups.

[a]Main effect of time of assessment, $p < .001$

Note. From "A Pilot Randomized Trial Evaluating Low-Level Laser Therapy as an Alternative Treatment to Manual Lymphatic Drainage for Breast Cancer-Related Lymphedema," by S. H. Ridner et al., 2013, *Oncology Nursing Forum*, *40*(4), p. 388 (https://doi.org/10.1188/13.onf.383-393). Copyright 2024 by the Oncology Nursing Society.

Lin et al. (2022), in a systematic review and meta-analysis on MLD, ultimately found that MLD had barely any effect on the volume of the affected area of BCRL.

In a randomized controlled study comparing PBMT (noted as LLLT) with both MLD and Kinesio-Taping, as shown in Table 2, Yilmaz and Ayhan (2023) found that the percentage of decreased volume (PDV) for patients with stage II BCRL was 8% 12 weeks after PBMT treatment and 2% 12 weeks after MLD treatment. The p-value for this comparison was 0.238.

Table 2. Percentage of decreased volume (PDV) and subsequent changes at follow-up of end of the treatment (1), 4th weeks (2) and 12th weeks (3)

	Percentage of decreased volume	**MLD (a)**	**Kinesio (b)**	**LLLT (c)**	**p-value**	**p-value**
PDV (1)	Mean ± SD	2.9±8.7	10.3±5.2	8.7±4.7	0.008[w]	a vs b=0.009[q]
	Median (25-75 CI)	2 (-3/9)	10 (5/14)	9 (5/12)		a vs c=0.059[q]
	Min-max	-14/17	4/21	1/18		b vs c≥0.999[q]
PDV (2)	Mean ± SD	0±12.3	8.2±8	4.9±8.4	0.04[x]	a vs b=0.039[y]
	Median (25-75 CI)	-1 (-1/4)	9 (3/14)	7 (2/10)		a vs c=0.284[y]
	Min-max	-33/24	-8/21	-15/16		b vs c≥0.999[y]
PDV (3)	Mean ± SD	4.1±11.9	9.4±8.3	7.4±5.8	0.042[x]	a vs b=0.042[y]
	Median (25-75 CI)	2 (0/6)	11 (5/15)	8 (5/10)		a vs c≥0.238[y]
	Min-max	-23/27	-12/22	-7/18		b vs c≥0.999[y]
	p-value	0.175z	0.945z	0.111z		

PDV (1): decreased volume percentage after treatment; PDV (2): decreased volume percentage 4 weeks after treatment; AVY (3): decreased volume percentage 12 weeks after treatment; SD: standard deviation; Median (25–75% CI): median (1st Quarter value/3rd Quarter value); Min–max: minimum – maximum; [w]: ANOVA test; [x]: Kruskal–Wallis test; [q]: post–hoc Bonferoni test; [z]: Friedman test; [y]:Dunn–Bonferoni Pairwise comparison test; CI: confidence interval; MLD: manual lymphatic drainage; ; LLLT: low-level laser therapy

Note. From "The Randomized Controlled Study of Low-Level Laser Therapy, Kinesio-Taping and Manual Lymphatic Drainage in Patients With Stage II Breast Cancer-Related Lymphedema," by S. S. Yilmaz and F. F. Ayhan, 2023, *European Journal of Breast Health*, *19*(1), p. 41 (https://doi.org/10.4274/ejbh.galenos.2022.2022-6-4). Copyright 2023 by the Turkish Federation of Breast Diseases Societies.

In a review of systematic reviews, Wang et al. (2021) found barely any difference between the effects of MLD and PBMT on limb volume. However, regarding the performance of PBMT and compression bandaging (CB) in decreasing limb circumference, the study also found that "The result showed a significant benefit of LLLT [another name for PBMT] at immediately post-treatment as compared to compression bandage (SMD [standardized mean difference] = 1.21, 95% CI [confidence interval]: 0.25 to 2.15)" (Wang et al.). Therefore, I wanted to see how MLD performed against CB in limb swelling reduction as well.

To do this, I observed the results of a randomized noninferiority prospective study by Gradalski et al. (2015). As shown in Table 3, they found that over six months, the group of women who received CB experienced an average 482.2 mL decrease in swollen limb volume and a 503.1 mL decrease in lymphedema volume. On the other hand, the group of women who received MLD as part of complex decongestive lymphatic therapy (CDT) experienced an average 418.9 mL decrease in swollen limb volume and a 392.2 mL decrease in lymphedema volume. The p-value at the end of the six months for both swollen limb and lymphedema volume was 0.3.

Table 3. SL and LE Volumes (CB Group vs. CDT (MLD) Group)

Measurement Before	CB Group		CDT Group		P-value [a]	
	SL	LE	SL	LE	SL	LE
Day 1	3431.4 (818.5)	1123.8 (548.8)	3264.8 (874.8)	897.8 (444.8)	0.6	0.6
Day 2	3230.7 (742.5) [b]	929.7 (449.8) [b]	3082.1 (825.6) [b]	731.6 (394.8) [b]	0.6	0.6
Day 3	3130.2 (685.7) [b]	824.1 (365.3) [b]	2982.7 (807.4) [b]	645.3 (382.2) [b]	0.6	0.6
Day 4	3042.2 (655.9) [b]	755.8 (327.2) [b]	2932.1 (788.4) [b]	590.4 (342.2) [b]	0.2	0.2
Day 5	2972.7 (641.6) [b]	658.4 (291.6) [b]	2912.8 (771.9) [b]	545.4 (309.8) [b]	0.3	0.3
Day 10	2895.8 (632.0) [b]	593.0 (278.1) [b]	2814.9 (744.5) [b]	472.0 (285.4) [b]	0.8	0.8
Month 1	3010.1 (647.8) [b]	707.4 (310.8)	2850.1 (703.7)	496.6 (261.3)	0.9	0.9
Month 3	2966.8 (609.7)	679.9 (302.9)	2856.2 (698.9)	482.8 (279.7)	0.9	0.9
Month 6	2949.2 (630.2)	620.7 (284.9)	2845.9 (680.6)	505.6 (263.1)	0.3	0.3

SL = swollen limb volume (milliliter); LE = lymphedema volume (milliliter); CB = compression bandaging; CDT = complex decongestive lymphatic therapy.
Mean values (standard deviations).
a *P*-values of between-group comparison.
b $P < 0.05$ in measurement comparisons of recorded volumes with the immediate previous values (compared within each respective subgroups).

Note. From "Complex Decongestive Lymphatic Therapy With or Without Vodder II Manual Lymph Drainage in More Severe Chronic Postmastectomy Upper Limb Lymphedema: A Randomized Noninferiority Prospective Study," by T. Gradalski et al., 2015, *Journal of Pain and Symptom Management*, *50*(6), p. 754 (https://doi.org/10.1016/j.jpainsymman.2015.06.017). Copyright 2015 by the American Academy of Hospice and Palliative Medicine.

Impact on Symptoms

This determiner is split into three subsections: impact on number of symptoms, impact on specific symptoms, and impact on quality of life (QOL).

Impact on Number of Symptoms

In the RCT mentioned previously, as shown in Table 4, Ridner et al. found that the median number of symptoms for BCRL patients treated with MLD decreased by 2 from the beginning to the end of the study, and the ES was -0.41. The median number of symptoms for BCRL patients treated with PBMT decreased by 1, and the ES was -0.16. The p-value for these results was 0.249.

Impact on Specific Symptoms

To compare the specific symptoms of patients receiving either treatment, as shown in Table 4, Ridner et al. also found that for patients treated with MLD, the average ES for 12 symptoms of BCRL (heavy arm, tight arm, numb arm, aching arm, swelling arm, hard arm, appearance concerns, fatigue, loss of sleep, lack of interest in sex, decrease in physical activity, and decrease in sexual activity) was 0, and the average ES for the same symptoms for the patients treated with PBMT was -0.34.

Table 4. Summaries of Symptom Measures at Baseline and End of Study (N=46)

	Study Group		
	MLD (N=16)	**LLLT (N=15)**	**Combined MLT & LLLT (N=15)**
	Median [IQR] (Min,Max)	**Median [IQR] (Min,Max)**	**Median [IQR] (Min,Max)**
Number of symptoms (*p* = .249)			
Baseline	14.5 [8,20] (3,35)	13.0 [8,16] (4,31)	14.0 [9,19] (4,31)
End of study	12.5 [6,16] (0,33)	12.0 [4,16] (2,34)	14.0 [10,19] (5,36)
Effect size	**−0.41**	**−0.16**	**0.15**
Overall symptom burden[a](*p* = .930)			
Baseline	2.4 [0,11] (0,26)	1.7 [1,13] (0,73)	6.1 [0,12] (0,22)
End of study	0.6 [0,6] (0,46)	0.4 [0,12] (0,53)	4.1 [0,8] (0,14)
Effect size	**−0.45**	**−0.41**	**−0.46**
Symptom Burden Subsets Effect Sizes			

	Study Group		
	MLD (N=16)	**LLLT (N=15)**	**Combined MLT & LLLT (N=15)**
	Median [IQR] (Min,Max)	**Median [IQR] (Min,Max)**	**Median [IQR] (Min,Max)**
Arm pain	0.15	−0.19	−0.06
Arm skin movement	−0.16	−0.31	0.00
Arm size[a]	−0.22	−0.59	−0.42
Insurance	−0.09	0.42	−0.02
Systemic[a]	−0.13	−0.48	−0.62
Neurological	−0.28	0.23	−0.21
Specific Symptoms [†]			
Heavy arm	0.01	−0.40	−0.33
Tight arm	−0.41	−0.43	0.02
Numb arm	−0.19	−0.17	−0.01
Aching arm	0.24	−0.31	−0.07
Swelling arm	−0.34	−0.53	−0.62
Hard arm	−0.03	−0.14	−0.11
Appearance concerns	−0.05	−0.15	−0.26
Fatigue	−0.12	−0.34	−0.46
Loss of sleep	−0.48	−0.43	−0.32
Lack of interest in sex	0.40	−0.45	−0.12
Decrease in physical activity	0.24	−0.19	−0.03
Decrease in sexual activity	0.73	−0.48	−0.02
Number of Skin Conditions Affected Arm[b](p = .031)			
Baseline	2.0 [2,3] (1,7)	3.0 [2,4] (1,6)	3.0 [2,5] (1,8)
End of Study	2.0 [1,3] (1,4)	1.0 [1,2] (1,3)	2.0 [1,2] (1,3)
Effect Size	**−0.44**	**−1.15**	**−1.65**
Unaffected Arm (p = .923)			
Baseline	1.5 [1,2] (1,3)	1.0 [1,2] (1,2)	1.5 [1,2] (1,3)
End of Study	1.0 [1,2] (1,6)	1.0 [1,2] (1,2)	1.0 [1,2] (1,2)
Effect Size	**−0.11**	**−0.13**	**−0.22**

[a]Main effect of time of assessment, $p < 0.05$
[b]Main effect of time of assessment, $p < 0.001$

†Effect sizes; At least 50% of the participants reported having the symptom at baseline.

IQR—interquartile range; LLLT—low-level laser therapy; MLD—manual lymphatic drainage

Note: The specific p-values report the results from the primary hypotheses of differences in the changes among the three study groups.

Note. From "A Pilot Randomized Trial Evaluating Low-Level Laser Therapy as an Alternative Treatment to Manual Lymphatic Drainage for Breast Cancer-Related Lymphedema," by S. H. Ridner et al., 2013, *Oncology Nursing Forum*, *40*(4), p. 389 (https://doi.org/10.1188/13.onf.383-393). Copyright 2024 by the Oncology Nursing Society.

Impact on Quality of Life (QOL)

I looked at information from Ridner et al.'s study on six instruments used in determining QOL to compare the QOL of BCRL patients treated with PBMT and those treated with MLD: the Center for Epidemiological Studies Depression Scale (CES-D) (p-value = 0.99), the Brief Fatigue Inventory (BFI) (p-value = 0.75), the Functional Assessment of Cancer Therapy - Breast (FACT-B) (p-value = 0.25), the Functional Assessment of Cancer Therapy - General (FACT-G) (p-value = 0.32), the Profile of Mood States (POMS) (p-value = 0.88), and the Upper Limb Lymphedema 27 (ULL-27) (p-value = 0.59).

As displayed in Table 5, the median CES-D for patients treated with MLD increased by 1 (ES = 0), and the median CES-D for patients treated with PBMT did not change (ES = -0.06). The median BFI for patients treated with MLD decreased by 1 (ES = -0.32), and the median BFI for patients treated with PBMT decreased by 0.1 (ES = -0.28). The median FACT-B for patients treated with MLD increased by 4.37 (ES = +0.12), and the median FACT-B for patients treated with PBMT increased by 2.5 (ES = +0.41). The median FACT-G for patients treated with MLD increased by 2.0 (ES = -0.01), and the median FACT-G for patients treated with PBMT increased by 3.7 (ES = +0.31). The median POMS for patients treated with MLD increased by 1.0 (ES = +0.04), and the median POMS for patients treated with PBMT did not change (ES = +0.03). The effect sizes for the POMS subcategories of tension, depression, anger, vigor, fatigue, and confusion are -0.13, +0.03, -0.05, +0.08, -0.25, and -0.05 respectively for patients treated with MLD and -0.05, +0.02, +0.04, +0.70, -0.15, and -0.04 respectively for patients treated with PBMT. The median ULL-27 for patients treated with MLD increased by 0.7 (ES = +0.13), and the median ULL-27 for patients treated with PBMT increased by 9.6 (ES = +0.52).

Table 5. Summaries of Depression, Fatigue, Psychological Distress, and Quality of Life (N=46)

	Study Group		
	MLD (N=16)	**LLLT (N=15)**	**Combined MLT & LLLT (N=15)**
	Median [IQR] (Min,Max)	**Median [IQR] (Min,Max)**	**Median [IQR] (Min,Max)**
CESD (*p* = .985)			
Baseline	13.0 [11,19] (8,31)	12.0 [9,15] (7,20)	12.0 [10,13] (9,38)
End of Study	14.0 [9,21] (8,29)	12.0 [8,14] (7,23)	11.0 [9,15] (8,22)
Effect Size	**0.00**	**−0.06**	**−0.04**
Brief Fatigue Inventory (*p* = .748)			

	Study Group		
	MLD (N=16)	**LLLT (N=15)**	**Combined MLT & LLLT (N=15)**
	Median [IQR] (Min,Max)	**Median [IQR] (Min,Max)**	**Median [IQR] (Min,Max)**
Baseline	2.4 [0,6] (0,7)	1.3 [0,4] (0,10)	1.2 [0,5] (0,8)
End of Study	1.4 [0,4] (0,8)	1.2 [0,3] (0,7)	1.6 [0,4] (0,6)
Effect size	**−0.32**	**−0.28**	**−0.07**
FACT B Total Score (*p* = .252)			
Baseline	111.88 [98,122] (52,136)	111.0 [97,118] (40,134)	116.0 [99,125] (64,133)
End of Study	116.25 [98,123] (51,136)	113.5 [100,129] (62,134)	110.0 [102,123] (91,136)
Effect Size	**0.12**	**0.41**	**−0.02**
Fact G Total Score (*p* = .319)			
Baseline	86.0 [75,100] (41,106)	87.8 [79,93] (32,107)	91.0 [75,99] (32,107)
End of Study	88.0 [74,99] (40,105)	91.5 [79,102] (50,105)	86.0 [74,95] (60,105)
Effect Size	**−0.01**	**0.31**	**−0.11**
Fact Subscales Effect Sizes			
Physical Well-being	0.30	0.20	0.00
Social Well-being	0.13	0.23	−0.13
Emotional Well-being	−0.20	0.27	0.04
Functional Well-being	−0.22	0.31	−0.07
Fact B Subscale[b]	0.27	0.49	0.47
POMS Total Score (*p* = .878)			
Baseline	34.5 [37,47] (25,58)	29.0 [26,32] (24,111)	35.0 [24,40] (24,88)
End of Study	35.5 [28,44] (24,60)	29.0 [25,41] (24,112)	31.0 [25,35] (24,49)
Effect Size	**0.04**	**0.03**	**−0.10**
POMS Subscales Effect Sizes			
Tension	−0.13	−0.05	−0.18
Depression	0.03	0.02	−0.01

	Study Group		
	MLD (N=16)	**LLLT (N=15)**	**Combined MLT & LLLT (N=15)**
	Median [IQR] (Min,Max)	**Median [IQR] (Min,Max)**	**Median [IQR] (Min,Max)**
Anger	−0.05	0.04	−0.10
Vigor[a]	0.08	0.70	0.31
Fatigue	−0.25	−0.15	−0.18
Confusion	−0.05	−0.04	−0.08
ULL-27 Total Score (*p* = .586)			
Baseline	81.5 [78,86] (74,92)	80.4 [69,89] (65,91)	68.5 [61,87] (52,88)
End of Study	82.2 [77,92] (58,95)	90.0 [71,96] (54,98)	78.9 [73,85] (62,91)
Effect Size	**0.13**	**0.52**	**0.42**
ULL Subscales Effect Sizes			
Physical	0.13	0.47	0.26
Psychological	0.28	0.01	−0.03
Social	−0.13	0.25	0.23

BFI—Brief Fatigue Inventory; CES-D—Center for Epidemiologic Studies–Depression; FACT-B—Functional Assessment of Cancer Therapy-Breast; FACT-G—Functional Assessment of Cancer Therapy–General; IQR—interquartile range; LLLT—low-level laser therapy; MLD—manual lymphatic drainage; POMS—Profile of Mood States; ULL-27—Upper Limb Lymphedema–27

Note. From "A Pilot Randomized Trial Evaluating Low-Level Laser Therapy as an Alternative Treatment to Manual Lymphatic Drainage for Breast Cancer-Related Lymphedema," by S. H. Ridner et al., 2013, *Oncology Nursing Forum*, *40*(4), p. 390 (https://doi.org/10.1188/13.onf.383-393). Copyright 2024 by the Oncology Nursing Society.

I also looked at information from Yilmaz and Ayhan's study to compare the effects of MLD and PBMT treatments on stage II BCRL patients' results on the lymphedema-specific QOL questionnaire (LymQoL). As shown in Table 6, patients treated with MLD had a median LymQoL percent change of -10% 12 weeks after treatment, while those treated with PBMT had a median LymQoL percent change of -8.39% 12 weeks after treatment (p-value = 0.326).

Table 6. Inter- and intra-group comparisons for LymQoL change (%)

	LymQoL	**MLD (a)**	**Kinesio (b)**	**LLLT (c)**	**p-value**
End of the treatment	Mean ± SD	-9.14±7.87	-11.97±10.95	-11.06±16.27	0.650[w]
	Median (25-75 CI)	-8.57 (-13.39-0)	-11.63 (-16.97/-5.88)	-3.85 (-17.39/0)	

	Min-max	-21.74/0	-44.83/0	-61.29/0	
4th weeks after treatment	Mean ± SD	-8.83±8.33	-13.77±16.99	-11.06±16.62	0.874[w]
	Median (25-75 CI)	-11.43 (-13.39/0)	-9.28 (-21.21/-1.64)	-11.61 (-23.24/0)	
	Min-max	-21.74/2.86	-56.12/5	-44.52/16.75	
12th weeks after treatment	Mean ± SD	-7.78±7.49	-14.58±13.11	-11.02±13.33	0.326[w]
	Median (25-75 CI)	-10 (-13.39/0)	-12.69 (-21.51/-5.88)	-8.39 (-17.39/0)	
	Min-max	-20/2.86	-49.25/0	-41.94/0	
	p-value	0.368 x	0.180 x	0.223 x	

SD: standard deviation, Median (25–75% CI): median (1st Quarter value/3rd Quarter value), Min–max: minimum–maximum, [w]: Kruskal–Wallis testi; x: Friedman test; CI: confidence interval; MLD: manual lymphatic drainage; ; LLLT: low-level laser theraphy

Note. From "The Randomized Controlled Study of Low-Level Laser Therapy, Kinesio-Taping and Manual Lymphatic Drainage in Patients With Stage II Breast Cancer-Related Lymphedema," by S. S. Yilmaz and F. F. Ayhan, 2023, *European Journal of Breast Health*, *19*(1), p. 41 (https://doi.org/10.4274/ejbh.galenos.2022.2022-6-4). Copyright 2023 by the Turkish Federation of Breast Diseases Societies.

Potential Risks

This determiner is split into two subsections: potential minor side effects and impact on tumor growth and recurrence.

Minor Side Effects

To start with the minor side effects, some potential side effects of MLD treatment include dizziness, nausea, fatigue, diarrhea, etc. However, it also has other side effects that can be more beneficial or at least not as troublesome that are important to acknowledge, such as increased energy, urination, and relaxation. According to a systematic review by de Pauli Paglioni et al. (2019), "Most studies showed that no side effects were observed with the use of PBMT" (de Pauli Paglioni et al.). As written in a study by El Mobadder et al. (2021) in which PBMT was used to treat symptoms of inferior alveolar nerve damage, "At the end of the treatment, all of the symptoms disappeared except for an abnormal sensation on touching the mucosa and gingiva of the concerned area. No side effects were noted" (El Mobadder et al.).

Impact on Tumor Growth and Recurrence

To move on to the impact of the two treatments on tumor growth and recurrence, a cohort study by Hsiao et al. (2015) initially stated that MLD may cause cancer cells to metastasize through the lymphatic system, causing the recurrence of breast cancer. However, the study disproved this claim in its conclusion; "MLD therapy is a safe procedure that does not increase the risk of disease recurrence in breast cancer survivors who developed BCRL after surgery, axillary LN dissection, and adjuvant therapy" (Hsiao et al.). Similarly, for PBMT, Mikhailov et al. (2000) found from a clinical trial study that "82.6% (about 66.6% in control group) of patients with II nd st. treated by LLLT had no recurrences in 10 years period. 77.7% (57.9% in control group) of patients with III rd st. treated by LLLT had no recurrences for the same period of time" (Mikhailov et al.). In addition, de

Pauli Paglioni et al. concluded their study with the observation that PBMT does not help in tumor growth and recurrence; "The results of this systematic review, based on current literature, suggest that the use of PBMT in the prevention and management of cancer treatment toxicities does not lead to the development of tumor safety issues" (de Pauli Paglioni et al.).

Discussion

Impact on Limb Swelling

In Ridner et al.'s study, as shown in Table 1, the arm volume for BCRL patients treated with PBMT decreased by 3.3 units (67%) more than that of patients treated with MLD. There was also a noticeable difference between the ES of the two treatments. Effect size is similar to p-value; though, the p-value determines if a finding is significant, while the ES indicates the size of the significance and the direction of the effect as well. According to an article by the Regional Education Laboratory at West Ed published by the Institute of Education Sciences (2021), if the goal of a tool is to promote a wanted or beneficial result, then the aim is to achieve a positive ES. On the other hand, if the goal of the tool is to lessen an unfavorable result, a negative ES is desired. Since MLD and PBMT both aim as BCRL treatments to substantially decrease arm volume (or decrease undesirable swelling of the arm) in Ridner et al.'s study, the desired ES for this would be one that is negative and farther from 0. Therefore, PBMT's ES of -0.64 shows that the reduction in arm volume caused by PBMT was more significant than that caused by MLD, which had an ES of -0.42. However, more information was needed.

In Yilmaz and Ayhan's study, as shown in Table 2, the PDV for patients with stage II BCRL decreased 6% more for patients treated with PBMT than those treated with MLD. These results also suggest that PBMT is more effective in decreasing limb volume than MLD is.

Since some sources stated that there was barely any difference between MLD and PBMT on limb volume, I decided to perform a transitive comparison. The baseline I used was compression bandaging (CB), a standard lymphedema treatment in which an elastic bandage is wrapped around the swollen area to exert pressure on it, pushing lymph fluids out of the affected area to decrease swelling. Based on Wang et al.'s findings, PBMT performed better than CB in reducing limb circumference. According to Gradalski et al., as shown in Table 3, MLD decreased swollen limb volume by 63.3 mL (13.1%) less and lymphedema volume by 110.9 mL (22.04%) less than CB did. Therefore, since PBMT was observed to have reduced limb swelling more effectively than CB, and CB was found to have decreased swelling more than MLD, the result of this transitive comparison is that PBMT better reduces limb swelling than MLD, reinforcing Ridner et al.'s and Yilmaz and Ayhan's findings previously mentioned.

Impact on Symptoms

Impact on Number of Symptoms

Ridner et al. found that, as shown in Table 4, the number of symptoms decreased by 1.0 more for patients who received MLD. As symptoms of BCRL are undesirable for the most part, and a goal of BCRL treatment is to lessen these symptoms, achieving a negative ES that further deviates from 0 would again be desired. Therefore, MLD's ES of -0.41 compared to PBMT's ES of -0.16 conveys that MLD more significantly decreased BCRL symptoms in patients than PBMT.

Impact on Specific Symptoms

Regarding specific symptoms in Ridner et al.'s study, as shown in Table 4, PBMT's average ES of -0.34 for the 12 symptoms is more favorable than MLD's ES of 0. It is also important to note that PBMT had negative ESs for all 12 symptoms, while MLD had negative ESs for 7 of them. Therefore, from this information, PBMT seems to have a better impact on specific BCRL symptoms than MLD.

Impact on Quality of Life (QOL)

Lastly, for QOL, in Ridner et al.'s study, as shown in Table 5, the median CES-D score for BCRL patients treated with MLD increased by 1.0 more than that for patients treated with PBMT (no change in score). CES-D scores range from 0 - 60, and a higher score often indicates a higher chance of having clinical depression and more depressive symptomatology. Therefore, an increase in patients' CES-D scores is unfavorable, meaning that PBMT patients' lack of change in their median CES-D score is more favorable than MLD patients' increase in their median score. The median BFI score for BCRL patients treated with MLD decreased by 0.9 more than that for PBMT patients. BFI scores range from 0 - 63, and a higher score indicates a higher severity of fatigue, so, similar to the CES-D, an increase in patients' BFI scores is undesirable. The median BFI scores for both MLD and PBMT patients decreased from the beginning to the end of the study, but since the median BFI score for MLD patients decreased more, MLD seems to perform slightly better in lessening BCRL patients' fatigue than PBMT.

The median FACT-B for patients treated with MLD increased by 1.87 more than that for PBMT patients. As a higher FACT-B score indicates better QOL (in the factors of physical, social, emotional, and functional well-being and breast cancer subscale), the higher score increase of MLD patients is more favorable in the FACT-B assessment. The median FACT-G for patients treated with PBMT increased by 1.7 more than that for MLD patients. As, similar to FACT-B, a higher FACT-G score indicates better QOL, the higher score increase of PBMT patients is more favorable in the FACT-G assessment.

The median POMS for patients treated with MLD increased by 1.0 more than that for PBMT patients (no change in score). Considering that the "POMS Total Score" in Table 5 refers to the Total Mood Disturbance (TMD) score, a higher TMD would be undesirable as it indicates higher levels of mood disturbance. Therefore, in this case, the lack of change in the median POMS score of PBMT patients is more favorable than the increase in the median POMS score of MLD patients. However, as I do not have absolute certainty that the "POMS Total Score" is referring to TMD, I compared the effect sizes of the POMS subscores for MLD and PBMT patients as well. Since the categories of tension, depression, anger, fatigue, and confusion indicate negative mood and MLD and PBMT are aiming to decrease these feelings in BCRL patients, a negative effect size would be desired. On the other hand, a positive effect size would be desired for vigor as it indicates a positive mood and the treatments are aiming to increase this feeling in BCRL patients. Therefore, PBMT seems to have a better effect on decreasing depression (ES 0.01 lower) and increasing vigor (ES 0.62 higher), while MLD seems to have a better effect on decreasing tension (ES 0.08 lower), anger (ES 0.09 lower), fatigue (ES 0.10 lower), and confusion (ES 0.01 lower). However, these differences in ES are very minor; the only notable one is the large positive ES of 0.70 for vigor for PBMT, which indicates that PBMT may be more effective in increasing feelings of vigor in BCRL patients than MLD. Other than this, the results for MLD and PBMT in POMS seem to be similar for the most part.

The median ULL-27 for patients treated with PBMT increased by 8.9 more than that for MLD patients. As higher ULL-27 scores suggest lower disability, and, therefore, better QOL, the much larger score increase for PBMT is more favorable for this assessment.

As shown in Table 6, the median LymQoL for patients treated with MLD decreased 1.61% more than that for PBMT patients. As a lower score on the LymQoL indicates better QOL, MLD's larger decrease in score is more favorable for this assessment, though the difference is very small.

Through the analysis of the results of these several QOL tools for the effects of MLD and PBMT on the QOL of BCRL patients, it seems that PBMT has a slightly better impact than MLD, as PBMT had relatively better results for the CES-D, FACT-G, and ULL-27 than MLD. Additionally, though the results for the POMS were very close for both treatments, the considerable effect of PBMT on patients' vigor is particularly notable.

Potential Risks

Minor Side Effects

Comparing the possible minor side effects of MLD and those of PBMT, the side effects of MLD have been found to include nausea, diarrhea, flu-like symptoms, headaches, and more. Even though MLD does come with some benefits along with its negative side effects, the lack of side effects of PBMT observed in the studies by de Pauli Paglioni et al. and El Mobadder et al. indicate that PBMT is a more favorable treatment in the context of minor side effects.

Impact on Tumor Growth and Recurrence

The possibility of MLD promoting metastasis and breast cancer recurrence was studied by Hsiao et al., and they eventually concluded that MLD does not do so. Similarly, for PBMT, Mikhailov et al. found that the majority of breast cancer patients did not have any recurrences of breast cancer over a decade. As well as this, de Pauli Paglioni et al. found that PBMT does not promote tumor development and recurrence. Further research delving deeper into the effects of PBMT on breast cancer recurrence in BCRL patients specifically may be helpful for a stronger comparison, though, with this information, both MLD and PBMT do not seem to promote tumor growth and recurrence.

Conclusion

Implications of this Review

There is limited information on MLD and PBMT as treatments for breast cancer-related lymphedema to have a clear answer on which one is the optimal treatment. However, from this study, PBMT seems to be slightly more favorable than MLD, primarily due to its impact on limb swelling, specific symptoms, and QOL, as well as its lack of side effects.

Limitations

This research has several limitations that are important to acknowledge. Firstly, for much of the data, the p-values were higher than 0.05, indicating that those data collected are likely to have been statistically weak and that we cannot reject the null hypothesis. Also, many ESs collected were small and had absolute values less than 0.5. This means that the data with these small ESs have limited practical applications and that the magnitude of the effects of MLD and PBMT on some of the determiners studied is likely to be low. However, some effect sizes were relatively high and at the medium level (around 0.5), which are essentially large enough to be visible to an observer.

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