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## **Original Article**

# The effect of massage as a complementary therapy on fatigue and quality of life in females with Multiple Sclerosis.

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# Abstract

**Background:** Multiple Sclerosis (MS) is a chronic central nervous system disorder that can impair the sensory and motor-nerve system by destroying the myelin sheath. These may lead to fatigue and Quality of Life (QoL). This study investigated the effect of eight-week massage as a complementary therapy on fatigue, Physical Component Health (PhCH), Psychological Component Health (PsCH), and QoL in MS female patients.

**Methods:** In this quasi-experimental study, 20 MS females with EDSS (Expanded Disability Status Score) = 2-5 were enrolled. After a briefing and obtaining consent, the subjects were pre-tested. The subjects were randomly divided into Control (n= 10) and experimental (n= 10) groups. The massage therapy was performed for eight-week (two sessions of 30 minutes per week). Fatigue and Quality of Life were assessed at the beginning and end of the protocol using the Modified Fatigue Impact Scale (MFIS) and Quality of Life Short Form Questionnaire (SF-36), respectively.

**Results:** Twenty females MS patients (age= 26-44 yr., weight= 53.-87 Kg, BMI (Body Mass Index) =24. 32 Kg.m-1) completed the study period. Data demonstrated a significant decrease in fatigue (F= 45.38, p= 0.001), a significant increase in PhCH (F= 21.60, P= 0.001), PsCH (F= 5.42, P= 0.001), and QoL (F= 22.67, P= 0.001).

**Conclusion:** Massage can be a non-invasive, safe, low-cost, and complementary intervention to improve fatigue and quality of life in MS patients.

Keywords: Fatigue, Massage, Multiple Sclerosis, Relapsing-Remitting, Quality of Life

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## Introduction

Demyelination and axon loss have accrued in Multiple Sclerosis (MS) as the inflammatory disease of the Central Nerve System (1). The prevalence of MS has increased around the world (2). The Multiple Sclerosis International Federation (MSIF) reported 75000 people in Iran (90/100000) in 2020 (3). In 2013, Isfahan was reported to have the highest MS prevalence in Iran (4). Also, the ratio prevalence of MS in females to males is approximately 2-3:1, meaning the diagnosis age is 32 years old (3). Several symptoms and signs, such as sensory impairment (pain, visual) and motor impairment (spasticity, weakness, ataxia, and balance) (5). Fatigue is one of the symptoms of MS, and the dysfunction in the thalamus and cortico-subcortical pathway has been suggested as pathogenic to fatigue (6). It has been reported that the prevalence of increased fatigue among MS patients affects daily tasks, mobility, and QoL; especially, it has been expected that this chronic condition will live its whole lifespan (7).

Massage therapy (MT) is an ancient form of treatment that is now gaining popularity as part of the complementary and alternative medical therapy movement (8). The intermittent pressure during a massage increases lymphatic drainage (9), blood circulation, adjusting blood pressure, and autonomic activity balance (10). By reducing pain, increasing alertness, diminishing depression, and enhancing immune function, the potential of biochemical and physiological mechanisms can be explained (11, 12). The usage of massage as any complementary and adjunct medical therapy was higher in MS patients after MS diagnosis (13, 14). Previous studies noted the effect of massage to improve fatigue (15-24), QoL (16, 17, 22, 25-27), muscle strength (28), mobility (18, 29), pain (19, 21, 29-31), quality of sleep (32), body image and image of disease progression (33), the Neurogenic Bowel Dysfunction Score, and a bowel diary (34, 35), motor-sensory and urinary symptoms (28), bladder dysfunction (25) constipation symptom in MS patients (27, 36), self-efficacy (14, 32, 37-40) anxiety and mood (14, 21, 33), social functional status (32), whereas another study reported massage therapy had no significant change in QoL and Six Minutes Walking Test following four-week in 24 MS patients with EDSS= 3-7 (27, 41).

The contradictory results made this research necessary by regarding the different types of massage, signs, and intensity of the disease, range of EDSS, motion, and motor-nerve disorder. This study aimed to measure the effect of massage as a complementary therapy on fatigue and QoL with managing the multiple accompanying symptoms and aspects of the treatment in patients with Multiple Sclerosis.

# Material and methods

## Design

This research was designed as a short-term quasi-experimental and randomized control trial. All subjects signed written informed consent and completed fatigue and QoL questionnaires as a pre-test. The decision was made to administer 16 sessions during eightweek according to the critical care plan during the study. The study protocol was approved by the Research Ethics Committees of the Sport Sciences Research Institute (SSRI), approval ID: IR.SSRC.REC.1400.043. This study was conducted under the auspices of the Najafabad Branch, Islamic Azad University, and Goldasht Multiple Sclerosis Center (GMSC). The volunteer participation was registered with GMSC.

#### **Participants**

The inclusion criteria were female as definite MS according to McDonald's criteria, with relapsing-remitting (RR) form of the disease and Expanded Disability Status Scale (EDSS) 2-5. The EDSS was determined by a neurologist who was blinded in this study. The exclusion criteria were back problems, pregnancy, epilepsy, and cancer. Sixty participants registered in GMSC were recruited. Twenty female patients (age= 26-44 yr., weight= 53.-87 Kg, BMI =24. 32 Kg.m<sup>-1</sup>) had the inclusion criteria and were randomly divided into two equal massage and control groups and enrolled in this study.

The topic of Swedish massage techniques consisted of five parts: Effleurage, Friction, Petrissage, Tapotement, and Vibration (42-44). These techniques were used to relax and rejuvenate after stress-ridden situations (43, 44).

- Effleurage: Effleurage is generally used in various massages, such as Swedish Massage. This technique (light/deep stroking) is done by the palm gliding over the body using oil to feel comfort and slight pressure on the skin. However, this technique caused increased blood circulation in various body parts. In addition, this technique can release muscle knots and body tension when used with negligibly more pressure (44).

 Friction: Friction contains deep and circular motion that produces a layer of tissue to run against each other and cause increased blood circulation and degenerate scar tissue (44).

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– Petrissage: Petrissage manipulates the fleshy area of the body. The manipulation consists of grasping, lifting, compressing, rolling, kneading, and chucking. The direction of hand movement is towards the center of the body (44).

- Tapotement: This technique consists of quick tapping of the hand that can be either cupped by the edge of the palm or fingertips tap the skin or tapping the skin when the hands are placed side by side on various parts of the body like the back, thighs, and buttock (44).

Vibration: This technique is like shakes and is done by the hand or fingertips moving from one point to another while repeating this stroke. This technique is designed to release muscle tension and is suitable for small muscles like the spinal muscles (44).
Each session was 30 minutes, which has been described in table 1. In addition, the massage

group received Swedish massage with bitter almond oil two times (30 minutes) per week for eight weeks, and the Control groups continued their routine life.

Techniques	Right Leg min. (sec.)	Left Leg min. (sec.)	Waist min.(sec.)	minutes
Effleurage	1.25 (75)	1.25 (75)	2.5 (150)	5
Friction	0.75 (45)	0.75 (45)	1.5 (90)	3
Petrissage	1.25 (75)	1.25 (75)	2.5 (150)	5
Tapotement	1.25 (75)	1.25 (75)	2.5 (150)	5
Vibration	0.75 (45)	0.75 (45)	1.5 (90)	3
Effleurage	4.5 (270)	4.5 (270)	4.5 (270)	9
Total	7.5 (450)	7.5 (450)	15 (900)	30

Table 1. The details of Swedish massage in each session

### Variables assessment

Fatigue severity by using Modified Fatigue Impact Scale (MFIS) was measured before and after the massage protocol. A lower score indicates a decrease in fatigue severity. Quality of life (QOL) was measured using SF-36 before and after the massage protocol. The SF-36 questionnaire consists of two parts: Physical Component Health (PCH), and Psychological Component Health (PsCH). The scores range from 0 to 100. A higher score indicates better QOL.

## **Statistical Analysis**

Descriptive statistic was reported as mean  $\pm$  Standard Deviation (SD) at baseline as Control and, following eight-week massage therapy in experimental groups. The inferential statistic was used for data processing using SPSS Statistics (Version 17.0). At first, the normal distribution was verified using Shapiro-Wilk Test (P> 0.05). Then, the independence T-Test (p< 0.05) assessed differences between baseline and demographic values. Next, the variables' homogeneity of variance was assessed using Levene's Test (P>0.05). Difference between groups were assessed by using Analysis of covariance (ANCOVA) (P<0.05). G-power 3.1 software was used to compute effect size, power, and sample size (45). The effect size of our total sample size (n=20) with two groups was moderate, as shown in figure 1.

Figure 1. Analysis of sensitively to compute required effect size based on central and non-central distributions



The clinical effect is calculated as the difference between pre-test and post-test value in percent by using the formula  $\% = [(post-test - pre-test)/ pre-test] \times 100$ 

# Results

The mean and Standard deviation (SD) of variables before and after massage therapy has been shown in Table 2.

Groups		Pre-test		Post-test	
		Mean	SD	Mean	SD
Fatigue	Control	9.90	2.37	10.30	2.83
	Experimental	10.23	2.94	4.30	2.26
PhCH	Control	43.10	4.22	44.00	4.59
	Experimental	40.00	4.71	47.10	2.18
PsCH	Control	47.30	3.88	47.30	4.47
	Experimental	45.70	2.66	49.60	2.79
QoL	Control	90.40	6.81	91.30	7.91
	Experimental	85.70	5.61	96.70	3.49

Table 2. The mean and standard deviation of pre-test and post-test variables in the studied subject's

PhCH, Physical Component Health; PsCH, Psychological Component Health; QoL, Quality of Life; SD, Standard Deviation.

The normality distribution, by using Shapiro-Wilk, reported a normal distribution, and the homogeneity of variance of variables, by using Levene's test, reported homogeny, shown in Table 3. (P> 0.05). Default homogeneity of regression slope of Fatigue (F= 2.843, p= 0.104), PhCH Component Health (F= 0.866, p= 0.360), Psychological Component Health (F= 1.263, p= 0.213), QoL (F=0.112, p=0.654) demonstrated the assumption of homogeneity of regression (P< 0.05).

Table 3. Shapiro-Wilk Test to assess the normality distribution, and Leven's F- Test to assess the
homogeneity of variance of variables in the studied subject's

Variable	Groups	Shapiro-Wilk Test				Leven's F-Test	
		Control		Experimental		- <b>df</b> (1,18)	
		Shapiro-	F	Shapiro-	F	F	Р
		Wilk Test		Wilk Test			
Fatigue	Pre-test	0.856	0.078	0.877	0.121	1.591	0.223
	Post-test	0.848	0.054	0.957	0.748	_	
PhCH	Pre-test	0.957	0.754	0.948	0.650	0.019	0.891
	Post-test	0.983	0.895	0.947	0.638	_	
PsCH	Pre-test	0.959	0.776	0.959	0.776	0.322	0.678
	Post-test	0.971	0.897	0.971	0.897	_	
QoL	Pre-test	0.909	0.227	0.916	0.326	0.450	0.223
	Post-test	0.947	0.631	0.926	0.278	_	

PhCH; Physical Component Health, PsCH; Psychological Component Health, QoL; Quality of

Life; df, degree of freedom; P>0.05.

Massage therapy had a significant effect on Fatigue, PhCH Components, Psychological Components, and QoL in female MS patients, which has been shown in Table 4. The significant clinical effect of Fatigue, PhCH, PsCH, and QoL in subjects following massage therapy was 57.96%, 17.75%, 3.38%, and 0.09%, respectively.

Table 4. Analysis of covariance (ANCOVA) on mean post-test scores variables in control and experiment groups

Variable	Total squares	F	Р	η	OP
Fatigue	193.680	45.38	0.001*	0.727	1.00
PhCH	112.907	21.60	0.001*	0.560	0.999
PsCH	52.619	5.42	0.032*	0.242	0.593
QoL	249.879	22.67	0.001*	0.571	0.994

F, F-Test; P, significant;  $\eta$ , partial eta- squared (demonstrated the change of variables); OP, Observed Power (the estimate of the power of study based on effect size in our study); df (1,18).

PhCH, Physical Component Health; PsCH, Psychological Component Health; QoL, Quality of Life; p<0.05.

## Discussion

The results of this study showed a 57.96% decrease in Fatigue. Previous studies reported improved fatigue following MT (15-21, 24, 26, 30, 31). Our result was in line with Backus et al. (16), Honarvar et al. (17), Arab (20), Naji, et al. (24), Arab et al. (20), Naji et al. (24), Frost-Hunt (18), and Atashi et al. (23). Although the methods, types of massage, duration of each session, and subjects were different that are mentioned in following lines. Backus et al., in 2016, following a nonrandomized post-design in a pilot study, reported a significant decrease in fatigue after one session per week for six weeks with a standardized MT routine in 24 female MS patients (16). Honarvar et al., following a Quasi-experimental study, reported that Effleurage MT caused a significant decrease in fatigue in 9 (Total subjects =17) MS patients with a range age 20-50 yrs. MT was down for 20-30-minute each session, three times per week for six week (17). Arab et al. reported that MT caused a significant decrease

in fatigue in 40 (Total subjects = 80) female MS patients with a mean age of  $33.38 \pm 8.28$ yrs. Standardized MT contains 13 techniques for 20-minute sessions, three times per week for four weeks (20). Naji et al., in a study on 36 MS patients based on 20-minute effleurage aromatherapy massage three times per week for four consecutive weeks reported a substantial decrease in fatigue severity score after intervention (24). Following a case report study on a 58-years old female diagnosed with MS 11 years earlier, Frost-Hunt reported a significant decrease in fatigue after 2200 hours over six weeks, with five MT treatments (18). Atashi et al., following a Quasi-experimental study, reported that Slow Stroke Back Massage (SSBM) treatment caused a significant decrease in fatigue in 32 (Total subjects = 62) MS patients with a range aged 20-45 yrs. The Slow Strock Back Massage (SSBM) was down for 10 minutes each session for ten sessions (23). A systematic review by Salarvand et al. reported significant improvement in fatigue in MS patients following MT in seven studies (19). Salarvand et al., in a review study, reported significant improvement in fatigue in MS patients following MT in seven studies (19). Significant decrease in fatigue in MS patients was reported after Reflexology post intervention (15, 21, 22, 26, 31). Nazari et al. studied a single-blinded randomized clinical trial. 75 MS patients were divided into three Reflexology, Relaxation (Jacobson and Benson), and Control equal groups. Foot Reflexology and relaxation were down for about 40 minutes each session, two times per week for four weeks, and the control group had routine medical treatment and received care. Immediately after intervention and two mounts after intervention, a significant decrease in the fatigue score has been shown in the reflexology group(31).

Ozdelikara et al., following a Quasi-experimental study, reported a significant decrease in fatigue in 15 (Total subjects =15) MS patients one year after MS was diagnosed, and the average age of the participant was determined to be  $39.20 \pm 11.89$  yrs. Reflexology was done for 60 minutes and 30 minutes for each leg in one session (21). Sajadi et al., following a Quasi-experimental study, reported a significant decrease in fatigue in (Total subjects =63). Dilek Dogan et al., following a Quasi-experimental study, reported a significant decrease in fatigue in 30 (Total subjects =60) MS patients six months after MS was diagnosed. Reflexology was down for 20-30-minute each session, three weekly sessions for 12 weeks (22). Hughes et al. reported that a double-blind, randomized, sham-controlled clinical trial study reported a significant decrease in fatigue in 73 MS patients by Sham Reflexology for about ten weeks (26). Sajadi et al. reported significant improvement in perceived fatigue following Foot Reflexology which was down four weeks to two times per week and each session was 30-40 minutes (15).

The plasma beta-endorphins (46), oxygen deficiency,  $K^+$ ,  $Ca^{2+}$ , and  $H^+$  intracellular are fatigue factors (47), which could be bold in MS subjects. Hypoxia affects the regulation of cellular respiration and impaired Ca2+, and the contraction cycle in muscle cells (47). Also, increased plasma beta-endorphins (46), decreased H+ accumulation, and increased K+ intracellular decrease fatigue, which occurs following MA (48).

Our study demonstrated 17.75% increase in PhCH, 3.38% increase in PsCH, and 0.09% increase in QoL following massage therapy in the experimental group. Honarvar et al. noted Effleurage MT caused a significant increase in psychological component health, whereas it had no significant effect on physical component health in QoL (17). Schroeder et al. reported that massage therapy had no significant change in QoL, and the Six Minutes Walking Test followed four-week in 24 MS patients with EDSS= 3—7 (41). Dilek Dogan et al., following a Quasi-experimental study, reported Reflexology significant improvement in QoL in 30 (Total subjects =60) MS patients six months after MS was diagnosed. The protocol of study was down for 20-30 minutes for each session, three sessions per week for 12 weeks, whereas Sajadi et al., following a quasi-experimental study, reported Foot Reflexology had no significant change in QoL (Total subjects =63). The protocol of study was down for about 30-40 minutes each session, twice a week for four weeks (27). Hughes et al. following a double-blind randomized sham-controlled clinical trial study reported Sham Reflexology significant decrease in QoL in 73 MS patients down about ten weeks (26).

Decreasing fatigue and pain is correlated with QoL improvement (16). There are many studies to show decreases in pain following massage therapy. Pain is one of the QoL components, so we assess these studies. Backus et al. reported a significant decrease in pain following one session per week for six weeks with a standardized MT routine in 24 female MS patients (16). Negahban et al. demonstrated 15 sessions, five weeks between 48 MS patients between four equal groups: Massage therapy, exercise therapy, combined massage exercise therapy, and control groups. Significant improvements were found in pain reduction. Also, they noted more significant MT improvement in pain reduction in combined massage and exercise therapy may be much more effective than exercise or massage alone (29). Following a case report study, Frost-Hunt demonstrated a significant decrease in fatigue, edema, and

increased mobility (18). Massage improves the sense of proprioception by stimulating the pressure receptors in skin, muscles, and joints that causes improved balance and muscle contraction, and movement, and affects physical health and QoL. Massage regulates the autonomic nervous system (49) and decreases autonomic activity. At the same time, parasympathetic nervous activity also decreased (10), increasing blood circulation (51). Lymphatic drainage (50), decreased cortisol (51-53), decreased adrenalin and noradrenalin (54), increased neurotransmitter serotonin and dopamine, following massage therapy effect on stress condition (55), which affect psychological health and QoL Muscle relaxation, reduced pain and anxiety effect on psychological health and QoL. Pain is one of the subcategories of PsCH, and massage by inducing an antinociceptive effect that activates oxytocin in pain controlling system. Also, beta-endorphin is linked to pain relief. Kaada et al. noted a significant increase in beta-endorphin and a decreased pain following MT (46), although Day et al. reported no significant change in beta-endorphin following MT in health without pain (56). These differences may be due to the difference in subjects with or without pain, and MT is recommended for pain relief. Massage stimulates sensory afferent C fiber in the skin and affects the human body and mind. McClurg et al. demonstrated that four weeks of abdominal massage caused significantly improved constipation symptoms in MS patients (36). Decreased cortisol (31%). A revived study noted the effectiveness of hand massage in improving relaxation in older people (57). Massage therapy is a non-invasive therapy to improve pain (59, 60), anxiety, depression (58, 59), stress, aggression, and agitation (60) in dementia elderly. This research suggests massage has stress-reliever effects (decrease cortisol), and activating effects (increase dopamine and serotonin) could be used as an adjunct therapy.

#### Conclusion

MS is a chronic disease that needs to be self-managed throughout treatment. Study results in Swedish support massage as an adjuvant treatment that offers non-invasive, safe, inexpensive (44) and reduces fatigue, pain, and spasticity, which are essential MS symptoms related to QoL. So MT, by improving the QoL, can be used as a treatment method along with drug treatment for MS patients.

# **Ethical Considerations**

Research Ethics Committees of Sport Sciences Research Institute (SSRI), approval ID: IR.SSRC.REC.1400.043.

# **Conflicts of interest**

The authors declare that they have no competing interests.

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#### Reference

Compston A, Coles A. Multiple sclerosis. Lancet (London, England). 2002;359(9313):1221-31.

Walton C, King R, Rechtman L, Kaye W, Leray E, Marrie RA, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. Mult Scler. 2020;26(14):1816-21.

Multiple Sclerosis International Federation. (MSIF). 2020.

- Etemadifar M, Izadi S, Nikseresht A, Sharifian M, Sahraian MA, Nasr Z. Estimated prevalence and incidence of multiple sclerosis in Iran. European neurology. 2014;72(5-6):370-4.
- Henze T, Rieckmann P, Toyka KV. Symptomatic treatment of multiple sclerosis. Multiple Sclerosis Therapy Consensus Group (MSTCG) of the German Multiple Sclerosis Society. European neurology. 2006;56(2):78-105.
- Capone F, Collorone S, Cortese R, Di Lazzaro V, Moccia M. Fatigue in multiple sclerosis: The role of thalamus. Mult Scler. 2020;26(1):6-16.
- Bass AD, Van Wijmeersch B, Mayer L, Mäurer M, Boster A, Mandel M, et al. Effect of Multiple Sclerosis on Daily Activities, Emotional Well-being, and Relationships: The Global vsMS Survey. International journal of MS care. 2020;22(4):158-64.
- Moyer CA, Rounds J, Hannum JW. A meta-analysis of massage therapy research. Psychological bulletin. 2004;130(1):3.
- Meftahi N, Bervis S, Taghizadeh S, Ghafarinejad F. Effects of Massage in Prone Position on Blood Pressure and Heart Rate in Healthy Women. Journal of Rehabilitation Sciences & Research. 2014;1(2):40-3.
- Lindgren L, Rundgren S, Winsö O, Lehtipalo S, Wiklund U, Karlsson M, et al. Physiological responses to touch massage in healthy volunteers. Autonomic neuroscience : basic & clinical. 2010;158(1-2):105-10.
- Field T, Diego M, Hernandez-Reif M. Massage therapy research. Developmental Review. 2007;27(1):75-89.
- Field TM. Massage therapy effects. American Psychologist. 1998;53(12):1270.
- Kim S, Chang L, Weinstock-Guttman B, Gandhi S, Jakimovski D, Carl E, et al. Complementary and Alternative Medicine Usage by Multiple Sclerosis Patients: Results from a Prospective Clinical Study. Journal of alternative and complementary medicine (New York, NY). 2018;24(6):596-602.
- Huntley A, Ernst E. Complementary and alternative therapies for treating multiple sclerosis symptoms: a systematic review. Complementary Therapies in Medicine. 2000;8(2):97-105.
- SAJADI M, Davodabady F, EBRAHIMI MONFARED M. The Effect of Foot Reflexology on Fatigue, Sleep Quality and Anxiety in Patients with Multiple Sclerosis: A Randomized Controlled Trial. ARCHIVES OF NEUROSCIENCE. 2020;7(3):-.
- Backus D, Manella C, Bender A, Sweatman M. Impact of Massage Therapy on Fatigue, Pain, and Spasticity in People with Multiple Sclerosis: a Pilot Study. Int J Ther Massage Bodywork. 2016;9(4):4-13.
- Honarvar s, rahnama n, nouri r. Effects of six weeks massage on the balance, fatigue and quality of life in patients with ms. Journal of research sport rehabilitation. 2015;2(4):-.
- Frost-Hunt A. Effects of Massage Therapy on Multiple Sclerosis: a Case Report. Int J Ther Massage Bodywork. 2020;13(4):35-41.
- Salarvand S, Heidari ME, Farahi K, Teymuri E, Almasian M, Bitaraf S. Effectiveness of massage therapy on

fatigue and pain in patients with multiple sclerosis: A systematic review and meta-analysis. Multiple sclerosis journal - experimental, translational and clinical. 2021;7(2):20552173211022779.

- Arab M, Radfar A, Madadizadeh N, Sadat Afsharian Pour Z, Karzari Z. The effect of massage therapy on fatigue of patients with multiple sclerosis. J Adv Pharm Educ Res. 2019;9:44-9.
- Ozdelikara A, Agcadiken Alkan S. The Effects of Reflexology on Fatigue and Anxiety in Patients With Multiple Sclerosis. Alternative therapies in health and medicine. 2018;24(4):8-13.
- Dilek Doğan H, Tan M. Effects of Reflexology on Pain, Fatigue, and Quality of Life in Multiple Sclerosis Patients: A Clinical Study. Alternative therapies in health and medicine. 2021;27(5):14-22.
- Atashi V, Siboni FS, Khatoni M, Alimoradi Z, Panah HM. The Effect of SSBM Massage on Anxiety and Fatigue of Patients with Multiple Sclerosis. Journal of Applied Environmental and Biological Sciences. 2014;4(8):217-23.
- Naji SA, Bahraini S, Mannani R, Bekhradi R. The Effect of Aromatherapy Massage on the Fatigue Severity in Women with Multiple Sclerosis. Journal of Sabzevar University of Medical Sciences. 1970;18(3):172-8.
- Miller L, McIntee E, Mattison P. Evaluation of the effects of reflexology on quality of life and symptomatic relief in multiple sclerosis patients with moderate to severe disability; a pilot study. Clinical rehabilitation. 2013;27(7):591-8.
- Hughes CM, Smyth S, Lowe-Strong AS. Reflexology for the treatment of pain in people with multiple sclerosis: a double-blind randomised sham-controlled clinical trial. Mult Scler. 2009;15(11):1329-38.
- Sajadi M, Davodabady F, Naseri-Salahshour V, Harorani M, Ebrahimi-Monfared M. The effect of foot reflexology on constipation and quality of life in patients with multiple sclerosis. A randomized controlled trial. Complement Ther Med. 2020;48:102270.
- Siev-Ner I, Gamus D, Lerner-Geva L, Achiron A. Refiexology treatment relieves symptoms of multiple sclerosis: a randomized controlled study. Multiple Sclerosis Journal. 2003;9(4):356-61.
- Negahban H, Rezaie S, Goharpey S. Massage therapy and exercise therapy in patients with multiple sclerosis: a randomized controlled pilot study. Clinical rehabilitation. 2013;27(12):1126-36.
- Backus D, Manella C, Bender A, Sweatman M. Impact of Massage Therapy on Fatigue, Pain, and Spasticity in People with Multiple Sclerosis: a Pilot Study. Int J Ther Massage Bodywork. 2016;9(4):4-13.
- Nazari F, Soheili M, Hosseini S, Shaygannejad V. A comparison of the effects of reflexology and relaxation on pain in women with multiple sclerosis. Journal of complementary & integrative medicine. 2016;13(1):65-71.
- Hernandez-Reif M, Field T, Field T, Theakston H. Multiple sclerosis patients benefit from massage therapy. Journal of Bodywork and Movement Therapies. 1998;2(3):168-74.

Bahraini s, naji sa, mannani r, bekhradi r. The effect of massage therapy on the quality of sleep in women with multiple sclerosis being admitted by isfahan m.s. association. Journal of urmia nursing and midwifery faculty. 2011;8(4):-.

McClurg D, Hagen S, Hawkins S, Lowe-Strong A. Abdominal massage for the alleviation of constipation symptoms in people with multiple sclerosis: a randomized controlled feasibility study. Multiple Sclerosis Journal. 2010;17(2):223-33.

McClurg D, Goodman K, Hagen S, Harris F, Treweek S, Emmanuel A, et al. Abdominal massage for

neurogenic bowel dysfunction in people with multiple sclerosis (AMBER - Abdominal Massage for Bowel Dysfunction Effectiveness Research): study protocol for a randomised controlled trial. Trials. 2017;18(1):150.

- McClurg D, Hagen S, Hawkins S, Lowe-Strong A. Abdominal massage for the alleviation of constipation symptoms in people with multiple sclerosis: a randomized controlled feasibility study. Mult Scler. 2011;17(2):223-33.
- Akbari A, Shamsaei F, Sadeghian E, Mazdeh M, Tapak L. Effect of progressive muscle relaxation technique on self-esteem and self-efficacy in multiple sclerosis patients: A clinical trial study. Journal of education and health promotion. 2022;11:8.
- Finch P, Bessonnette S. A pragmatic investigation into the effects of massage therapy on the self efficacy of multiple sclerosis clients. Journal of Bodywork and Movement Therapies. 2014;18(1):11-6.
- Finch P, Bessonnette S. A pragmatic investigation into the effects of massage therapy on the self efficacy of multiple sclerosis clients. J Bodyw Mov Ther. 2014;18(1):11-6.
- Finch P, Becker P. Changes in the self-efficacy of multiple sclerosis clients following massage therapy. Journal of Bodywork and Movement Therapies. 2007;11(3):267-72.
- Schroeder B, Doig J, Premkumar K. The effects of massage therapy on multiple sclerosis patients' quality of life and leg function. Evidence-based complementary and alternative medicine : eCAM. 2014;2014;640916.
- Elliott JA, Smith HS. Handbook of Acute Pain Management: CRC Press; 2016.
- Norris CM. The Complete Guide to Clinical Massage: Bloomsbury Publishing; 2013.
- McAtee RE. Sport Massage for Injury Care: Human Kinetics; 2019.
- Cohen J. Statistical power analysis for the behavioral sciences: Routledge; 2013.
- Kaada B, Torsteinbø O. Increase of plasma beta-endorphins in connective tissue massage. General pharmacology. 1989;20(4):487-9.
- Hepple RT. The role of O2 supply in muscle fatigue. Canadian journal of applied physiology = Revue canadienne de physiologie appliquee. 2002;27(1):56-69.
- Nielsen OB, de Paoli F, Overgaard K. Protective effects of lactic acid on force production in rat skeletal muscle. The Journal of physiology. 2001;536(Pt 1):161-6.
- Guan L, Collet J-P, Yuskiv N, Skippen P, Brant R, Kissoon N. The Effect of Massage Therapy on Autonomic Activity in Critically Ill Children. Evidence-Based Complementary and Alternative Medicine. 2014;2014:656750.
- Bakar Y, Coknaz H, Karlı Ü, Semsek Ö, Serın E, Pala Ö O. Effect of manual lymph drainage on removal of blood lactate after submaximal exercise. Journal of physical therapy science. 2015;27(11):3387-91.
- Field T, Grizzle N, Scafidi F, Schanberg S. Massage and relaxation therapies' effects on depressed adolescent mothers. Adolescence. 1996;31(124):903-11.
- Moyer CA, Rounds J, Hannum JW. A meta-analysis of massage therapy research. Psychol Bull. 2004;130(1):3-18.
- Moyer CA, Seefeldt L, Mann ES, Jackley LM. Does massage therapy reduce cortisol? A comprehensive quantitative review. J Bodyw Mov Ther. 2011;15(1):3-14.

- Ulrich-Lai YM, Herman JP. Neural regulation of endocrine and autonomic stress responses. Nature reviews Neuroscience. 2009;10(6):397-409.
- Field T, Hernandez-Reif M, Diego M, Schanberg S, Kuhn C. Cortisol decreases and serotonin and dopamine increase following massage therapy. The International journal of neuroscience. 2005;115(10):1397-413.
- Day JA, Mason RR, Chesrown SE. Effect of massage on serum level of beta-endorphin and beta-lipotropin in healthy adults. Physical therapy. 1987;67(6):926-30.
- Harris M, Richards KC. The physiological and psychological effects of slow-stroke back massage and hand massage on relaxation in older people. Journal of clinical nursing. 2010;19(7-8):917-26.
- Rodríguez-Mansilla J, González López-Arza MV, Varela-Donoso E, Montanero-Fernández J, González Sánchez B, Garrido-Ardila EM. The effects of ear acupressure, massage therapy and no therapy on symptoms of dementia: a randomized controlled trial. Clinical rehabilitation. 2015;29(7):683-93.
- Yang YP, Wang CJ, Wang JJ. Effect of Aromatherapy Massage on Agitation and Depressive Mood in Individuals With Dementia. Journal of gerontological nursing. 2016;42(9):38-46.
- Zhao H, Gu W, Zhang M. Massage Therapy in Nursing as Nonpharmacological Intervention to Control Agitation and Stress in Patients With Dementia. Alternative therapies in health and medicine. 2020;26(6):29-33.