ORIGINAL RESEARCH

Bagcilar Med Bull 2025;10(3):273-278 **DOI:** 10.4274/BMB.galenos.2025.29290



Quality of Life Outcomes in Lower Extremity Lymphedema After Manual Lymphatic Drainage Therapy

Manuel Lenfatik Drenaj Terapisi Sonrasi Alt Ekstremite Lenfödeminde Yaşam Kalitesi Sonuçları

- ▶ Sedef Ersoy¹,
 ▶ Büşra Şirin Ahısha²,
 ▶ Nur Kesiktaş¹,
 ♠ Cansın Medin Ceylan¹,
 ♠ Nurdan Paker¹,
 ♠ Derya Buğdaycı¹,
 ♠ Eser Kalaoğlu¹
- ¹University of Health Sciences Turkey, İstanbul Physical Therapy and Rehabilitation Training and Research Hospital, Department of Physical Therapy and Rehabilitation, İstanbul, Turkey
- ²Beylikdüzü State Hospital, Clinic of Physical Therapy and Rehabilitation, İstanbul, Turkey

Abstract

Objective: Lymphedema is a complex condition, and there is limited evidence regarding the impact of lower extremity lymphedema on patients' health and quality of life (QoL). This study aims to evaluate the QoL in individuals diagnosed with secondary lymphedema affecting the lower limbs.

Method: This cross-sectional study collected data from outpatient and inpatient lymphedema management units. Assessments included lymphedema quality of life (LQoL), body mass index (BMI), characteristics of secondary lymphedema and demographic details. LQoL scores were recorded both before and after 20 sessions of manual lymphatic drainage (MLD) therapy.

Results: A total of 67 patients diagnosed with secondary lower-extremity lymphedema were included in the study. Lymphedema severity was evaluated through circumferential measurements, with nearly all participants exhibiting moderate to severe swelling. The majority of the participants (79.1%) were female, while 14 were male. The patients' ages ranged from 34 to 83 years, with a mean age of 58.67±10.97 years. The mean BMI was calculated as 34.41±713. The mean LQoL score before treatment was 2.53±0.63. A paired samples t-test demonstrated a statistically significant improvement in LQoL scores after MLD therapy (p=0.035), confirming its effectiveness. Furthermore, a significant correlation was identified between BMI and LQoL (r=0.291, p<0.021, Pearson correlation test).

Öz

Amaç: Lenfödem, özellikle alt ekstremitelerde görüldüğünde hastaların yaşam kalitesini (QoL) olumsuz etkileyen karmaşık bir hastalıktır. Ancak, bu durumun QoL üzerindeki etkilerine dair sınırlı sayıda çalışma bulunmaktadır. Bu çalışmanın amacı, alt ekstremitelerde sekonder lenfödem tanısı konmuş bireylerde QoL'yi değerlendirmektir.

Yöntem: Bu çalışmada, alt ekstremite sekonder lenfödemi tanısı almış ve ayakta ya da yatarak tedavi gören hastalardan, lenfödem yönetim birimlerinde veriler toplanmıştır. Katılımcıların demografik özellikleri, lenfödemin klinik parametreleri ve beden kitle indeksleri (BKİ) kaydedilmiştir. Yaşam kalitesini değerlendirmek için lenfödem yaşam kalitesi (LQoL) ölçeği kullanılmış olup, LQoL skorları 20 seanslık MLD tedavisi öncesi ve sonrası olmak üzere iki farklı dönemde ölçülmüştür. Bu sayede, MLD tedavisinin yaşam kalitesi üzerindeki etkileri karşılaştırmalı olarak analiz edilmistir.

Bulgular: Sekonder alt ekstremite lenfödemi tanısı konmuş toplam 67 hasta çalışmaya dahil edilmiştir. Lenfödem şiddeti, çevresel ölçümlerle değerlendirilmiş ve katılımcıların büyük çoğunluğunda orta ile ileri derecede şişlik tespit edilmiştir. Çalışmaya katılanların %79,1'i kadın, geri kalan 14'ü ise erkektir. Hastaların yaş aralığı 34 ile 83 yıl arasında değişmekte olup, ortalama yaş 58,67±10,97 yıl olarak hesaplanmıştır. Ortalama BKİ ise 34,41±7,13 olarak bulunmuştur. Tedavi öncesinde ortalama LQoL skoru 2,53±0,63 olarak ölçülmüştür. Eşleştirilmiş örneklem t-testi sonuçları, MLD tedavisi sonrasında LQoL skorlarında istatistiksel



Address for Correspondence: Lec, Sedef Ersoy, MD, University of Health Sciences Turkey, İstanbul Physical Therapy and Rehabilitation Training and Research Hospital, Department of Physical Therapy and Rehabilitation, İstanbul, Turkey

E-mail: sedef_ersoy@yahoo.com ORCID: orcid.org/0000-0001-9018-7937

Received: 10.07.2025 Accepted: 29.08.2025 Epub: 03.09.2025 Publication Date: 12.09.2025

Cite this article as: Ersoy S, Ahısha BŞ, Kesiktaş N, Medin Ceylan C, Paker N, Buğdaycı D, et al. Quality of life outcomes in lower extremity lymphedema after manual lymphatic drainage therapy. Bagcilar Med Bull. 2025;10(3):273-278



°Copyright 2025 by the Health Sciences University Turkey, İstanbul Bagcilar Training and Research Hospital. Bagcilar Medical Bulletin published by Galenos Publishing House. Licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License.

Abstract

Conclusion: This study highlights a significant association between BMI and QoL in patients with secondary lower-extremity lymphedema. MLD was found to be an effective therapeutic approach.

Keywords: Lymphatic, lymphedema, phlebolymphedema, quality of life

Öz

olarak anlamlı bir iyileşme olduğunu göstermiştir (p=0,035) ve bu durum tedavinin etkinliğini desteklemektedir. Ayrıca, BKİ ile LQoL skorları arasında Pearson korelasyon testi ile anlamlı bir pozitif ilişki saptanmıştır (r=0,291, p<0,021).

Sonuç: Bu çalışma, sekonder alt ekstremite lenfödemi olan hastalarda BKİ ile yaşam kalitesi arasında anlamlı bir ilişki olduğunu ortaya koymaktadır. MLD ise etkili bir tedavi yöntemi olarak bulunmuştur.

Anahtar kelimeler: Flebolenfödem, lenfatik, lenfödem, yaşam kalitesi

Introduction

Chronic lymphedema is a condition characterized by inflammatory and lymphostatic changes affecting the interstitial space and lymphatic drainage. It occurs due to mechanical restrictions in the lymphatic system, including lymphatic collectors, trunks, or lymph nodes, rather than congenital or acquired structural damage (1). Lymphedema manifests with a variety of symptoms and clinical features. The most frequently reported complaints include pain, itching, a sensation of heaviness, fatigue, skin changes, and recurrent infections (2). Although lymphedema causes physical and psychological problems and impairs quality of life (QoL), it is underrecognized and undertreated. The diagnosis of lymphedema is clinical and depends on a detailed history and thorough physical examination. In addition, quantitative measurements of functional disability and QoL and the psychological context of the disease (anxiety, depression, sleep disturbances, fear of cancer recurrence and sexuality issues) need to be addressed (3). As lymphedema progresses into a chronic and often irreversible condition, it necessitates continuous care and management, often incorporating psychosocial support. The ongoing requirement for therapy does not imply inadequate treatment but rather reflects the chronic nature of the disease, where outcomes may still be suboptimal. Patient adherence to treatment regimens plays a crucial role in achieving better clinical results. Early diagnosis and intervention are associated with improved treatment efficacy and potential cost reductions through conservative management strategies, including the use of compression garments, self-care education (covering aspects such as skin hygiene, weight management, and anatomy), selfadministered or caregiver-assisted manual lymphatic drainage (MLD), psychosocial support, and physical activity. Additionally, timely identification of the condition may facilitate the use of advanced surgical interventions, such as lymphatic-venous shunting, in appropriate cases,

potentially reducing the need for lifelong treatment (1). Although studies have shown that MLD therapy is an effective treatment for patients with lymphedema, there is a limited number of studies in the literature examining changes in QoL before and after treatment. This study aims to evaluate the clinical impact of lymphedema, which significantly reduces QoL, and to assess the improvement in QoL following MLD therapy.

Materials and Methods

Patients diagnosed with lymphoedema and followed up at the outpatient clinics of University of Health Sciences Turkey, İstanbul Physical Therapy and Rehabilitation Training and Research Hospital, were included in this study. Ethical approval for the study was obtained from the Clinical Research Ethics Committee of University of Health Sciences Turkey, İstanbul Physical Therapy and Rehabilitation Training and Research Hospital on 02.07.2024 with protocol number 2024-39. Pre- and posttreatment data from 67 patients were obtained from both outpatient and inpatient lymphedema management centers. Recorded variables included lymphedema quality of life (LYMQoL), body mass index (BMI), lymphedema characteristics, disease stage, and demographic data. The severity and presence of lymphedema were assessed through circumferential measurements of the lower extremities. Specifically, measurements were taken at the level of the metatarsophalangeal joint, the narrowest point above the ankle malleolus, and at distances of 10, 20, and 30 cm proximal to the lateral malleolus. Patients underwent 20 sessions of MLD therapy performed by trained therapists. Following the completion of treatment, all measurements were repeated to evaluate post-treatment changes. All patients suffered from lower extremity lymphedema (LEL). Patients with lipedema, venous insufficiency, lower extremity edema due to systemic disease, ulcer or infection were excluded. All patients had received MLD and compression and exercise therapy. The LYMQoL is a disease-specific health-related quality of life (HRQoL) assessment tool designed to evaluate function, appearance, symptoms, and mood in individuals with lymphedema. It comprises 22 items, each scored on a four-point Likert scale: 1= Not at all, 2= A little, 3= Fairly, 4= A lot. The total score for each domain is derived by summing the item scores and dividing by the total number of items answered. The overall LYMQoL score ranges from 1 to 4, with higher scores indicating a poorer QoL. The scale was originally developed by Keeley et al. (4) in 2010 to assess QoL in individuals with lymphedema. The Turkish adaptation and validation of the scale were conducted by Borman et al. (5). The validated version consists of 21 items categorized into function, appearance, symptoms, and mood, each rated from 1 to 4, where higher scores indicate better QoL.

Statistical Analysis

The normality of the data was analyzed using the Shapiro-Wilk test. Quantitative data were summarized as mean and standard deviation values, while categorical variables were presented as percentages. The relationship between dependent variables was evaluated using the paired sample t-test, and correlations between variables were assessed with the Pearson correlation test. P-value \leq 0.05 was considered statistically significant. Statistical analyses were performed using SPSS 21.0 software.

Results

The study included 67 patients with LEL. The presence and severity of lymphedema were evaluated by circumferential measurement and clinical examination. 66.7% of the patients had bilateral lymphedema, 23.3% right and 10% left LEL. Lymphedema developed after gynecologic malignancy in 38% of the patients. The other patients suffered from lymphedema as a result of primary or infection, fracture and surgery. We did not group our patients according to the presence of malignancy. 83.58% of the patients were staged as stage 2 and 16.42% as stage 3 lymphedema. 79.1% of the participants were female. The ages of the patients ranged between 34-83 years. The mean age was 58.67±10.97 years. The mean BMI was 34.40±7.13. 60% of the patients complained of pain and 80% complained of fullness (Table 1).

LQoL was 2.53±0.63 before treatment and 2.31±0.66 after treatment. When the LQoL scores of all patients with LEL were compared with the paired sample test, the p-value was 0.035 and the difference between the LQoL scores

before and after manual lymph massage was statistically significant (Table 2).

There was a statistically significant correlation between BMI and LQoL scores before treatment (r=0.291, p<0.021 Pearson correlation test) (Table 3).

Discussion

In this study, MLD therapy was found to be an effective treatment in improving QoL in patients with LEL. Additionally, a weak but statistically significant correlation was observed between BMI and QoL scores. While most lymphedema research has primarily focused on upper extremity lymphedema in breast cancer patients, studies on LEL remain limited despite its frequent occurrence, particularly among individuals with gynecologic cancers. By evaluating QoL outcomes in patients with LEL, our study addresses an important gap in the existing literature.

Table 1. Descriptive data				
		Mean ± SD/(%)		
Age		58.67±10.97		
Gender	Male	(20.9%)		
	Female	(79.1%)		
ВМІ		34.40±7.13		
Stage	2	(83.58%)		
	3	(16.42%)		
Extremity	Bilateral	(66.7%)		
	Right	(23.3%)		
	Left	(10%)		
Pain		(60%)		
Fullness		(80%)		

BMI: Body mass index, SD: Standard deviation

Table 2. Comparison of LYMQOL scores before and after treatment

	Mean ± SD	p-value	%95 confidence interval
LYMQOL before	2.53±0.63	0.035^{t}	0.016-0.427
LYMQOL after	2.32±0.67		

LYMQOL: Lymphedema quality of life, SD: Standard deviation, T: Paired samples t-test

Table 3. Correlation between BMI and LYMQOL before treatment

LYMQO	L before
-------	----------

	r	p-value
ВМІ	0.291*	0.021 ^p

LYMQOL: Lymphedema quality of life, BMI: Body mass index. P: Pearson correlation test *: Correlation is significant at the 0.05 level (2-tailed)

In patients with lymphedema, disturbances in body image often contribute to diminished self-esteem, heightened anxiety regarding disease progression, and impaired extremity function, all of which adversely affect overall QoL. In cases of LEL, these symptoms tend to be more pronounced, and QoL is reported to be significantly lower compared to upper extremity involvement. The deterioration in QoL has been closely associated with the reduction in lower limb functional capacity (6,7). Moffatt et al. (8) screened 823 patients and found that lymphedema incidence increases with age, with a higher prevalence among women. Furthermore, it has been reported that 80% of affected individuals experience work productivity loss, and their QoL is significantly lower than normal. Lymphedema has also been recognized as an important public health concern due to its impact on morbidity and social participation. In the study by Greene and Meskell (9), 77% of the participants were female, while another study reported the proportion of females as 71% (10). In an epidemiological study conducted by Grigorean et al. (11), it was confirmed that lymphedema is more frequently observed in females. Similarly, in our study, 79.1% of the patients were female, supporting the observation that lymphedema is more prevalent among women.

In this study, MLD, compression therapy, and therapeutic exercises were administered to all patients as part of a standardized conservative treatment protocol. These interventions have well-established efficacy. A weak but statistically significant association was observed between BMI and QoL scores before the application of the treatment protocol. Furthermore, a significant improvement was noted in QoL scores following the treatment. In a study investigating the effectiveness of compression therapy in patients with LEL, it was shown that the group receiving compression had better physical functioning after 12 months compared to those who did not. However, no significant differences were observed between the two groups in terms of emotional, cognitive, and social functioning, or symptoms such as pain, constipation, diarrhea, dyspnea, loss of appetite, and insomnia (12). Stolldorf et al. (7) conducted a study involving 213 patients with lymphedema to examine the impact of LEL symptoms on QoL. The study utilized the lymphedema symptom intensity and distress questionnaire-leg alongside an open-ended qualitative question. The findings revealed that a significant proportion of participants experienced psychological and physical symptoms, including depression (65.9%), anxiety about appearance (81.9%), negative body image perception (67.8%), fatigue (75.7%), weakness during leisure activities

(65%), and reduced physical activity (69.5%). These factors collectively contributed to a substantial decline in the QoL among individuals with LEL (7). Additionally, studies have identified skin quality as a key determinant in the reduction of QoL among patients with LEL. Proper skin care and cellulitis prevention have been suggested as essential strategies to enhance QoL in these individuals (13).

A study conducted in Bangladesh reported that the QoL of women with LEL, including their mental health, was adversely affected. Participants complained of limited access to healthcare services, the belief that the disease could not be effectively treated, and negative perceptions within society (14). Another study, which included 122 participants receiving MLD at vascular and wellness clinics in Ireland, aimed to assess the effects of chronic LEL on patients' OoL. The results indicated that a majority of participants reported physical difficulties such as limb heaviness (74%), weakness (44%), pain (38%), walking difficulties (53%), standing impairments (51%), and difficulty bending (45%). Furthermore, 76% of patients expressed concerns about poor body image, while 59% reported challenges in finding properly fitting shoes due to edema. Additionally, 55% experienced reduced socialization, and emotional symptoms such as irritability (42%), anxiety (41%), and tension (40%) were commonly observed. These findings emphasize that chronic LEL contributes to significant physical, psychological, and social burdens, ultimately leading to a reduced QoL (9). Schulz et al. (15) administered the LYMQoL questionnaire and demonstrated that patients with LEL experience significantly lower QoL compared to those with UEL. In the systematic review published in 2022, the impact of LEL on the HRQoL and the methodologies used to evaluate HRQoL and compliance with the HRQoL dimensions recommended by the World Health Organization (WHO) were examined. Although LYMQoL is the most widely used questionnaire, studies that include all the elements recommended by WHO have not yet been conducted (16). Therefore, despite the need for a universal, disease-specific methodology to ensure that HRQoL data accurately reflect the impact of the disease, such an approach is still lacking.

Bowman et al. (17) demonstrated that the complex interaction between the QoL, anxiety, depression and psychosocial well-being of LEL patients and supportive care emphasizes the importance of a multidisciplinary approach and services that provide psychosocial support. In another study, it was observed that exercise programs, both with and without resistance, led to improvements in QoL in LEL patients compared to pre-treatment

levels (18). Angst et al. (19) found evidence that patients with LEL benefited significantly from a comprehensive inpatient rehabilitation program and achieved HRQoL levels equal to or higher than expected when compared with general population norms, thus strengthening the recommendation of multidisciplinary inpatient rehabilitation. In this study, LYMQoL, the most commonly used scale, was also employed, and post-treatment findings revealed a significant improvement in scores. This indicates the positive impact of therapeutic interventions on the QoL of individuals with LEL.

Study Limitations

This study has several limitations that should be considered when interpreting the results. First, the retrospective design restricted the available data to information recorded in patient files. As a result, some important variables, such as circumferential measurements and BMI before and after MLD, were not consistently documented and could not be analyzed. Although information regarding the underlying cause of lymphedema (malignant vs. non-malignant) was available, subgroup analyses were not performed due to the limited sample size, to avoid underpowered and potentially misleading results. The relatively small sample size also limits the generalizability and statistical robustness of our findings. While a statistically significant correlation between BMI and LYMQoL scores was observed, the correlation was weak. Therefore, these findings should be interpreted with caution. Additionally, potential confounding factors, such as the stage of lymphedema or the type of underlying pathology, could not be fully accounted for in the analysis. Although all circumferential measurements were performed by a single experienced specialist, eliminating interrater variability, interrater reliability could not be evaluated. Furthermore, minimal detectable change and minimal clinically important difference values specific to the LYMQoL for LEL are not clearly established in the literature, limiting the interpretation of the clinical significance of the changes observed.

Despite these limitations, our study has several strengths. Unlike most studies that primarily focus on upper extremity lymphedema following breast cancer, our research provides valuable insights into QoL changes in patients with LEL after MLD treatment, an area with limited existing research. Additionally, all circumferential measurements were conducted by the same specialist using standardized methods, ensuring consistency and reducing measurement bias.

Conclusion

In conclusion, this study highlights the impact of secondary lower-extremity lymphedema on patients' QoL and reveals a weak but statistically significant correlation between BMI and QoL. The findings support the effectiveness of MLD in improving QoL among affected individuals. Given the limited number of studies focusing specifically on lower-extremity lymphedema, our research contributes valuable insights to a relatively underexplored area. Although lymphedema is often managed within oncology or vascular specialties, the growing field of lymphology underscores the importance of interdisciplinary collaboration and specialized care. Many patients continue to face unmet clinical, psychological, and rehabilitative needs. Future prospective studies with larger sample sizes and objective evaluation tools are warranted to further refine treatment approaches and improve outcomes in this patient population.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Clinical Research Ethics Committee of University of Health Sciences Turkey, İstanbul Physical Therapy and Rehabilitation Training and Research Hospital on 02.07.2024 with protocol number 2024-39.

Informed Consent: Written İnformed consent was obtained from all subjects involved in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.E., N.K., C.M.C., E.K., Concept: S.E., B.Ş.A., N.P., D.B., Design: S.E., B.Ş.A., N.K., N.P., D.B., E.K., Data Collection or Processing: S.E., N.K., C.M.C., Analysis or Interpretation: S.E., B.Ş.A., N.K., N.P., D.B., Literature Search: B.Ş.A., N.K., C.M.C., Writing: S.E., B.Ş.A., N.K., E.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

- Executive Committee of the International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2023 consensus document of The International Society of Lymphology. Lymphology. 2023;56(4):133-151.
- Schiltz D, Eibl D, Mueller K, Biermann N, Prantl L, Taeger CD. Therapist versus machine-immediate effects of manual versus

- mechanical lymphatic drainage in patients with secondary lymphedema. J Clin Med. 2024;13(5):1277.
- 3. Borman P. Lymphedema diagnosis, treatment, and follow-up from the view point of physical medicine and rehabilitation specialists. Turk J Phys Med Rehabil. 2018;64(3):179-197.
- Keeley V, Crooks S, Locke J, Veigas D, Riches K, Hilliam R. A quality of life measure for limb lymphoedema (LYMQOL). J Lymphoedema. 2010;5(1):26-37.
- Borman P, Yaman A, Denizli M, Karahan S. The reliability and validity of lymphedema quality of life questionnaire-leg in Turkish patients with lower limb lymphedema. Lymphat Res Biol. 2020;18(1):42-48.
- Kalemikerakis I, Evaggelakou A, Kavga A, Vastardi M, Konstantinidis T, Govina O. Diagnosis, treatment and quality of life in patients with cancer-related lymphedema. J BUON. 2021;26(5):1735-1741.
- Stolldorf DP, Dietrich MS, Ridner SH. Symptom frequency, intensity, and distress in patients with lower limb lymphedema. Lymphat Res Biol. 2016;14(2):78-87.
- Moffatt CJ, Franks PJ, Doherty DC, Williams AF, Badger C, Jeffs E, et al. Lymphoedema: an underestimated health problem. QJM. 2003;96(10):731-738.
- 9. Greene A, Meskell P. The impact of lower limb chronic oedema on patients' quality of life. Int Wound J. 2017;14(3):561-568.
- Franks PJ, Moffatt CJ, Doherty DC, Williams AF, Jeffs E, Mortimer PS. Assessment of health-related quality of life in patients with lymphedema of the lower limb. Wound Repair Regen. 2006;14(2):110-118.
- Grigorean A, Voci D, Farmakis IT, Hobohm L, Keller K, Kucher N, et al. Prevalence of lymphedema using large data sets: an epidemiological analysis in the United States and in Italy. Lymphology. 2023;56(4):178-187.

- 12. Kurpiewska-Pieniążek J, Ochałek K, Grądalski T, Szuba A. Efficacy of compression stockings in prophylaxis of lower limb lymphedema in women undergoing treatment for gynecological malignancies: a prospective randomized study. Cancers (Basel). 2025;17(15):2530.
- Eidenberger M. Patient-reported outcome measures with secondary lower limb lymphedemas: a systematic review. J Adv Pract Oncol. 2021;12(2):174-187.
- 14. Koly KN, Saba J, Nessa Z, Luba FR, Hossain I, Aktaruzzaman MM, et al. Social and healthcare-seeking experiences of people affected with lymphedema in Bangladesh. PLoS Negl Trop Dis. 2025;19(8):e0013384.
- 15. Schulz T, Lee Warg M, Kurow O, Langer S, Nuwayhid R. The burden of lymphedema on quality of life. Vasa. 2025;54(2):124-132.
- Chima C, Murray B, Moore Z, Costello M, George S. Healthrelated quality of life and assessment in patients with lower limb lymphoedema: a systematic review. J Wound Care. 2022;31(8):690-699
- 17. Bowman C, Oberoi D, Radke L, Francis GJ, Carlson LE. Living with leg lymphedema: developing a novel model of quality lymphedema care for cancer survivors. J Cancer Surviv. 2021;15(1):140-150.
- 18. Hsu YY, Lin CF, Liang PC, Nguyen TTB, Hsu KF. Effects of resistance exercise on reducing the risk of lower-limb lymphedema after gynecological cancer surgery. Asia Pac J Oncol Nurs. 2025;12:100756.
- 19. Angst F, Benz T, Lehmann S, Sándor PS, Wagner S. Effects of inpatient rehabilitation in leg lymphedema: a naturalistic prospective cohort study with intra-individual control of effects. Arch Phys Med Rehabil. 2023;104(12):2035-2042.