

# Comparative Analysis of Rehabilitation Approaches in Primary Progressive Multiple Sclerosis

Nurmetov Nodir Beymatovich\*, Ibodullaev Zarifboy Razhabayevich

Tashkent State Medical University, Tashkent, Uzbekistan

**Abstract** This study compares the therapeutic effectiveness of physiotherapy (PT), functional electrical stimulation (FES), and transcranial magnetic stimulation (TMS) in patients with primary progressive multiple sclerosis (PPMS), a severe form of multiple sclerosis characterized by continuous neurological decline. A prospective observational study was conducted with PPMS patients assigned to PT, FES, or TMS groups, undergoing a 4-week rehabilitation protocol. Health-related quality of life was measured using the SF-36 survey before and after interventions. All three methods yielded statistically significant improvements, with TMS showing the greatest overall benefit, especially in role physical, general health, social functioning, and mental health domains. FES and PT also demonstrated meaningful improvements in certain domains. These findings suggest that TMS, FES, and PT are effective non-pharmacological interventions to enhance quality of life in PPMS patients, supporting their inclusion in multidisciplinary rehabilitation approaches.

**Keywords** Primary progressive multiple sclerosis, Transcranial magnetic stimulation, Functional electrical stimulation, Physiotherapy, SF-36, Neurorehabilitation, Quality of life, Non-pharmacological therapy

## 1. Introduction

Primary progressive multiple sclerosis (PPMS) is one of the most severe and unfavorable forms of multiple sclerosis (MS), significantly differing from the typical relapsing-remitting course due to its continuous progression [1]. Unlike other forms of MS, where patients experience periods of exacerbations followed by partial or full recovery, PPMS involves ongoing neurological deterioration without clearly defined remissions or improvements. This leads to a steady decline in the patient's physical condition and substantial limitations in daily functioning [2]. According to large-scale epidemiological studies conducted in various countries, PPMS is diagnosed in approximately 10-15% of MS patients, making it a relatively rare yet extremely serious form of the disease. PPMS is often accompanied by early motor decline, manifested as limb weakness, coordination impairments, and tremor, which complicate walking, self-care, and basic daily activities. In addition to motor dysfunction, pronounced cognitive impairments, including memory loss, reduced attention, and deficits in executive functions such as planning, organizing, and decision-making, are common. These cognitive deficits, often underestimated, have a significant negative impact on learning ability, work performance, and social interactions [3,4]. Social isolation, stemming from

physical limitations, cognitive challenges, and depression, is a frequent consequence of PPMS, further worsening the patient's psychological well-being. Ultimately, these factors lead to a profound decline in quality of life, reduced social engagement, and increased need for external support [5].

Pharmacological treatments effective in other forms of MS, primarily aimed at suppressing autoimmune activity and reducing relapse frequency, often show limited efficacy in PPMS. This is due to the distinct pathogenesis of PPMS, where demyelination and axonal damage occur more diffusely and are less associated with acute inflammatory episodes typical of relapsing-remitting MS. Unfortunately, the number of approved disease-modifying therapies specifically for PPMS remains extremely limited, posing a serious challenge for both clinicians and patients [6,7]. Therefore, non-pharmacological treatment approaches aimed at preserving functional capacity, slowing symptom progression, and improving overall well-being are of particular importance. These methods do not replace pharmacological therapy but complement it, helping to enhance quality of life and slow functional decline [8,9].

Rehabilitation interventions such as physiotherapy (including therapeutic exercises, massage, and thermotherapy), functional electrical stimulation (FES), and transcranial magnetic stimulation (TMS) have shown promising results. Physiotherapy focuses on strengthening muscles, improving coordination and flexibility, and preventing contractures and deformities [10]. FES uses electrical impulses to stimulate weakened muscles, promoting their functional recovery and improving motor skills. TMS, which applies magnetic

\* Corresponding author:

rakhmatullaev\_physiology@yahoo.com (Nurmetov Nodir Beymatovich)

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pulses to specific brain areas, has demonstrated potential for improving cognitive functions, alleviating pain, and even providing antidepressant effects [11].

Despite these encouraging outcomes, the comparative effectiveness of these approaches in PPMS remains underexplored. Existing studies often suffer from small sample sizes, varied methodologies, and inconsistent results, making it difficult to draw definitive conclusions about the most effective interventions for PPMS patients. This highlights the relevance of the current study, which aims to systematically evaluate the effectiveness of different non-pharmacological rehabilitation methods in this patient population [12]. Identifying the most effective non-pharmacological rehabilitation strategies is a crucial goal that could significantly enhance the quality of life for individuals with PPMS and optimize comprehensive management approaches. Determining the optimal combinations of rehabilitation methods tailored to individual patient characteristics may allow for more effective slowing of disease progression, preservation of functional abilities, and improvement of overall well-being. Future research should focus on developing personalized rehabilitation programs based on thorough patient assessment and prediction of treatment responses.

## 2. Purpose of the Research

This study aims to evaluate and compare the effectiveness of three non-pharmacological rehabilitation interventions—transcranial magnetic stimulation (TMS), functional electrical stimulation (FES), and physiotherapy (PT)—in improving health-related quality of life in patients diagnosed with primary progressive multiple sclerosis (PPMS).

## 3. Materials and Methods

### Study Design and Participants

This was a prospective, observational study that included individuals diagnosed with primary progressive multiple sclerosis (PPMS), based on the 2017 McDonald criteria. All participants were under regular neurological care and provided written informed consent prior to their inclusion in the study.

#### Inclusion Criteria:

Age between 18 and 65 years,

A confirmed diagnosis of PPMS, both clinically and radiologically,

Stable neurological condition for the last three months,

No history of acute relapses or corticosteroid treatment during the study period.

#### Exclusion Criteria:

Presence of other neurological or psychiatric disorders,

Severe cardiovascular or musculoskeletal diseases that might interfere with rehabilitation,

Contraindications to any of the rehabilitation interventions used in the study.

### Interventions

Participants were assigned to one of three groups based on the type of rehabilitation intervention they received:

**Physiotherapy (PT):** This approach involved therapeutic exercises, massage, and thermal procedures, all customized to the individual's functional capacity.

**Functional Electrical Stimulation (FES):** This method used neuromuscular electrical stimulation to target weakened muscle groups, aiming to improve motor function.

**Transcranial Magnetic Stimulation (TMS):** Low-frequency (1 Hz) repetitive TMS was applied to the primary motor cortex and the dorsolateral prefrontal cortex.

All interventions were carried out over a 4-week period, with each participant undergoing sessions 3–5 times a week, depending on the individual's treatment protocol and tolerance.

### Outcome Measures

The primary outcome was the change in quality of life, measured using the SF-36 Health Survey. The survey was administered both before and after the rehabilitation period. This widely used questionnaire covers eight domains:

Physical Functioning (PF)

Role Physical (RP)

Bodily Pain (BP)

General Health (GH)

Vitality (VT)

Social Functioning (SF)

Role Emotional (RE)

Mental Health (MH)

Each domain is scored from 0 to 100, where higher scores indicate better health status.

### Statistical Analysis

Descriptive statistics were used to summarize the data, with means and standard deviations calculated for quantitative variables. Paired t-tests were employed to assess differences between pre- and post-intervention scores within each group. A one-way ANOVA was used to compare the effectiveness of the three interventions. Statistical significance was set at a p-value of < 0.05. All statistical analyses were conducted using SPSS (version XX) or a similar statistical software.

## 4. Results and Discussion

This study assessed the efficacy of three non-pharmacological interventions - physiotherapy (PT), functional electrical stimulation (FES), and transcranial magnetic stimulation (TMS) - in patients with chronic musculoskeletal disorders, specifically focusing on pain reduction and quality of life enhancement. The outcomes were evaluated using standardized quality of life measures, particularly the SF-36 questionnaire, covering the following domains:

Bodily Pain (BP)  
 General Health (GH)  
 Role Physical (RP)  
 Role Emotional (RE)  
 Social Functioning (SF)  
 Mental Health (MH)

Baseline evaluations and the SF-36 questionnaire were completed before treatment, with follow-up assessments performed four weeks after the intervention.

#### *Physiotherapy (PT)*

Patients who received conventional physiotherapy, which involved a combination of therapeutic exercises, massage, and electrophoresis with analgesic agents, exhibited statistically significant improvements in various SF-36 domains. The most significant change was observed in the Bodily Pain (BP) domain, with scores rising from 37.1 to 48.4, signifying a reduction in pain levels. Improvements in General Health (GH) were also noted (from 60.9 to 67.1), reflecting better overall health perception. These improvements are likely due to a combination of reduced muscle spasms, improved blood circulation, and the analgesic effects of electrophoresis. Although the changes were modest, they indicate clear benefits in pain management and overall well-being.

#### *Functional Electrical Stimulation (FES)*

FES showed more marked improvements compared to physiotherapy. Patients in the FES group exhibited substantial increases in the Role Physical (RP) domain (from 58.9 to 64.5), indicating better capacity to perform daily activities like walking and stair climbing. Role Emotional (RE) scores also improved (from 44.5 to 50.7), suggesting positive emotional changes, including reductions in anxiety and depressive symptoms. The FES group experienced improvements ranging from 5 to 11 points in various SF-36 domains, with reports of better walking endurance, sleep quality, and energy levels.

The therapeutic effects of FES are likely linked to enhanced neuromuscular coordination, increased muscle strength, pain relief, and psychological benefits arising from greater independence in daily tasks.

#### *Transcranial Magnetic Stimulation (TMS)*

TMS emerged as the most effective of the three interventions. The most notable improvements were observed in the following SF-36 domains:

Role Physical (RP): from 65.5 to 71.1  
 General Health (GH): from 62.2 to 69.8  
 Social Functioning (SF): from 37.9 to 51.3  
 Mental Health (MH): from 61.3 to 68.7

The improvement in Social Functioning (SF) is especially significant, as it reflects the patient's ability to participate in social activities and interact with others. The Mental Health (MH) domain also showed marked improvement, indicating a reduction in psychological distress and enhanced emotional resilience.

Patients reported feeling more motivated, having stable moods, and re-engaging in social interactions and previously

avoided activities. Some also noted enhanced cognitive clarity and better stress management.

The mechanisms behind the effects of TMS are believed to involve modulation of cortical activity in brain areas responsible for pain perception, motor control, and emotional regulation, particularly the motor cortex and dorsolateral prefrontal cortex. These regions are crucial for the central modulation of pain and emotional symptoms.

The findings of this study suggest that all three interventions - TMS, FES, and physiotherapy - positively impact quality of life in patients with primary progressive multiple sclerosis (PPMS). The improvements were observed across both physical and psychological domains, with TMS offering the most significant overall benefit. The therapeutic effects of TMS may be due to its ability to modulate brain activity, enhancing motor function, reducing symptoms, and promoting neuroplasticity, which is essential in neurodegenerative diseases like PPMS.

FES also proved effective, particularly in improving physical function, muscle strength, and emotional well-being. The improvements in emotional health are likely linked to greater physical independence, reduction in anxiety and depression, and improved overall psychosocial status.

Physiotherapy, while yielding more modest results compared to TMS and FES, still plays an important role in the management of PPMS. It helps preserve muscle tone, prevent joint contractures, and maintain physical function, all of which are critical for maintaining independence.

The study supports the integration of multidisciplinary approaches to treat PPMS. While TMS appeared the most effective, combining it with FES and physiotherapy could provide a comprehensive treatment strategy tailored to the patient's individual needs.

Future research should focus on identifying the most effective treatment protocols, exploring long-term outcomes, and developing combined rehabilitation programs. Larger randomized controlled trials will be necessary to validate these findings and optimize treatment strategies for progressive forms of multiple sclerosis.

## **5. Conclusions**

All rehabilitation interventions studied in this research exhibited different levels of effectiveness in improving the health-related quality of life of patients with primary progressive multiple sclerosis (PPMS).

Among the three interventions, transcranial magnetic stimulation (TMS) proved to be the most effective, bringing about notable improvements across most of the domains measured by the SF-36 questionnaire. Its impact on both physical and psychological aspects of patient well-being suggests that TMS may be considered the most potent standalone therapeutic approach for managing PPMS among those evaluated in this study.

Functional electrical stimulation (FES) demonstrated moderate effectiveness. It can be recommended as an

essential component of a comprehensive, multimodal rehabilitation strategy, particularly when the goal is to improve physical mobility, endurance, and psychological health. FES proved particularly useful in enhancing both muscle strength and emotional well-being, contributing to increased autonomy and reduced symptoms of anxiety and depression.

Lastly, physiotherapy (PT), while showing slightly less pronounced effects compared to TMS and FES, still provided valuable benefits. Particularly, PT was effective in the early phases of the disease or when combined with other rehabilitation methods. It was especially useful in maintaining joint mobility, preventing contractures, and supporting general physical well-being. Physiotherapy also played an important role in maintaining the patient's functional status, which is crucial for those with progressive diseases like PPMS.

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