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Sistematik Derleme/Systematic Review

The Use of Therapeutic Interventions for Improving Balance and Gait in People with Multiple Sclerosis: A Systematic Review of Studies Conducted in Turkey

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ABSTRACT

This systematic review aimed to evaluate the effectiveness of therapeutic interventions used in the treatment of balance and gait in multiple sclerosis by reviewing studies conducted in Turkey. Studies were included according to the following eligibility criteria: Population, Multiple Sclerosis patients; Intervention, non-pharmacological therapeutic interventions for balance and gait; Comparison, usual intervention and no intervention/no special balance intervention; Outcome, balance and gait clinical scales; Study design, randomized controlled trials. A literature search was conducted in CENTRAL, MEDLINE/PubMed, EMBASE, ClinicalTrials.gov, TR Index for studies published between January 2013 and August 2023. The methodological quality of the included studies was assessed by the Quality Checklist for Randomized Controlled Trials published by the Joanna Briggs Institute. A total of 1023 participants (n) were included in this review. The average sample size per study was 37.88± 16.73. While 78% of the studies reported that the interventions they applied had a positive effect on walking and recovery outcomes in MS, 22% of the studies reported no significant superiority in balance and walking outcomes. The evidence showed that although a wide range of therapeutic interventions are available for balance and gait in people with MS, there is a serious lack of high-quality evidence demonstrating the effectiveness of these modalities.

Keywords: Postural balance, gait, multiple sclerosis, therapeutics

Multipl Sklerozlu Kişilerde Denge ve Yürüyüşü İyileştirmek İçin Terapötik Müdahalelerin Kullanımı: Türkiye'de Yapılan Çalışmaların Sistematik Derlemesi

ÖZET

Bu sistematik derleme, Türkiye'de yapılan çalışmaları gözden geçirerek multipl sklerozda denge ve yürüme tedavisinde kullanılan terapötik müdahalelerin etkinliğini değerlendirmeyi amaçlamaktadır. Çalışmalar aşağıdaki uygunluk kriterlerine göre dahil edilmiştir: Popülasyon, Multipl Skleroz hastaları; Müdahale, denge ve yürüyüş için farmakolojik olmayan terapötik müdahaleler; Karşılaştırma, olağan müdahale ve müdahale yok/özel denge müdahalesi yok; Sonuç, denge ve yürüyüş klinik ölçekleri; Çalışma tasarımı, randomize kontrollü çalışmalar. Ocak 2013 ile Ağustos 2023 tarihleri arasında yayınlanan çalışmalar için CENTRAL, MEDLINE/PubMed, EMBASE, ClinicalTrials.gov, TR Dizin'de literatür taraması yapılmıştır. Dahil edilen çalışmaların metodolojik kalitesi Joanna Briggs Enstitüsü tarafından yayınlanan Randomize Kontrollü Çalışmalar için Kalite Kontrol Listesi ile değerlendirilmiştir. Bu incelemeye toplam 1023 katılımcı (n) dahil edilmiştir. Çalışma başına ortalama örneklem büyüklüğü 37.88± 16.73'tür. Çalışmaların %78'i uyguladıkları müdahalelerin MS'te yürüme ve iyileşme sonuçlarına olumlu etkisinin olduğunu bildirirken, çalışmaların %22'si ise denge ve yürüme sonuçlarında anlamlı bir üstünlük olmadığını bildirmiştir. Bu inceleme sonucunda bulunan kanıtlar, MS'li kişilerde denge ve yürüme için çok çeşitli terapötik müdahalelerin mevcut olmasına rağmen, bu yöntemlerin etkinliğini gösteren yüksek kaliteli kanıtların ciddi şekilde eksik olduğunu göstermiştir.

Anahtar Kelimeler: Duruş dengesi, yürüyüş biçimi, multipl skleroz, tedavi ediciler

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INTRODUCTION

Multiple sclerosis (MS) is a chronic, demyelinating, autoimmune disorder of the central nervous system (CNS) which is characterised by a wide range of symptoms affecting different functional systems (gait, balance, bowel, bladder, vision, and cognition) (Zurawski & Stankiewicz, 2018). Impairments in cognition, muscle strength, muscle tone, sensation, coordination and gait due to damage to central nervous system structures cause balance and walking problems in MS (Cattaneo et al., 2002; Cameron & Nilsagard, 2018). In people with MS (PwMS), balance and gait impairments become more pronounced as disease duration increases, affecting the performance of activities of daily living and reducing quality of life (Chee et al., 2021).

It is of critical importance to select and regularly implement appropriate rehabilitation approaches to address the problems that increase disability in MS. There have been several therapeutic intervention strategies developed recently to improve balance in people with MS (Khan et al., 2017). Interventions aimed at improving balance and gait in people with MS often include strengthening, endurance and resistance exercises, pilates, orthotics, casting, transcutaneous electrical nerve stimulation, acupressure, hippotherapy, vibration therapy, acupuncture, cognitive interventions, telerehabilitation, fatigue management, upper limb rehabilitation and spasticity management (Arik et al., 2022; Glinsky et al., 2007; Haselkorn et al., 2015; Rodríguez-Fuentes et al., 2022; Yeni et al., 2022).

Individuals with MS identified wellness interventions as a high priority over pharmacological interventions in symptom management. They also expressed the importance of the healthcare providers' critical role in promoting these behaviors (Motl et al., 2018). Gunn et al. (2015) reported that therapeutic interventions including gait, balance and functional training had a higher impact on balance and gait outcomes than other interventions. A number of recent studies demonstrating the clinical effectiveness of different rehabilitation interventions have been incorporated into the management of people with MS, transforming these interventions from a preventive or symptomatic approach to a therapeutic intervention (Centonze et al., 2020). While various rehabilitation approaches have been proven to be effective, understanding the optimal modality of a particular therapeutic intervention is critical to implementing evidence-based practice and improving the effectiveness of interventions (Dijkers et al., 2014).

MS rehabilitation is a long-term process and it is essential to incorporate therapeutic interventions into programmes to increase patient motivation and engagement. While a broad range of therapeutic interventions has been evaluated in people with multiple sclerosis (pwMS), the evidence for their effectiveness could be strengthened. A synthesis of the available evidence on the effectiveness and safety of therapeutic interventions in the context of MS rehabilitation is essential to guide practitioners and caregivers in achieving optimal patient outcomes. As a consequence, this systematic review aimed to determine the current status of therapeutic interventions for balance and gait in people with multiple sclerosis by reviewing studies conducted in Turkey.

MATERIAL AND METHOD

Study Type

The type of the study is systematic review.

Population and Sampling

The literature search for this study was conducted in the following electronic databases for studies published between January 2013 and August 2023: CENTRAL, MEDLINE/PubMed, EMBASE, ClinicalTrials.gov and TR Index. Appropriate keywords and MeSH titles were generated through conversation between the study authors ("multiple sclerosis" OR "postural balance" OR "gait" OR " randomised controlled" OR "clinical trials" OR "therapeutic intervention" OR "Turkey"). The search algorithm was adapted to each database and filters were used to refine the searches (year of publication and language). For example, the search term for Pub Med was; ("multiple sclerosis" OR 'postural balance OR 'gait OR 'therapeutic intervention' AND Turkey). Exclusion criteria were non-randomised controlled trials, review articles, feasibility and protocol studies, case-control studies, book chapters, conference

abstracts, unpublished abstracts, qualitative studies and letters. We also excluded studies with multiple diagnoses without separate analysis for MS, published in languages other than English and Turkish, and without full text.

Studies eligible for this systematic review were selected according to the following PICOs: (P) Population: Individuals aged 18 years and older diagnosed with MS; (I) Intervention: all interventions specifically aimed at improving balance and walking; (C) Comparison: usual intervention or no intervention; (O) Outcome: clinical scales of gait or balance; (S) Study types: Randomized controlled trials.
Exclusion criteria were non-randomized controlled trials, review articles, feasibility and protocol studies, case-control studies, book chapters, conference abstracts, unpublished abstracts, qualitative studies and letters. We also excluded studies with multiple diagnoses without separate analyses for MS, published in languages other than English and Turkish, and without full text.

Data Collection Tools

In the review, the researchers developed an electronic data extraction tool to obtain the data. This tool extracted the first author's full name, year of publication, study design, sample size (experimental and control groups), clinical and demographic characteristics of the sample (mean age, sex, EDSS (Expanded Disability Status Scale) score, disease duration), description of the experimental and control interventions, intervention characteristics (setting, duration, frequency, intensity and dose of the intervention), gait and balance outcome measures (primary or secondary outcomes).

Data Collection

The systematic review protocol and its details were registered in the International Prospective Database of Systematic Reviews (PROSPERO) under the registration number CRD42023410986. In the reporting of this systematic review, we also followed the protocol described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Page et al., 2021).

Two authors (MKT and GYY) independently screened all titles and abstracts of the articles. Relevant articles were then retrieved for full-text assessments, and the same authors independently assessed all full-text articles to identify eligible studies. In case of disagreement, a third senior author (IT) assessed the article to reach a consensus.For the methodological quality of the studies included in this systematic review, we used the 13-item Quality Checklist for Randomized Controlled Trials published by the Joanna Briggs Institute (JBI) (Barker et al., 2023). Each item on this list is rated as "yes, no, uncertain, and not applicable." A "quality score" was assigned to the assessment results of each included study. The methodological quality of the studies was assessed as "mediocre" if less than 50% of the items were rated "yes," "fair quality" if 51-80% of the items were rated "yes," and "good quality" if more than 80% of the items were rated "yes." Quality assessment was carried out by two independent authors. In case of differences in the authors' responses, the two authors discussed and reached a consensus, and the final responses were then compiled into a single text.

The first literature search revealed 4715 studies. After removing duplicates (n=1117), 3598 studies remained. After excluding studies based on title and abstract screening (n=3424), 174 studies were included in the full-text review. One hundred forty-seven studies were excluded because they did not meet the eligibility criteria, and 27 were included in the systematic review (Figure 1).

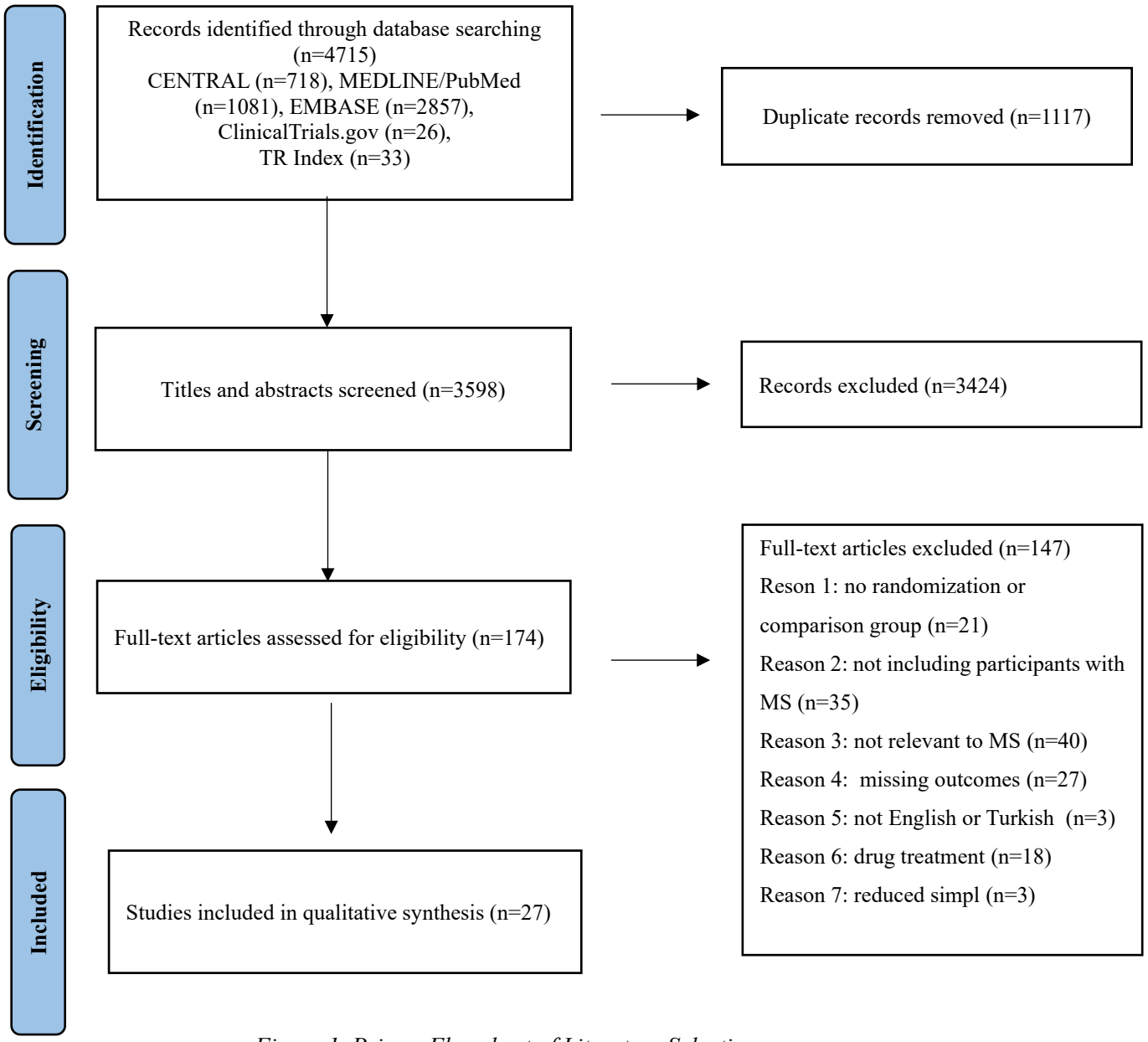

Figure 1. Prisma Flowchart of Literature Selection

Data Analysis

The studies included in the systematic review differed in methodology, participant characteristics, evaluation strategies, and outcome factors. Since meta-analysis was impossible, the results are summarized and presented as a narrative.

Ethical Committee Approval

The studies that were open to access were included in the research. In this direction, the articles that were allowed to be accessed in the database were examined.

RESULTS

All of the studies included in the systematic review were randomized controlled trials. A total of 1023 participants (n) were included in this review. The mean sample size per study was 37.88±16.73. The sample sizes of the studies were heterogeneous, ranging from 16 to 99 participants. The study included 671 (74%) female participants and 239 male participants, except for four studies that did not specify the

gender of the participants (Ayvat et al., 2021; Bulguroğlu et al., 2017; Gürpınar et al., 2020; Salbaş et al., 2022).

The EDSS scores of the included participants ranged from 0 to 7, except for one uninformative study (Salbaş et al., 2022). The participants' illness duration ranged from 3 months to 29 years. One RCT included participants with severe disabilities (EDSS 5.5-7), while all others included mild to moderate disabilities (Özsoy-Ünübol et al., 2022). All studies had a pretest and posttest follow-up immediately after the intervention (n = 27). The characteristics of the included studies are listed in Table 2.
Eight studies had only balance as the primary outcome (Doğan et al, 2023; Gürpınar et al., 2020; Kahraman et al., 2020; Özkan et al., 2022; Özkul et al., 2020a; Salbaş et al., 2022; Tomruk et al., 2016 Yazgan et al., 2020) and one study had only balance as the secondary outcome (Özkul et al., 2018). Three studies had only walking as the primary outcome (Bilek et al., 2023; Kırmacı et al., 2021; Tarakçı et al., 2021). Eleven studies used both balance and gait as primary outcomes (Abasıyanık et al., 2020; Aydın et al., 2014; Bulguroğlu et al., 2027; Eldemir et al., 2023; Küçük et al., 2016; Özkul et al., 2020c; Özkul et al., 2023; Özsoy- Ünübol et al., 2022; Salcı et al, 2017; Tarakçı et al., 2013; Yaşa et al., 2022), while two studies used both walking and balance as secondary outcomes (Ayvat et al., 2021; Özdoğar et al., 2020). Only two studies had balance as the primary outcome and walking as the secondary outcome (Kahraman et al., 2020; Özkan et al., 2022). Details of 27 interventions to improve balance or gait in people with MS are shown in Table 1.

Table 1. Interventions Included in the Systematic Review

Study	Intervention
Özkul, 2020a	Immersive virtual reality
Gürpınar, 2020	Aquatic exercises
Salbaş, 2022	Hippotherapy simulation exercise
Abasıyanık, 2020; Küçük, 2016; Tomruk, 2016	Clinical pilates training
Özdoğar, 2020	Video-based exergaming
Özkul, 2020b; Özkul, 2018	Combined exercise training
Kahraman, 2020	Telerehabilitation-based motor imagery training
Ayvat, 2021	High-frequency local vibration on mild-moderate
Özkan, 2022	Aerobic training and combined trunk stabilization training
Güngör, 2022	Pilates-based core stability training
Özkul, 2023	Multi-task training
Bilek, 2023	Self-acupressure
Yazgan, 2020	Exergaming (Nintendo Wii Fit)
Tarakçı, 2013	Group exercise
Özkul, 2020c	Task-oriented circuit training
Bulguroğlu, 2017	Mat Pilates and reformer pilates
Yaşa, 2022	Core stability-based balance training and kinesio taping
Doğan, 2023	Virtual reality supported task-oriented circuit therapy
Salcı, 2017	Lumbar stabilization, Balance and a task-oriented training
Kırmacı, 2021	Eccentrıc and concentrıc exercıse traınıng
Özsoy Ünübol, 2022	Robot-assisted gait training
Aydın, 2014	Home based or hospital based calisthenic exercises training
Tarakçı, 2021	Structured supervised exercise
Eldemir, 2023	Pilates-based telerehabilitation

The balance and walking intervention's duration, frequency, and intensity varied across studies. Four studies lasted 12 weeks, one study 10 weeks, seventeen studies 8 weeks, three studies 6 weeks, and 2 studies 4 weeks. Twenty-five studies had a frequency of 2/3 per week. Two studies had 1 frequency per week. The dose of frequencies in the studies ranged from 27 minutes to 90 minutes. The intervention setting included Inpatient or outpatient/day treatment environments of private/public hospital patients' homes. All but three of the twenty-seven included studies explained participant withdrawal and loss to follow-up. No participants withdrew from the two studies. In studies with loss to follow-up or withdrawal from the study, participants who did not continue were excluded from the analysis. Additionally, no adverse events or side effects were related to the interventions used in the included studies. Only one study reported that a patient in the home exercise group fell. The Berg Balance Scale (BBS), Activities-Specific Balance Confidence (ABC), Posturography (Biodex Balance Systems) tools were frequently used to obtain balance result measurements of the studies, while Timed Up & Go test (TUG), The Six-Minute Walk Test (6MWT), Timed 25-Foot Walk (T25FW): Multiple Sclerosis Walking Scale-12 (MSWS-12), 2-Minute Walk Test (2MWT) tools were frequently used for walking results (Table 2).

Table 2. Characteristics and Main Findings of The Studies Included in The Systematic Review

Study	Study Design	Gait/ Balance Measures	Population (Intervention/Comparison)	Participants Characteristics	Intervention/ Comparison	Follow Up/Lost to Follow-Up(n)	Results
Özkul, 2020a	RCT Single blind	BBS Posturography TUG	Immersive virtual reality group (IVRG):13, Balance training group (BTG):13, Control group (CG):13	IVRG: age (years) 29 (25–41), gender (f/m): 9/4, EDSS score: 1 (1–3), disease duration (years): 4 (4–6.5) BTG: age (years) 34 (25.5–45.5), gender (f/m): 11/2, EDSS score: 1 (0.75–3), disease duration (years): 4 (3–6.5) CG: age (years) 34 (32–42.5), gender (f/m): 10/3, EDSS score: 2 (1–2.5), Disease duration (years): 4 (2.5–14.5)	Duration: 8 weeks/ Frequency: two session IVRG: 5 min warm-up + 20 min Pilates + 5 min cooldown + 10 min rest + 20 min IVR or balance training. BTG: 5 min warm-up + 20 min Pilates + 5 min cooldown + 10 min rest performed two tasks: hitting and avoiding the ball. CG: 20 min Jacobson's progressive relaxation exercise.	At baseline and 8th week / 12	IVRG had beneficial effects similar to those of balance training on balance mobility, in MS patients.
Gürpınar, 2020	RCT Single blind	Posturography	Aquatic plyometric group (APE): 15 Halliwick group (Hallw): 13	APE: age (years) 51 (49.5- 63.5), gender unclear, EDSS score: 2.5 (2.5-5.5), disease duration (years): 15 (11.0-22.5) Hallw: age (years) 56.8 (47.3-65.8), gender unclear, EDSS score: 2.7 (2.3-5.4), Disease duration (years): 15 (7.0-29.0)	Duration: 8 weeks/ Frequency: two session APE: 5 min warm-up + 35 min aquatic plyometric exercise + 5 min cool down. Hallw: 5 min warm up + 35 min halliwick programme+ 5 min cool down.	At baseline and 8th week / 2	APE is a safe and effective intervention for balance in MS.
Salbaş, 2022	RCT Single blind	BBS TUG	Hippotherapy simulation exercise groups (HSE): 17 Conventional home exercise groups (CHE): 18	HSE: age (years) 37.6±6.3, gender (f/m): 14/3, EDSS score unclear, disease duration (years): 8.1±2.7 CHE: age (years) 38.8±4.6 gender (f/m): 15/3, EDSS score unclear, disease duration (years): 8.0±2.4	Duration: 12 weeks/ Frequency: three session HSE: 5 min warm up + 5 min static stretching + 20 Hippotherapy simulation exercise + 5 min static stretching CHE: 5 min warm up + 5 min static stretching + 20 conventional home exercise + 5 min static stretching	At baseline and 12th week / 5	HSE is effective at improving balance in MS.
Abasıyanık, 2020	RCT Unclear	6MWT T25FW TUG MSWS-12 Posturography ABC	Clinical pilates group: 16 Control group: 17	Clinical pilates group: age (years) 42.50 (6.76), gender (f/m): 12/4, EDSS score 3.06 (1.65), disease duration (years): 12.59 (6.23) Control group: age (years) 48.24 (11.79), gender (f/m): 11/6, EDSS score 3.24 (1.77), disease duration (years): 9.83 (8.7)	Duration: 8 weeks/ Frequency: one session Clinical pilates group: 10 min warm-up + 40 min pilates + 5–10 min cooldown + two-day home exercise Control group: Duration: 8 weeks, frequency: three session standardized home exercises	At baseline and 8th week / 9	Clinical pilates training is effective in improving balance and gait in MS.
Özdoğar, 2020	RCT Unclear	ABC T25FW MSWS-12 SSST	Video-based exergaming group:21 Conventional rehabilitation group: 19 Control group: 20	Video-based exergaming: age (years) 39.2 (8.6), gender (f/m): 16/5, EDSS score 2.7 (1.8), disease duration (years): 7.5 (4.5) Conventional rehabilitation: age (years) 43.6 (10.5), gender (f/m): 13/6, EDSS score 2.11 (0.9), disease duration (years): 6.43 (5.9) Control group: age (years) 37.9 (12.4), gender (f/m): 15/5, EDSS score 2.25 (1.2), disease duration (years): 5.93 (4.2)	Duration: 8 weeks/ Frequency: one session Video-based exergaming group: 45 min video-based exergaming. Conventional rehabilitation group: 5-10 min warm up + 40 min conventional rehabilitation. Control Group: No intervention	At baseline and 8th week/ 3	Video-based exercise game is effective in improving balance and walking functions in MS.

Table 2. Characteristics and Main Findings of The Studies Included in The Systematic Review (continued)

Özkul, 2020b	RCT Single blind	6MWT	Combined exercise group (CEG):17 Control group (CG):17	CEG: age (years) 35.88 ± 9.74, gender (f/m): 13/4, EDSS score 1.50±0.77, disease duration (years): 14.65 ± 4.08 CG: age (years) 36.76 ± 9.02, gender (f/m): 13/4, EDSS score 1.71±0.94, disease duration (years): 5.71 ± 4.90	Duration: 8 weeks/ Frequency: three session CEG: 5 min warm up + 20 min aerobic training + 5 min cool down+15 min rest+5 min warm up + 50 min pilates training + 5 min cool down CG: 15-20 min Jacobson's progressive relaxation exercise.	At baseline and 8th week / no losses	Combined exercise is effective in improving walking capacity.
Kahraman, 2020	RCT Single blind	TUG DGI T25FW 2MWT MSWS-12 ABC Posturography	Intervention group:20 MS control group:15 Healthy group: 20	Intervention group: age (years) 34.5 (30–38.75), gender (f/m): 16/4, EDSS score 1 (0–1.75), disease duration (years): 4 (1.5–8) MS control group: age (years) 36 (28–45), gender (f/m): 14/1, EDSS score 2 (0–2.5), disease duration (years): 4 (6.2–5.3) Healthy group: age (years) 31 (27–45.5), gender (f/m): 14/6, EDSS score not available, disease duration (years): not available	Duration: 8 weeks/ Frequency: two session İntervention group: 20–30 min telerehabilitation-based motor imaging training (Tele-MIT). MS control group: no intervention Healthy group: no intervention	At baseline and 8th week / 2	Tele-MIT has been shown to improve dynamic balance, walking speed perceived walking ability, and balance confidence in MS.
Ayvat, 2021	RCT Single blind	Posturography SLST GAITRite	Group 1:10 Group 2:10 Group 3:7	Group 1: age (years) 37.70±9.70), gender (f/m): unclear, EDSS score 3.00±1.08, Disease duration (month): 135.60±77.15 Group 2: age (years) 38.40±11.07, gender (f/m): unclear, EDSS score 2.75±1.00, disease duration (month): 84.00±56.92 Group 3: age (years) 33.86±6.74, gender (f/m): unclear, EDSS score 3.00±0.81, disease duration (month): 127.00±84.36	Duration: 8 weeks/ Frequency: three session Group 1: 10 min +50 Hz local vibration + 50 min standard exercise treatment. Group 2: 10 min +100 Hz local vibration 50 min standard exercise treatment. Group 3: 60 min standard exercise treatment.	At baseline and 8th week /6	Improvement in all gait parameters three was similar between the groups: Local vibration did not offer a significant improvement for balance and gait.
Özkan, 2022	RCT Unclear	Posturography	Combined exercise group:8 Control group:8	Combined exercise group: age (years) 37.88±9.73, gender (f/m): 6/2, EDSS score 3.50 (3.25-3.75), disease duration (years): 7.50 (5.50-10.50) Control group: age (years) 35.88±11.53, gender (f/m): 5/3, EDSS score 3.25 (3-3.75), disease duration (years): 8.00 (5.00-12.50).	Duration: 8 weeks/ Frequency: two session Combined exercise group: 5 min warm-up + 20 min aerobic training + 5 min cooldown +15 min rest + 30 min trunk stabilization training. Control group: 5 min warm-up + 20 min aerobic training + 5 min cooldown	At baseline and 8th week / 2	In the combined exercise group compared to the control group in balance meaningful development was identified.
Güngör, 2022	RCT Single blind	Posturography 2MWT TUG	Supervised pilates-based core Stability training group (Supervised PBCST Group): 22 Home pilates-based core stability training group (Home PBCST Group): 20	Supervised PBCST group: age (years) 41.2 ± 9.9 (20–57), gender (f/m): 20/2, EDSS score 3.03 ± 1.25 (1–5.5), disease duration (years): 7.4 ± 6.1 (1–21) Home PBCST group: age (years) 37.5 ± 11.9 (22–58), gender (f/m): 16/4, EDSS score 2.95 ± 1.29 (1.5–5.5), disease duration (years): 7.9 ± 5.4 (1–19)	Duration: 8 weeks/ Frequency: two session Supervised PBCST group: 60-75 min standard exercise treatment. Home PBCST group: 60-75 min standard exercise treatment.	At baseline and 8th week / 8	The Supervised PBCST Group showed significant improvement in all sub-parameters of postural balance compared to the Home PBCST Group.

Table 2. Characteristics and Main Findings of The Studies Included in The Systematic Review (continued)

Özkul, 2023	RCT Single blind	Posturography TUG	Multi-task training group (MTTG):13 Single-task training group (STTG): 13 Control group (CG): 13	MTTG: age (years) 34.31 ± 12.13, gender (f/m): 10/3, EDSS score 1.23 ± 0.26, Disease duration (years): 4.15 ± 2.15 STTG: age (years) 36.31 ± 11.59, gender (f/m): 11/2, EDSS score 1.27 ± 0.26, Disease duration (years): 4.77 ± 2.31 CG: age (years) 36.31 ± 11.59, gender (f/m): 10/3, EDSS score 1.23 ± 0.26, Disease duration (years): 5.08 ± 4.05	Duration: 6 weeks/ Frequency: two session MTTG: 60 min task-oriented training program + cognitive task STTG: 60 min task-oriented training program CG: 15-20 min Jacobson's progressive relaxation exercises	At baseline and 6th week / 3	After 6 weeks, postural balance and walking speed did not change significantly in any group.
Bilek, 2023	RCT Single blind	T25FW	Study group: 31 Control group: 31	Study group: age (years) 32.58 ± 9.78, gender (f/m): 25/6, EDSS score 1.87 ± 0.64, disease duration (years): 5.75±4.49 Control group: age (years) 34.22 ± 9.30, gender (f/m): 21/10, EDSS score 1.98 ± 0.55, disease duration (years): 6±4.06	Duration: 4 weeks/ Frequency: two session Study group: 27 min acupressure application Control group: no intervention	At baseline and 4th week / no losses	Compared to the control group, there was a significant improvement between the pre-and post-study walking speeds of the study group.
Yazgan, 2020	RCT Single blind	BBS TUG 6MWT	Nintendo Wii Fit group (Group I):15 Balance trainer (Group II): 12 Control group (Group III): 15	Group I: age (years) 47.46 (10.53), gender (f/m): 13/2, EDSS score 4.16 (1.37), disease duration (years): 12.06 (6.56) Group II: age (years) 43.08 (8.74), gender (f/m): 12/0, EDSS score 3.83 (1.49), disease duration (years): 14.91 (6.54) Group III: age (years) 40.66 (8.82), gender (f/m): 13/2, EDSS score 4.06 (1.26), disease duration (years): 11.06 (5.70)	Duration: 8 weeks/ Frequency: two session Group I: 10 min warm up+ 50 min Nintendo Wii fit training Group II: 10 min warm-up + 50 min balance trainer-based exercise Group III: no intervention	At baseline and 4th week / 5	It was observed that exergaming with Nintendo Wii Fit and Balance Trainer improved balance and walking and increased functionality in PwMS compared to no intervention.
Tarakçı, 2013	RCT Single blind	BBS 10MWT 10 SCT	Exercise group:51 Control group:48	Exercise group: age (years) 41.49 ±9.37, gender (f/m): 34/17, EDSS score 4.38 ±1.37, disease duration (years): 9 ±4.71 Control group: age (years) 39.65 ±11.18, gender (f/m): 30/18, EDSS score 4.21 ±1.44, disease duration (years): 8.42 ±5.38	Duration: 12 weeks / Frequency: three session Exercise group: 60 min group exercise program Control group: no intervention	At baseline and 12th week / 7	Exercise training showed significant improvement in balanced gait measurements compared to the control group.
Özkul, 2020c	RCT Single blind	Posturography BBS ABC TUG FGA MSWS-12	Task-oriented circuit training group (TOCTG): 10 Control group (CG): 10)	TOCTG: age (years) 46 (29–47), gender (f/m): 6/4, EDSS score 4 (3.37–4.25), disease duration (years): 16 (7–20.75) CG: age (years) 41.5 (28.25–47.25), gender (f/m): 6/4, EDSS score 3.75 (3–4.25), disease duration (years): 13.5 (6.75–20)	Duration: 6 weeks/ Frequency: two session TOCTG: 60 min Task-oriented circuit training CG: 15-20 min Jacobson's progressive relaxation exercises	At baseline and 6th week / 1	There were significant improvements in balance and gait after TOCT.

Table 2. Characteristics and Main Findings of The Studies Included in The Systematic Review (continued)

Bulguroğlu, 2017	RCT Single blind	TUG ABC SLST	Mat pilates group:12 Reformer pilates group:13 Control group:13	Mat pilates group: age (years) 45 (39.3– 49.5), gender (f/m): unclear, EDSS score: 1.8 (1.1–3.3), disease duration (years): 4.5 (3–13.3) Reformer pilates group: age (years) 37 (29.5–40), gender (f/m): unclear, EDSS score 2 (1–3), disease duration (years): 5 (2–10) Control group: age (years) 40 (26–43), gender (f/m): unclear, EDSS score 1 (0.5–2), disease duration (years): 3 (1–8.5)	Duration: 8 weeks/ Frequency: two session Mat pilates group: warm up + 60-90 min mat pilates. Reformer pilates group: warm-up + 60-90 min reformer pilates Control group: Relaxation and respiration exercises	At baseline and 8th week / unclear	Mat pilates and reformer pilates have improved balance in MS patients.
Yaşa, 2022	RCT Single blind	Mini BESTest 2MWT TIS	Kinesio taping group (KT):15 Control group(CG):15	Kinesio taping group: age (years) 41 (33–46), gender (f/m): 9/6, EDSS score: 3 (2.5–3.5), disease duration (years): 8 (4–11) Control Group: age (years) 35 (31–48), gender (f/m): 11/4, EDSS score 2.5 (2–3.5), disease duration (years): 6 (4–9)	Duration: 8 weeks / Frequency: two session Kinesio taping group: 60 min Core stability-based balance training+ Kinesio Taping + 60 min home exercises Control group: 60 min core stability-based balance training+ 60 min home exercises	At baseline and 8th week / 2	After 8 weeks, balance, trunk control, and walking capacity increased in both groups.
Doğan, 2023	RCT Single blind	TIS ICARS	Virtual reality-supported task-oriented circuit training group (V-TOCT): 17 Mobil application-based telerehabilitation group (TR):15	V-TOCT: age (years) 38.76±5.53, gender (f/m): 13/2, EDSS score: 3.94±1.04, disease duration (years): unclear TR: age (years) 36±8.19, gender (f/m): 15/2, EDSS score 3.74±0.92, disease duration (years): unclear	Duration: 8 weeks/ Frequency: three session V-TOCT: 60 min virtual reality-supported task-oriented circuit training TR: 60 min mobile application-based telerehabilitation	At baseline and 8th week/ 2	The results of the study showed that V-TOCT and TR improved dynamic balance.
Salcı, 2017	RCT Unclear	BSS ICARUS FRT 2MWT Posturography	Balance Training Group (BT):14 Lumbar Stabilization Group (LS): 14 Task-Oriented Training Group (TT):14	BT: age (years) 35.36 ± 8.14, gender (f/m): 6/8, EDSS score: 3.5 (3–4), disease duration (years): 6,18 ± 4,08 LS: age (years) 37.29 ± 9.75, gender (f/m): 9/5, EDSS score 3.5 (3–4), disease duration (years): 8.54 ± 8.44 TT: age (years) 34.36±7.90, gender (f/m): 10/4, EDSS score 3.5 (3.5–4), disease duration (years): 5.82 ± 4.50	Duration: 8 weeks/ Frequency: unclear BT: 45 min balance training LS: 45 min balance training+ lumbar stabilization exercises TT: 45 min balance training + task-oriented training	At baseline and 8th week/ unclear	LS produced better improvements in postural control and gait performance than BT alone. TT provided better postural control improvements than BT alone. The balance results of LS and TT were similar.
Kırmacı, 2021	RCT Single blind	6MWT	Excentric exercise training group:10 Concentric exercise training group:10	Eccentric exercise training group: age (years) 34.8±8.02, gender (f/m): unclear, EDSS score: 1.60±0.84, disease duration (years): 6.7±6.42 Concentric exercise training group: age (years) 37.80±7.06, gender (f/m): unclear, EDSS score 1.65±0.57, disease duration (years): 5.2±3.96	Duration: 8 weeks/ Frequency: two sessions Eccentric exercise training group: 5 min warm-up + 20 min eccentric exercise training + 5 min cooldown Concentric exercise training group: 5 min warm-up + 20 min concentric exercise training + 5 min cool down	At baseline and 8th week / no losses	Walking distance improved significantly in both groups. There is no significant difference between the groups.

Table 2. Characteristics and Main Findings of The Studies Included in The Systematic Review (continued)

Özsoy Ünübol, 2022	RCT Single blind	BBS 6MWT	Robot-assisted gait training Group (RAGT):18 Conventional gait training group (CGT):19	RAGT: age (years) 45.05 ± 9.22, gender (f/m): 11/7, EDSS score: 4.5 (5.5–7), disease duration (years): 14.11 ± 5.94 CGT: age (years) 44.73 ± 8.43, gender (f/m): 13/6, EDSS score 4.75 (5.5–7), disease duration (years): 13.47 ± 6.21	Duration: 4 weeks / Frequency: three sessions RAGT: 60 min inpatient rehabilitation program + 30 min robot-assisted gait training CGT: 60 min inpatient rehabilitation program + 30 min conventional walking training.	At baseline and 8th week/ unclear	In general, both groups showed significant improvements in balance and gait scores. However, no superior effect of RAGT on walking endurance was found.
Özkul, 2018	RCT Single blind	Posturography 6MWT	Combined exercise group (MS-EX): 18 Control Group (MS-C): 18 Healthy Group (HC): 18	MS-EX: age (years) 34.5 (26-43.25), gender (f/m): 14/4, EDSS score: 1 (0.87-2.12), disease duration (years): 4 (2.75-11.25) MS-C: age (years) 34 (32-43.75, gender (f/m): 14/4, EDSS score 1 (1-2), disease duration (years): 4(2-7) HG: age (years) 33 (26.75-43.25), gender (f/m): 14/4, EDSS score not available, disease duration (years): not available	Duration: 8 weeks/ Frequency: three session MS-EX: 5 min warm up + 20 min aerobic training + 5 min cool down+ 15 min rest+ 5 min warm up+ 50 min Pilates training+ 5 min cool down MS-C: 60 min relaxation exercise HC: No intervention	At baseline and 8th week/ 5	MS-EX was significantly improved in terms of gait and balance. No significant change was observed in MS-C.
Aydın, 2014	RCT Unclear	10MWT BBS	Hospital-based exercise group: 16 Home-based exercise group: 20	Hospital-based exercise group: age (years) 32.62 ± 3.15, gender (f/m): 9/7, EDSS score: 3.6 ± 1.3, disease duration (years): 6.43 ± 2.78. Home-based exercise group: age (years) 33.00 ± 4.06, gender (f/m): 11/9, EDSS score 3.4 ± 2.1, Disease duration (years): 7.40 ± 3.43	Duration: 12 weeks/ Frequency: five session Hospital-based exercise group: 15 min warm up + 20 min calisthenic exercises (3 days a week) + 10 min cool down+ 15 min rest+ 20 min relaxation exercises (twice a week) Home-based exercise group: 15 min warm up + 20 min calisthenic exercises (3 days a week) + 10 min cool down+ 15 min rest+ 20 min relaxation exercises (twice a week)	At baseline and 12th week/ no losses	Balance and walking results showed significant improvement in both groups. Although there was no significant difference between the groups, balance measurements were higher in the hospital group.
Tarakçı, 2021	RCT Single blind	FIM NHP-I	Structured supervised exercise group (Group 1): 15 Telerehabilitation group (Group 2): 15	Group 1: age (years) 41± 11.09, gender (f/m): 12/3, EDSS score: 3.40 ± 1.53, disease duration (years): 6.20 ± 3.96 Group 2: age (years) 39.46 ± 10.59, gender (f/m): 11/4, EDSS score 3.46 ± 1.31, disease duration (years): 8.86 ± 4.50	Duration: 12 weeks /Frequency: three session Group 1: 10 min warm up + 40 min structured exercise program + 5 min cool down Group 2: 10 min warm up + 40 min home-based exercise program + 5 min cool down	At baseline and 12th week/ 5	A structured home-based exercise program can be an alternative to supervised exercises with no side effects in patients with multiple sclerosis.

Table 2. Characteristics and Main Findings of The Studies Included in The Systematic Review (continued)

Küçük, 2016	RÇT, Single blind	BBS TUG TIS	Pilates group: 11 Control group: 9	Pilates group: age (years) 47.2±9.5, gender (f/m): 7/4, EDSS score: 3.2 ± 2.2, disease duration (years): 14.8 ± 7.4. Control group: age (years) 49.7 ± 8.9, gender (f/m): 6/3, EDSS score 2.8 ± 1.4, disease duration (years): 14.2 ± 9.5	Duration: 8 weeks/ Frequency: two session Pilates group: 10 min warm-up + 25-45 min clinical pilates Control group: 10 min warm-up + 25-45 min traditional exercise program	At baseline and 8th week/ 8	Due to its positive effects on balance, Clinical Pilates can be used as an effective treatment for MS.
Eldemir, 2023	RCT Single blind	BBS 6MWT Posturography G-Walk Sensor System	Pilates-based telerehabilitation group (Pilates-TR): 15 Control group (CG): 15	Pilates-TR: age (years) 41±7.82, gender (f/m): 14/1, EDSS score: 1.5 (1–2.5), disease duration (years): 10 (6–13). CG: age (years) 38.4±10.86, gender (f/m): 14/1, EDSS score 1.5 (1–3), disease duration (years): 8 (6–13).	Duration: 6 weeks/ Frequency: three session Pilates-TR Group: 5 min warm up+ 50 min Pilates-based telerehabilitation + 5 cool down Control Group: No intervention	At baseline and 6th week/ unclear	Functional balance and walking speed improved significantly in the Pilates-TR group compared to the control group.
Tomruk, 2016	RCT Single blind	Posturography	MS patients:11 Healthy controls:12	MS patients: age (years) 52 (35–66), gender (f/m): 7/4, EDSS score: 3.5 (2.0–5.0), disease duration (years): unclear. Healthy controls: age (years) 50 (38–65), gender (f/m): 7/5, EDSS score not available, disease duration (years): Not available	Duration: 10 weeks/ Frequency: two session MS patients: 60 min modified clinical pilates training Healthy controls: no intervention	At baseline and 10th week/ unclear	Pilates training alone is not effective in improving balance.

EDSS: Expanded Disability Status Scale; TUG: Timed Up and Go Test; BBS: Berg Balance Scale, FRT: Functional Reach Test; 6MWT: The Six-Minute Walk Test; T25FW: Timed 25-Foot Walk; MSWS-12: Multiple Sclerosis Walking Scale-12; ABC: Activities-Specific Balance Confidence; DGI: Dynamic Gait Index; 2MWT: 2-Minute Walk Test; SLST: Single Leg Stance Test; FGA: The Functional Gait Assessment; K- ICARS: The International Cooperative Ataxia Rating Scale; NHP-I: First Section of Nottingham Health Profile; Mini BESTest: Balance Evaluation Systems Test; TIS: The Trunk Impairment Scale; GAITRite: Electronic walkway system.

The assessment of methodological quality using the JBI Critical Appraisal Checklist showed that three of the studies were found to have " good quality" and twenty-four had " moderate quality" (Table 3). The JBI quality scores of the included studies ranged from 70 to 85 points, with a mean score of 75. Three studies were evaluated as "good quality" (Doğan et al., 2023; Kahraman et al., 2020; Özkul et al., 2020b).

The study evidence included in this review was highly heterogeneous, particularly in terms of intervention characteristics and the various outcome measures used. In all twenty-seven studies, the assignment of participants to intervention groups and blinding of intervention implementers were not specified. In addition, most did not report information on the confidentiality of participants' assignment to intervention groups. Several trials were underpowered with small sample sizes.

Table 3. Results of Quality Assessment

	JBI Critical Appraisal Checklist for Randomised Controlled Trials Questions													
Studies	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**	**S11**	**S12**	**S13**	**Quality Score (%)**
Özkul, 2020a	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Gürpınar, 2020	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Salbaş, 2022	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Abasıyanık, 2020	Y	U	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	70
Özdoğar, 2020	Y	U	Y	U	U	N	Y	Y	Y	Y	Y	Y	Y	70
Özkul, 2020b	Y	Y	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	85
Kahraman, 2020	Y	Y	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	85
Ayvat, 2021	Y	Y	Y	U	U	Y	Y	U	Y	Y	Y	Y	Y	77
Özkan, 2022	Y	Y	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	77
Güngör, 2022	Y	U	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	70
Özkul, 2023	Y	U	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	70
Bilek, 2023	Y	U	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	70
Yazgan, 2020	Y	U	Y	U	U	N	Y	Y	Y	Y	Y	Y	Y	70
Tarakçı, 2013	Y	U	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	70
Özkul, 2020c	Y	U	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	70
Bulguroğlu, 2017	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Yaşa, 2022	Y	U	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	70
Doğan, 2023	Y	Y	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	85
Salcı, 2017	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Kırmacı, 2021	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
ÖzsoyÜnübol, 2022	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Özkul, 2018	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Aydın, 2014	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Tarakçı, 2021	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Küçük, 2016	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Eldemir, 2023	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77
Tomruk, 2016	Y	U	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	77

Y: yes, N: no, U: uncertain

DISCUSSION

This systematic review aimed to determine the current status of therapeutic interventions used to improve balance and gait in individuals with multiple sclerosis by reviewing studies conducted in Turkey. We identified 27 studies of moderate to good methodological quality that tested different interventions for MS patients with an EDSS score between 0 and 7.

Twenty one trials (Abasıyanık et al., 2020; Aydın et al., 2014; Bilek et al., 2023; Bulguroğlu et al., 2017; Doğan et al., 2023; Eldemir et al., 2023; Güngör et al., 2022; Gürpınar et al., 2020; Kahraman et al., 2020; Kırmacı et al., 2021; Küçük et al., 2016; Özdoğar et al., 2020; Özkan et al., 2022; Özkul et al., 2018, 2020b, 2020c; Salbaş et al., 2022; Salcı et al., 2017; Tarakçı et al., 2013; Yaşa et al., 2022; Yazgan

et al., 2020) reported improved effects on gait and recovery outcomes in MS, while 6 trials (Ayvat et al., 2021; Özkul et al., 2020a, 2023; Özsoy- Ünübol et al., 2022; Tarakçı et al., 2021; Tomruk et al., 2026) reported no significant superiority in balance and gait outcomes.

Overall, evidence suggests that exercise interventions are generally effective for people with MS (Pilutti et al., 2014). In the literature, specific walking, balance, and functional exercises have been identified as the only balance intervention by The Prevention of Falls Network Europe group (Sherrington et al., 2019) and have shown a moderate effect on balance outcomes in PwMS (Gunn et al., 2015). A meta-analysis of data from 13 studies showed significant improvements in balance and walking speed in PwMS who exercised (Pearson et al., 2015). In contrast, another meta-analysis found low evidence for the effectiveness of specific balance exercises, resistance, and aerobic exercises in improving balance among people with multiple sclerosis (Paltamaa et al., 2012). Again, according to the literature, the results of vibration training show that, unlike our study, it has the potential to increase walking endurance in MS patients with low disability status (Kantele et al., 2015).

Although some aspects of improvements in balance and gait were found in this review, the limited number of studies and heterogeneous outcome measures make it difficult to provide conclusive evidence. Clinicians, researchers, and participants need to have studies with larger sample sizes, longer follow-up periods, and appropriate intervention protocols (dose/intensity) to determine the effect of interventions. In this study, different intervention protocols and outcomes made it difficult to compare the findings. Furthermore, many studies in the reviewed reviews had a small sample size. Lack of information about blinding procedures or blinding of staff among participants and missing outcome data made it difficult to make informed judgments about the fidelity of the authors' conclusions.

CONCLUSION

This review shows that therapeutic interventions improve balance and walking outcomes for people with MS. Although the interventions under review showed superiority in certain outcomes in terms of balance and gait, it should be noted that the effect size of these interventions on recovery outcomes may not be sufficient. However, the evidence for many rehabilitation interventions needs to be interpreted with caution as the majority of included studies found only moderate-quality evidence. The evidence showed that although a wide range of therapeutic interventions for balance and walking in people with MS are available, high-quality evidence demonstrating the effectiveness of various modalities is severely lacking. In addition, the gaps in interventions and reporting identified in this study may guide future studies.

ETHICAL COMMITTEE APPROVAL

The studies that were open to access were included in the research. In this direction, the articles that were allowed to be accessed in the database were examined.

AUTHOR'S CONTRIBUTION

Idea/concept: MKT, İT, GYY; Design: MKT, İT, GYY; Consultancy: İT; Data collection: MKT, GYY; Data Processing: MKT, GYY; Analysis and/or Interpretation: MKT, İT, GYY; Literature review: MKT, GYY; Writing of the article: MKT, İT, GYY; Critical review: İT, MKT, GYY

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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REFERENCES

Abasıyanık, Z., Ertekin, Ö., Kahraman, T., Yiğit, P., & Özakbaş, S. (2020). The effects of clinical pilates training on walking, balance, fall risk, respiratory, and cognitive functions in persons with multiple sclerosis: A randomized controlled trial. *Explore*, *16*(1), 12–20. https://doi.org/10.1016/j.explore.2019.07.010

Arık, M. I., Kiloatar, H., & Saraçoğlu, I. (2022). Do Pilates exercises improve balance in patients with multiple sclerosis? A systematic review and meta-analysis. *Multiple Sclerosis and Related Disorders, 57*(1), 103410. https://doi.org/10.1016/j.msard.2021.103410

Aydın, T., Akif Sarıyıldız, M., Güler, M., Çelebi, A., Seyithanoğlu, H., Mirzayev, I., Peru, C., Sezer, E., & Batmaz, I. (2014). Evaluation of the effectiveness of home based or hospital based calisthenic exercises in patients with multiple sclerosis. *European Review for Medical and Pharmacological Sciences*, *18*(8), 1189–1198

Ayvat, F., Özçakar, L., Ayvat, E., Aksu Yıldırım, S., & Kılınç, M. (2021). Effects of low vs. high frequency local vibration on mild-moderate muscle spasticity: Ultrasonographical and functional evaluation in patients with multiple sclerosis. *Multiple Sclerosis and Related Disorders*, *51*(6*)*, 102930. https://doi.org/10.1016/j.msard.2021.102930

Barker, T. H., Stone, J. C., Sears, K., Klugar, M., Tufanaru, C., Leonardi-Bee, J., Aromataris, E., & Munn, Z. (2023). The revised JBI critical appraisal tool for the assessment of risk of bias for randomized controlled trials. *JBI Evidence Synthesis*, *21*(3), 494–506. https://doi.org/10.11124/JBIES-22-00430

Bilek, F., Bahçecioğlu-Turan, G., & Özer, Z. (2023). The effect of self-acupressure on quality of life, physical and cognitive function in relapsing remitting multiple sclerosis patients: A randomized controlled study. *Explore*, *19*(1), 84–90. https://doi.org/10.1016/j.explore.2022.03.002

Bulguroğlu, I., Güçlü-Gündüz, A., Yazıcı, G., Özkul, C., İrkeç, C., Nazlıel, B., & Batur-Çaglayan, H. Z. (2017). The effects of mat pilates and reformer pilates in patients with multiple sclerosis: A randomized controlled study. *NeuroRehabilitation*, *41*(2), 413–422. https://doi.org/10.3233/NRE-162121

Cameron, M. H., & Nilsagard, Y. (2018). Balance, gait, and falls in multiple sclerosis. *Handbook of Clinical Neurology*, *159*, 237–250. https://doi.org/10.1016/B978-0-444-63916-5.00015-X

Cattaneo, D., Marazzini, F., Crippa, A., & Cardini, R. (2002). Do static or dynamic AFOs improve balance? *Clinical Rehabilitation*, *16*(8), 894-899.

Centonze, D., Leocani, L., & Feys, P. (2020). Advances in physical rehabilitation of multiple sclerosis. *Current Opinion in Neurology*, *33*(3), 255–261. https://doi.org/10.1097/WCO.0000000000000816

Chee, J. N., Ye, B., Gregor, S., Berbrayer, D., Mihailidis, A., & Patterson, K. K. (2021). Influence of multiple sclerosis on spatiotemporal gait parameters: A systematic review and meta-regression. *Archives Of Physical Medicine and Rehabilitation*, *102*(9), 1801–1815. https://doi.org/10.1016/j.apmr.2020.12.013

Dijkers, M. P., Hart, T., Tsaousides, T., Whyte, J., & Zanca, J. M. (2014). Treatment taxonomy for rehabilitation: past, present, and prospects. *Archives of Physical Medicine and Rehabilitation*, *95*(1 Suppl), S6–S16. https://doi.org/10.1016/j.apmr.2013.03.032

Doğan, M., Ayvat, E., & Kılınç, M. (2023). Telerehabilitation versus virtual reality supported task-oriented circuit therapy on upper limbs and trunk functions in patients with multiple sclerosis: A randomized controlled study. *Multiple Sclerosis and Related Disorders*, *71*(2), 104558. https://doi.org/10.1016/j.msard.2023.104558

Eldemir, K., Güçlü-Gündüz, A., Eldemir, S., Saygılı, F., Özkul, C., & İrkeç, C. (2023). Effects of pilates-based telerehabilitation on physical performance and quality of life in patients with multiple sclerosis. *Disability and Rehabilitation, 45*(1), 1–8. https://doi.org/10.1080/09638288.2023.2205174

Glinsky, J., Harvey, L., & Van Es, P. (2007). Efficacy of electrical stimulation to increase muscle strength in people with neurological conditions: A systematic review. *Physiotherapy Research International, 12*(3), 175–194. https://doi.org/10.1002/pri.375

Gunn, H., Markevics, S., Haas, B., Marsden, J., & Freeman, J. (2015). Systematic review: the effectiveness of ınterventions to reduce falls and ımprove balance in adults with multiple sclerosis. *Archives of Physical Medicine and Rehabilitation*, *96*(10), 1898–1912. https://doi.org/10.1016/j.apmr.2015.05.018

Gürpınar, B., Kara, B., & İdiman, E. (2020). Effects of aquatic exercises on postural control and hand function in multiple sclerosis: Halliwick versus aquatic plyometric exercises: A randomised trial. *Journal of Musculoskeletal and Neuronal İnteractions*, *20*(2), 249–255.

Güngör, F., Tarakcı, E., Özdemir-Acar, Z., & Soysal, A. (2022). The effects of supervised versus home pilates-based core stability training on lower extremity muscle strength and postural sway in people with multiple sclerosis. *Multiple Sclerosis (Houndmills, Basingstoke, England) Journal*, *28*(2), 269–279. https://doi.org/10.1177/13524585211012202

Haselkorn, J. K., Hughes, C., Rae-Grant, A., Henson, L. J., Bever, C. T., Lo, A. C., Brown, T. R., Kraft, G. H., Getchius, T., Gronseth, G., Armstrong, M. J., & Narayanaswami, P. (2015). Summary of comprehensive systematic review: Rehabilitation in multiple sclerosis: Report of the guideline development, dissemination, and ımplementation subcommittee of the American Academy of Neurology. *Neurology, 85*(21), 1896–1903. https://doi.org/10.1212/WNL.0000000000002146

Kahraman, T., Savcı, S., Özdoğar, A. T., Gedik, Z., & İdiman, E. (2020). Physical, cognitive and psychosocial effects of telerehabilitation-based motor imagery training in people with multiple sclerosis: A randomized controlled pilot trial. *Journal of Telemedicine and Telecare*, *26*(5), 251–260. https://doi.org/10.1177/1357633X18822355

Kantele, S., Karinkanta, S., & Sievänen, H. (2015). Effects of long-term whole-body vibration training on mobility in patients with multiple sclerosis: A meta-analysis of randomized controlled trials. *Journal of The Neurological Sciences*, *358*(1-2), 31–37. https://doi.org/10.1016/j.jns.2015.09.357

Kırmacı, Z. İ., Fırat, T., Sağlam, M., Neyal, A., Neyal A. M., & Ergun, N.(2021). A comparison of the effects of eccentric and concentric exercise training on hemodynamic response, functional capacity, and fatigue in patients with multiple sclerosis. *Turkish Journal of Physiotherapy and Rehabilitation*, *32*(1), 10-19.

Khan, F., Amatya, B., Galea, M. P., Gonzenbach, R., & Kesselring, J. (2017). Neurorehabilitation: applied neuroplasticity. *Journal of Neurology, 264*, 603-615.

Küçük, F., Kara, B., Poyraz, E. Ç., & İdiman, E. (2016). Improvements in cognition, quality of life, and physical performance with clinical pilates in multiple sclerosis: A randomized controlled trial. *Journal of Physical Therapy Science*, *28*(3), 761-768.

Motl, R. W., Mowry, E. M., Ehde, D. M., LaRocca, N. G., Smith, K. E., Costello, K., Shinto, L., Ng, A. V., Sullivan, A. B., Giesser, B., McCully, K. K., Fernhall, B., Bishop, M., Plow, M., Casaccia, P., & Chiaravalloti, N. D. (2018). Wellness and multiple sclerosis: The National MS Society establishes a Wellness Research Working Group and research priorities. *Multiple Sclerosis (Houndmills, Basingstoke, England), 24*(3), 262–267. https://doi.org/10.1177/1352458516687404

Özdoğar, A. T., Ertekin, O., Kahraman, T., Yiğit, P., & Özakbaş, S. (2020). Effect of video-based exergaming on arm and cognitive function in persons with multiple sclerosis: A randomized controlled trial. *Multiple Sclerosis and Related Disorders*, *40*(1), 101966. https://doi.org/10.1016/j.msard.2020.101966

Özkul, C., Eldemir, K., Apaydın, Y., Gülşen, C., İrkeç, C., & Güçlü-Gündüz, A. (2023). Effects of multi-task training on motor and cognitive performances in multiple sclerosis patients without clinical disability: A single-blinded randomized controlled trial. *Acta Neurologica Belgica*, *123*(4), 1301–1312. https://doi.org/10.1007/s13760-023-02172-7.

Özkul, C., Güçlü-Gündüz, A., Eldemir, K., Apaydın, Y., Gülşen, C., Yazıcı, G., Söke, F., & İrkeç, C. (2020c). Effect of task-oriented circuit training on motor and cognitive performance in patients with multiple sclerosis: A single-blinded randomized controlled trial. *NeuroRehabilitation*, *46*(3), 343–353. https://doi.org/10.3233/NRE-203029

Özkul, C., Güçlü-Gündüz, A., Eldemir, K., Apaydın, Y., Yazıcı, G., & İrkeç, C. (2020b). Combined exercise training improves cognitive functions in multiple sclerosis patients with cognitive impairment: A single-blinded randomized controlled trial. *Multiple Sclerosis and Related Disorders*, *45*(7), 102419. https://doi.org/10.1016/j.msard.2020.102419

Özkul, C., Güçlü-Gündüz, A., İrkeç, C., Fidan, I., Aydın, Y., Özkan, T., & Yazıcı, G. (2018). Effect of combined exercise training on serum brain-derived neurotrophic factor, suppressors of cytokine signaling 1 and 3 in patients with multiple sclerosis. *Journal of Neuroimmunology*, *316*(1), 121–129. https://doi.org/10.1016/j.jneuroim.2018.01.002

Özkul, C., Güçlü-Gündüz, A., Yazıcı G., Güzel, N. A., & İrkeç, C. (2020a). Effect of immersive virtual reality on balance, mobility, and fatigue in patients with multiple sclerosis: A single-blinded randomized controlled trial. *European Journal of Integrative Medicine*, *35*(3), 101092.

Özsoy-Ünübol, T., Ata, E., Cavlak, M., Demir, S., Candan, Z., & Yılmaz, F. (2022). Effects of robot-assisted gait training in patients with multiple sclerosis: A single-blinded randomized controlled study. *American Journal of Physical Medicine and Rehabilitation*, *101*(8), 768–774. https://doi.org/10.1097/PHM.0000000000001913

Özkan, T., & Ünlüer, N. Ö. (2022). Investigation of the effects of trunk stabilization training combined with aerobic training on balance, lower limb muscle strength, and core stability in patients with Multiple Sclerosis: a randomized controlled study. *Journal of Exercise Therapy and Rehabilitation*, *9*(1), 20-29.

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *British Medical Journal, 372*, 71. https://doi.org/10.1136/bmj.n71

Paltamaa, J., Sjögren, T., Peurala, S. H., & Heinonen, A. (2012). Effects of physiotherapy interventions on balance in multiple sclerosis: A systematic review and meta-analysis of randomized controlled trials. *Journal of Rehabilitation Medicine*, *44*(10), 811–823. https://doi.org/10.2340/16501977-1047

Pearson, M., Dieberg, G., & Smart, N. (2015). Exercise as a therapy for improvement of walking ability in adults with multiple sclerosis: A meta-analysis. *Archives of Physical Medicine and Rehabilitation, 96*(7), 1339–1348.e7. https://doi.org/10.1016/j.apmr.2015.02.011

Pilutti, L. A., Platta, M. E., Motl, R. W., & Latimer-Cheung, A. E. (2014). The safety of exercise training in multiple sclerosis: A systematic review. *Journal of The Neurological Sciences, 343*(1-2), 3–7. https://doi.org/10.1016/j.jns.2014.05.016

Rodríguez-Fuentes, G., Silveira-Pereira, L., Ferradáns-Rodríguez, P., & Campo-Prieto, P. (2022). Therapeutic effects of the pilates method in patients with multiple sclerosis: A systematic review. *Journal of Clinical Medicine*, *11*(3), 683. https://doi.org/10.3390/jcm11030683

Salbaş, E., & Karahan, A. Y. (2022). Effects of hippotherapy simulation exercise vs. conventional home exercises on muscle strength and balance in people with multiple sclerosis: A randomized controlled trial. *Multiple Sclerosis and Related Disorders*, *68*(12), 104111. https://doi.org/10.1016/j.msard.2022.104111

Salcı, Y., Fil, A., Armutlu, K., Yıldız, F. G., Kurne, A., Aksoy, S., Nurlu, G., & Karabudak, R. (2017). Effects of different exercise modalities on ataxia in multiple sclerosis patients: a randomized controlled

study. *Disability and Rehabilitation*, *39*(26), 2626–2632. https://doi.org/10.1080/09638288.2016.1236411

Sherrington, C., Fairhall, N. J., Wallbank, G. K., Tiedemann, A., Michaleff, Z. A., Howard, K., ... & Lamb, S. E. (2019). Exercise for preventing falls in older people living in the community. *Cochrane Database of Systematic Reviews*, *1*(1), CD012424. doi: 10.1002/14651858.CD012424.pub2.

Tomruk, M.S, Uz, M. Z., Kara, B., & İdiman, E. (2016). Effects of Pilates exercises on sensory interaction, postural control and fatigue in patients with multiple sclerosis. *Multiple Sclerosis and Related Disorders*, *7*(12), 70–73. https://doi.org/10.1016/j.msard.2016.03.008

Tarakçı, E., Tarakçı, D., Hajebrahimi, F., & Budak, M. (2021). Supervised exercises versus telerehabilitation: Benefits for persons with multiple sclerosis. *Acta Neurologica Scandinavica*, *144*(3), 303–311. https://doi.org/10.1111/ane.13448

Tarakçı, E., Yeldan, I., Hüseyinsinoğlu, B. E., Zenginler, Y., & Eraksoy, M. (2013). Group exercise training for balance, functional status, spasticity, fatigue and quality of life in multiple sclerosis: A randomized controlled trial. *Clinical Rehabilitation*, *27*(9), 813–822. https://doi.org/10.1177/0269215513481047

Walton, C., King, R., Rechtman, L., Kaye, W., Leray, E., Marrie, R. A., Robertson, N., La Rocca, N., Uitdehaag, B., Vander Mei, I., Wallin, M., Helme, A., Angood Napier, C., Rijke, N., & Baneke, P. (2020). Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. *Multiple Sclerosis (Houndmills, Basingstoke, England) Journal*, *26*(14), 1816–1821. https://doi.org/10.1177/1352458520970841

Yaşa, M. E., Özkan, T., Ünlüer, N. Ö., Çelenay, Ş. T., & Anlar, Ö. (2022). Core stability-based balance training and kinesio taping for balance, trunk control, fear of falling and walking capacity in patients with multiple sclerosis: A randomized single-blinded study. *Multiple Sclerosis and Related Disorders*, *68*(12), 104178. https://doi.org/10.1016/j.msard.2022.104178

Yazgan, Y. Z., Tarakçı, E., Tarakçı, D., Özdinçler, A. R., & Kürtüncü, M. (2020). Comparison of the effects of two different exergaming systems on balance, functionality, fatigue, and quality of life in people with multiple sclerosis: A randomized controlled trial. *Multiple Sclerosis and Related Disorders*, *39*(4), 101902. https://doi.org/10.1016/j.msard.2019.101902

Yeni, K., Tülek, Z., & Terzi, M. (2022). Effect of self-acupressure on fatigue in patients with multiple sclerosis. *Complementary Therapies in Clinical Practice, 47*(5), 101572. https://doi.org/10.1016/j.ctcp.2022.101572

Zurawski, J., & Stankiewicz, J. (2018). Multiple sclerosis re-examined: Essential and emerging clinical concepts. *The American Journal of Medicine*, *131*(5), 464–472. https://doi.org/10.1016/j.amjmed.2017.11.044