Abstract

Objective: The aim of this paper is to review literature systematically and quantify the effects of leg spasticity on gait parameters in PwMS.

Methods and Materials: This study is a systematic review and meta-analysis of observational studies. Articles were included if they met the following inclusion criteria: They were original, observational studies, participants were PwMS, study the effects of leg spasticity on gait in MS patients compared with MS patients without spasticity. The included articles were assessed by modified Downs and Black checklist. The difference between the groups using standardized mean differences and 95% confidence intervals were calculated for meta-analyses.

Results: The review included 3 studies with a total of 156 participants; 78 participants were with spasticity, and 78 without spasticity. The lower limb spasticity was detected by modified Ashworth scale self-rating spasticity. The gait was assessed by clinical scales, spatial and temporal gait analyses, free-living walking for a 7 days, O2 consumption during gait, kinematic parameters within the gait, and lower limb muscles range of motion and activity. The included studies and meta-analyses show that the spasticity affected negatively gait with significant differences in comparison with non-spasticity PwMS.

Conclusion: Spasticity affects negatively on gait and walking mobility. Those walking impairments lead to increase level of disability, and risk of fall. Gait training is required in MS rehabilitation protocols especially for PwMS with spasticity.

Keywords: Multiple Sclerosis, Spasticity, Gait, Walking
INTRODUCTION

Multiple Sclerosis (MS), a chronic autoimmune demyelinating central nervous system disease, is the leading cause of disability in young adults \(^1\). MS symptoms include accumulations of irreversible neurological deficits, and is characterized by visual, brainstem, cerebellar, cognitive, motor and sensory symptoms \(^2\). Spasticity is a significant problem for 60%-80% of patients with MS (pwMS) \(^3\). The spasticity was defined by Lance in 1980 \(^4\) as "Spasticity is a motor disorder characterized by a velocity-dependent increase in muscle tone with exaggerated tendon jerks, resulting from hyper-excitability of the stretch reflex as one component of the upper motor neuron syndrome". Regarding to the lance definition, the spasticity is considered as positive upper motor neuron sign since it represents excessive muscle tone and stretch reflex. Furthermore, spasticity represents as clonus and spasms \(^5\). Gait is perceived as the most important bodily function across the MS \([6]\). Gait parameters are used as indicators of ambulatory ability and consequence of MS progression\(^7\). Furthermore, gait need to be identified and managed early in the course of MS \(^8\). Lower limb spasticity has negative impacts on postural control and gait in MS patients \(^9\).

Therefore, the aim of this study is to review systematically and quantify the effects of leg spasticity on gait parameters in PwMS. The determining precisely of the gait disorders will help us in order to conclude better protocols to rehab PwMS.

Method and Materials

Study design

This study design is a systematic review and meta-analysis of observational studies. The recommendations of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group \(^10\).

Eligibility criteria and search procedure.

The eligibility criteria were assessed by an author (E.M). Articles were included if they met the following inclusion criteria: (1) they were original, observational studies; (2) participants were PwMS, (3) study the effects of leg spasticity on gait in MS patients compared with MS patients without spasticity. The following databases were searched from date of inception to August 2017: MEDLINE, EMBASE, CINHAL, and Scopus. A combination of the following keywords and MeSH headings were utilized as search terms: (multiple sclerosis OR MS) AND (Spasticity OR Hyperton* OR Clonus OR Spasm OR Excitability*).
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Table 1. Demographic data, sample details, course of MS, and methodological quality of included articles.

| Study          | Sample details | Disability level measured with EDSS | Course of MS | Methodological Quality |
|----------------|----------------|-------------------------------------|--------------|------------------------|
| Balantrapu 2014 [13] | N=84 44 with spasticity, 40 without spasticity | 2-6.5 with average of 4.81 for all sample 2-6.5 with average of 3.5 for participants without spasticity 2.5-6.5 with average of 6 in participants with spasticity | RRMS PMS | 14/16 |
| Pau 2015 [14]     | N=38 19 with spasticity, 19 without spasticity | 2.5-6.5 with average of 3.8 for all sample 2.5-4.5 with average of 3.4 for participants without spasticity 3.5-6.5 with average of 4.4 in participants with spasticity | RRMS PMS | 14/16 |
| Sosnoff 2011 [15] | N=34 15 with spasticity, 17 without spasticity | 3.5-6.5 with median of 6 for all sample 3.5-6.5 with median of 4 for participants without spasticity 3.5-6.5 with median of 6 in participants with spasticity | RRMS PMS | 14/16 |

OR Hyperexcitability OR Stretch reflex) AND (Gait or Walking or Ambulation*).

Studies Selection and data extraction
Studies selection was performed independently in un-blinded standardized manner by the authors on the base of title and abstract. Full-text articles were then read. The extracted were the following data: study design, sample size, MS course, level of disability, spasticity outcomes, gait outcomes and their values.

Quality of the articles
The included articles were assessed by modified Downs and Black checklist for observational studies. It consists of 17 items assess reporting, external validity, internal validity and power of the studies. The checklist criteria is as follow: (1) Clarity of the hypothesis, (2) Descriptions of outcomes, (3) Characteristics of participants, (4) Baseline comparability, (5) Clarity of the main finding, (6) Estimate of the random variability, (7) Actual probability for the main outcomes, (8) Origin of the participants,
(9) between-group comparison, (10) Blinding of the outcome assessors, (11) Data degrading, (12) Statistical tests for the difference, (13) Validity and reliability of outcomes, (14) study groups are from same population, (15) study

Table 2. Spasticity level and outcomes, gait parameters, and main results of the included articles.

| Study            | Spasticity level in spasticity groups | Gait parameters                                      | Main results                                                                                                                                 |
|------------------|--------------------------------------|------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| Balantrapu 2014[13] | 1.8-2 on Modified Ashworth scale in hip flexor, knee extensor, and ankle dorsiflexion | - 6 Minutes- walk test  
- Timed 25 foot walk test  
- Timed-up and go test  
- O2 consumption  
- Spatial and temporal gait analysis  
- Multiple sclerosis walk test  
- Accelerometer for live walking for 7 days  | -6 Minutes-walk test  
Timed 25 foot walk test  
Timed-up and go test  
O2 consumption, Multiple sclerosis walk test, and free-living walking were significantly worse in spasticity group.  
- Spatial and temporal gait analysis showed that the velocity and cadence were worse significantly in spasticity group. No significant difference between groups in base of support, or single or double support time.  |
| Pau 2015 [14]    | 7.7 on Numerical rating scale ranged from 0 to 10 for assessing self-perceived spasticity | - Spatial and temporal gait analysis  
- Kinematic parameters within the gait cycle represented with pelvic tilt, rotation, obliquity, hip flexion-extension, adduction-abduction and rotation, knee flexion-extension, ankle dorsiflexion and foot progression.  
- Range of motion for hip and knee flexion-extension and ankle dorsiplantarflexion.  
- EMG for muscular activity for rectus femoris, Tibialis anterior, and Gastocnemius lateralis.  | - Kinematic parameters within the gait cycle represented with pelvic tilt, rotation, obliquity, hip flexion-extension, adduction-abduction and rotation, knee flexion-extension, ankle dorsiflexion and foot progression were significantly worse in spasticity group. No significant difference between groups in hip rotation.  
- Spatial and temporal gait analysis showed that the stride length, cadence, swing phase, double support time were significantly worse in spasticity group. No significant difference between group in step width, and stance phase.  
- Range of motion for hip and knee flexion-extension were lesser significantly in spasticity group, while no significant difference between groups in ankle d ankle dorsiplantarflexion.  
- Muscular activation showed higher significant value for Rectus femoris muscle but not Tibialis anterior or Gastocnemius lateralis.  |
| Sosnoff 2011 [15] | 1-3 on Modified Ashworth scale for leg muscles | - 6 Minutes- walk test  
- Timed 25 foot walk test  
- Timed-up and go test  
- Multiple sclerosis walk test  | All outcomes were significantly worse in spasticity group.  |
groups were recruiting at the same time, (16) Adequate adjustment for confounding, (17) Statistical power sample size. The item 14 was not assessed due to the nature of the included studies.

**Statistical analysis**

Meta-analyses were conducted using the comprehensive meta-analysis version 3.3.070 software package (Biostat, New Jersy, USA)) to determine the differences between individuals with spasticity and without spasticity. For continuous variables, the difference between the groups using standardized mean differences (SMD) and 95% confidence intervals were calculated. The level of significant was set at $p \leq .05$

**Results**

**Study Selection and Studies Characteristics**

The included studies are 3 studies [13-15]. They enrolled a total of 156 participants, 78 participants were with spasticity, and 78 without spasticity. The included participants were in relapsing remitting and progressive MS courses. The Expanded disability status scale was used to determine the level of disability. The level of disability ranged from 2 to 6.5. All included participants were ambulatory with or without assistive device. The level of disability was significantly higher in participants with spasticity than participants without spasticity in the included articles.

**Methodological quality**

All 3 studies reported all required items on modified Downs and Black checklist except 2 items. The missing items were that study groups were recruiting at the same time, and statistical power sample size.

**Spasticity and gait parameters:**

The lower limb spasticity was detected by modified Ashworth scale in 2 studies and by self-rating spasticity in one study. The included studies used following clinical scales to assess the gait: 6 Minutes-walk test, timed 25 foot walk test, timed-up and go test, O2 consumption, and multiple sclerosis walk test. Kinematic parameters within the gait cycle represented with pelvic tilt, rotation, obliquity, hip flexion-extension, adduction-abduction and rotation, knee flexion-extension, ankle dorsiflexion and foot progression were used. The spatial and temporal analyses items were as velocity, cadence, and base of support, step time, step width, stride length, stance phase, swing phase, and single and double support time of the gait cycle. The participants in one study wore an accelerometer over a seven days period to assess free-living walking. Finally, one study has assessed the lower limb muscles activity.

**Effect of spasticity on gait parameters**

Table 2 summarizes the effect of spasticity on the used gait parameters for each included
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study. Clinical scales represented with six scales, Figure 1. All used Spatial and temporal gait analysis showed that the velocity and cadence were worse significantly in spasticity group except base of support, single limb support, step width, and stance phase.

Figure 1. Forest plot of the effect of spasticity on gait clinical scales. 6MWT; six minutes-walk test, MSW-12; multiple sclerosis walking test-12, T25FW; timed 25 foot walk, TUG; timed up-and go test

Figure 2. Forest plot of the effect of spasticity on spatial and temporal gait parameters.

Figure 2 showed that the spasticity worse significantly in spasticity group, while no significantly spatial and temporal gait parameters. Range of motion for hip and ankle dorsi-planterflexion. Muscular knee flexion-extension were lesser activation showed higher significant value for
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Rectus femoris muscle but not Tibialis anterior or Gastocnemius lateralis.

Discussion

The aim of this review was to clarify the effects of lower limb spasticity on gait in PwMS. The review included the articles that study the effect of lower limb spasticity on gait in comparison with PwMS without spasticity. The search strategy found 3 studies. The results of the included articles and the meta-analysis found that the spasticity worsen markedly the most of used kinematic, dynamic, and clinical outcomes of the gait. The lower limb muscles range of motion, and activation were worse in spasticity group’s especially hip flexion-extension range of motion and rectus femoris activation. To the best of our knowledge, the current review is the first review studies the gait disorders according to the spasticity.

Previous review found that the PwMS reported significant impairments in gait compared with healthy people regardless the spasticity.

The review results are not in consistence with other report in other neurological disorders, which have shown no association between spasticity and mobility impairments in persons with stroke and cerebral palsy. This consistency may be due to that the spasticity in PwMS is more difficult because the fluctuation and progressive courses in MS. Furthermore, an observational study compared between the spasticity impairments in PwMS and stroke patients. It found that the spasticity in PwMS affected highly the ankle range of motion. However, A cross sectional study found planter flexor weakness negatively impact walk more than planter flexor spasticity in ambulatory pwMS.

The review results and high prevalence confirm that the walking difficulties in PwMS are one of the most disabling symptoms as it affects mobility and quality of life. The disability level was worse in spasticity groups as gait impairments. The review and analysis showed that is spasticity reduces the walkin
speed. Recently, Karlon et al [21] suggested that the walking speed may be preferred predictor of spasticity. Furthermore, the low walking speed is associated with poor performance in walking and balance, and high risk of fall [21]. The impairments in spatial and temporal gait parameters as shown in the review lead to a high risk of fall [22]. In this line, previous study showed that posture deficits and high risk of fall are correlated with high spasticity in PwMS [23].

One of included study [14] indicates that the spasticity lead to significant hyperactivity in rectus femoris muscle, and lower hip flexion-extension range of motion. This finding indicates that the spasticity affects highly two joint muscles. The rehabilitation interventions target rectus femoris muscles and other two joint muscles are highly required. Walking was the most common type of physical activity self-selected by pwMS [24]. The review results and high prevalence of spasticity indicate that the gait training is required in MS rehabilitation protocols. The interventions should to reduce spasticity as well as improve the gait.

**Conclusion**

Spasticity affects negatively on gait and walking mobility. Those walking impairments lead to increase level of disability, and risk of fall. Gait training is required in MS rehabilitation protocols especially for PwMS with spasticity.

**Conflict of Interest:** None declared

**Source of Funding:** None

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