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Plantarflexor weakness negatively impacts walking in persons with multiple sclerosis more than plantarflexor spasticity

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Abstract

Objective—To determine if plantarflexor (PF) spasticity or ankle strength best predicts variance in walking capacity or self-perceived limitations in walking in persons with multiple sclerosis (pwMS), and if pwMS with PF spasticity are weaker and have greater walking dysfunction than pwMS without PF spasticity.

Design—Cross-sectional study.

Setting—University research laboratory.

Participants—Forty-two pwMS (age: 42.9 ± 10.1 years; Expanded Disability Status Scale (EDSS): median = 3.0, range = 0–6) and 14 adults without disability (WD) (age: 41.9 ± 10.1 years).

Intervention—Not applicable.

Main Outcome Measures—PF spasticity and dorsiflexion (DF) and PF maximum voluntary isometric torque (MVIT) were assessed using the Modified Ashworth Scale (MAS) and a computerized dynamometer, respectively. The Timed 25-Foot Walk Test (T25FWT) was the primary outcome measure of walking capacity. Secondary measures included the Six Minute Walk Test (6MWT) and 12-item Multiple Sclerosis Walking Scale (MSWS-12).

Results—PF strength was the most consistent predictor of the variance in walking capacity (T25FWT: R^2 change = 0.23 to 0.29, $p = 0.001$; 6MWT: R^2 change = 0.12 to 0.29, $p = 0.012$), and

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self-perceived limitations of walking (MSWS-12: R^2 change = 0.04 to 0.14, $p < 0.18$). There were no significant differences ($p > 0.05$) between the pwMS with PF spasticity and pwMS without PF spasticity for any of the outcome measures.

Conclusions—Our study suggests a unique contribution of PF weakness to walking dysfunction in pwMS, and highlights the importance of evaluating PF strength in this clinical population.

Keywords

multiple sclerosis; strength; spasticity; walking; ankle

Corticospinal tract demyelination and axon loss typically result in lower extremity spasticity and muscle weakness in persons with multiple sclerosis (pwMS)^{1, 2}. These impairments are considered key contributors to walking dysfunction. Consequently, rehabilitation strategies are targeted at reducing spasticity³ and increasing strength⁴ to improve walking in pwMS.

The association between lower limb spasticity and walking dysfunction in pwMS is poorly understood^{5–7}. While pwMS report spasticity to be related to gait impairments⁸ and disability⁷, these self-report tools are not limited to the lower limbs and often include non-specific descriptors of “pain”, “jumping of the legs”, “spasms”, and “muscle stiffness”^{7, 8}. PwMS with plantarflexor (PF) spasticity quantified by the Modified Ashworth Scale (MAS)⁹ were noted to have reduced walking capacity and greater self-perceived walking limitations compared to those without PF spasticity⁶. However, the group with PF spasticity had a greater median Expanded Disability Status Scale (EDSS)¹⁰ score compared with those without PF spasticity, and other impairments (i.e. weakness) may have contributed to the group differences.

In contrast to pwMS, lower limb spasticity and walking function appear unrelated in persons post-stroke^{11–13, 14}. Weakness, rather than spasticity, is reported to be a major contributing factor to walking dysfunction when both impairments are measured concurrently in persons post-stroke^{12, 13, 15}. In pwMS, lower limb muscle weakness is associated with reduced walking speed^{16, 17} and endurance¹⁸. However, no single study has examined both lower limb spasticity and weakness in the same group of pwMS. An understanding of the relative contribution of spasticity and weakness to walking dysfunction in pwMS is required for targeted therapeutic interventions.

Spasticity and weakness may be present in several lower limb muscles of pwMS. Our study focused on the ankle because dorsiflexors (DF) are important for swing phase foot clearance, whereas PFs help generate the energy for forward propulsion^{19, 20}. Other investigators have found PFs to be particularly critical for ambulation in persons with other neurological conditions^{15, 21, 22}. Similarly, we hypothesized that in pwMS, PF weakness would be a superior predictor of walking speed, endurance, and self-reported limitations in walking, when PF spasticity is assessed concurrently. We also hypothesized that pwMS with PF spasticity would not be weaker or have greater walking dysfunction than pwMS without PF spasticity.

METHODS

Participants

Forty-two pwMS were recruited from the greater St. Louis area via the MS Clinic at Saint Louis University, the John L. Trotter MS Center at Washington University School of Medicine, and the Gateway Chapter of the National Multiple Sclerosis Society. PwMS were included if they: (1) had a confirmed diagnosis of MS using McDonald criteria²³, including relapsing-remitting, secondary progressive, and primary progressive MS; (2) were 18–65 years of age; (3) had minimal to moderate clinical disability as evidenced by an EDSS score ranging from 0.0 to 6.0; and (4) for those with RRMS, were at least 6 months following their last clinical exacerbation of MS. A certified neurologist determined the EDSS¹⁰. PwMS were excluded if they had lower extremity orthopedic conditions that limited ambulation, or if they were pregnant.

Fourteen control subjects without disability (WD) were recruited from the community if they were 18 years or older and excluded if they: (1) had a history of neurological disease, (2) had orthopedic conditions that limited ambulation, (3) had a history of cardiovascular or pulmonary conditions that would limit participation, (4) were pregnant or (5) unable to provide informed consent. The study was approved by the Saint Louis University Institutional Review Board and the Washington University Human Research Protection Office, and all participants provided informed consent prior to participation.

Clinical and self-report measures

Both pwMS and those WD participated in clinical measures of spasticity and walking capacity. Spasticity of the PFs was measured bilaterally using the Modified Ashworth Scale (MAS)⁹. The MAS ranges from 0–4, where 0 = no increase in muscle tone, and 4 = affected part(s) rigid in flexion or extension. Walking capacity was assessed using the Timed 25-Foot Walk Test (T25FWT)²⁴ and the Six Minute Walk Test (6MWT)²⁵. The T25FWT, a component of the Multiple Sclerosis Functional Composite²⁴, is a standardized clinical measure of short-distance maximal walking speed. The T25FWT was the main outcome measure. The 6MWT is a standardized clinical measure of walking endurance. Participants with MS also completed the 12-item Multiple Sclerosis Walking Scale (MSWS-12)²⁶. The MSWS-12 provides a score from 0–100, with larger values indicating greater perceived walking difficulty due to MS. These tests were administered by a physical therapist.

Instrumented Assessment of Ankle Dorsiflexor and Plantarflexor Strength

All participants underwent a dynamometry-based assessment of ankle strength using a Biodex System IV computerized dynamometer^a. Participants were positioned in a semi-supine position on the Biodex chair with the tested limb in 0° of knee extension. Waist and knee straps were used to stabilize the pelvis and lower limb, and a foot rest provided support for the non-tested limb. Prior to testing, each ankle was passively rotated from 30° of PF to 10° of DF with the foot secured in the Biodex attachment to ensure that all participants had a minimum of 40° of passive ankle motion. Both ankles were tested in a random order. The

^aBiodex Medical Systems, Inc., Shirley, NY, USA

maximal voluntary isometric torques (MVIT) for DF and PF were measured with the ankle in a neutral position (0° DF)⁴. Three, 5-second trials were collected for each muscle group in an alternating order. A minute rest period was provided between each trial. Participants were instructed to contract each specific muscle group as “hard and fast as possible”, with verbal encouragement. Analog torque (ft-lbs), position (degree), and velocity (degree/sec⁻¹) signals were sampled directly from the dynamometer at a rate of 1kHz using a Powerlab 16/30 A/D system^b and LabChart Pro (version 7.2.1)^b software.

Data Analysis

Because the MAS includes a score of 1+, raw MAS scores were transformed to a 0–5 scale.²⁷ The maximum PF MAS score (MaxPFMAS) from either leg was identified and used for subsequent statistical analysis. PwMS with MAS scores 1.0 or more for either leg were classified as being in the spasticity group, whereas pwMS with MAS scores of zero were in the no spasticity group⁶.

For the instrumented strength measure, data analyses were performed using LabChart (version 7.2.1)^b and MATLAB (version 2011b) software^c. Torque-angle data were low-pass filtered (50Hz) then processed to correct for the effects of limb weight and gravity using an anthropomorphic method²⁸. The maximum voluntary isometric torque (MVIT) value was identified for each of the trials, converted to Newton-meters (Nm), normalized by body mass (Nm/kg), and averaged across trials for each muscle group in each leg. The lowest mean normalized MVIT value for each muscle group from either leg was identified (MinDFMVIT, MinPFMVIT) and analyzed as the measure of muscle weakness.

SPSS software (version 20.0)^d was used for all analyses, with significance set at $p = 0.05$. Prior to performing the statistical analyses, distributions of the variables were examined for normality using the Shapiro-Wilk W test. Variables that were not normally distributed (EDSS, T25FWT, MaxPFMAS) were transformed to minimize skewness. Fisher’s exact tests were used to assess differences in gender and ethnicity between MS and WD groups. T-tests were used to assess differences in age, BMI, ankle strength and walking performance between MS and WD groups. Pearson product moment or Spearman rank order correlation coefficients indexed associations between PF spasticity, ankle strength, and measures of walking in the MS group ($r < 0.25$: little or none; $r > 0.25 - 0.50$: fair; $r > 0.50 - 0.75$: moderate; and $r > 0.75$: excellent association)²⁹. Based on our sample size, correlation coefficients greater than 0.30 and 0.49 were statistically significant at the $p < 0.05$ and $p < 0.001$ levels, respectively. A series of hierarchical linear multiple regression analyses, entering each of the independent variables in turn as last, was used to determine the amount of unique variance in walking speed, walking endurance, and self-perceived limitations in walking that was explained by PF spasticity, DF and PF strength. This method was used to assess the consistency of the IVs to predict the variance in walking dysfunction given the moderate association between DF and PF strength (see Results)³⁰. T-tests and Mann-Whitney U tests as appropriate were used to assess differences between spasticity (MAS

^bADInstruments, Inc., Colorado Springs, CO, USA

^cMathworks, Inc., Natick, MA, USA

^dIBM Inc., Armonk, New York, USA

1) and no spasticity (MAS = 0) groups for clinical disability, PF spasticity, ankle strength, walking capacity, and MSWS12, using $P < 0.008$ to correct for multiple comparisons. The magnitude of the difference between groups (MS vs. WD, spasticity vs. no spasticity) was estimated by calculating Cohen's d effect size³¹, with the absolute value reported. Effect size values > 0.2 were considered small; $> 0.5 - 0.8$ were moderate; and values > 0.80 were large³¹.

RESULTS

Demographics between the MS and WD groups were well matched for age, BMI, gender, and ethnicity ($p > 0.05$; Table 1). PwMS had mild clinical disability based upon a median EDSS score of 3.0 (range 0 – 6.0), and self-perceived limitations in walking documented by the MSWS12 (Table 2). Twelve (29%) pwMS reported using a straight cane for community ambulation, seven (17%) used a cane during the T25FWT, and nine (21%) used a cane during the 6MWT. Two of individuals wore a unilateral ankle-foot orthosis in addition to a cane during testing. Six (14%) pwMS reported the use of oral anti-spasticity medications (Table 1).

The MS group had mild PF spasticity (MaxPFMAS: median 1 (range 0 – 4)). Compared to the WD group, pwMS had lower PF strength (MinPFMVIT: $p = 0.02$, $|d| = 0.80$), a trend for lower DF strength (MinDFMVIT: $p = 0.10$, $|d| = 0.50$), and reduced walking capacity as indexed by the T25FWT ($p = 0.0002$, $|d| = 1.07$) and 6MWT ($p = 0.0001$, $|d| = 1.59$) (see Table 2). There were no missing values in the data set.

No association was found between PF spasticity and ankle strength ($r = -0.18$). PF spasticity had little association with walking capacity or self-perceived walking limitations ($|rs| = 0.27$). Dorsiflexor strength was moderately associated to PF strength ($r = 0.65$). Greater DF and PF strength were associated with longer distance walked during the 6MWT (DF: $r = 0.42$; PF: $r = 0.54$) and lower self-perceived limitations in walking by the MSWS-12 (DF: $r = -0.33$; PF: $r = -0.39$). Greater PF strength was also associated with shorter time to complete the T25FWT ($r = -0.54$) (see Table 3).

The results of the hierarchical regression (Table 4) indicated that the three predictors (PF spasticity, DF and PF strength) together explained 33% of the variance in walking speed ($R^2 = 0.33$, $F(3,38) = 7.62$, $p = 0.001$). PF strength increased by the highest amount the explained variance in walking speed (incremental R^2 change = 0.23 to 0.29) once all remaining IVs were in the model, regardless of the entry order of IVs into the equation. DF strength did not make a significant unique contribution to the prediction of walking speed irrespective of the order of entry into the model (incremental R^2 change = 0.01 to 0.07). In the final model, PF spasticity and PF strength significantly predicted walking speed, with PF strength recording a higher beta value ($\beta = 0.634$, $p = 0.001$) than PF spasticity ($\beta = -0.265$, $p = 0.046$). The three predictors together explained 33% of the variance in walking endurance ($R^2 = 0.33$, $F(3,38) = 6.14$, $p = 0.002$). The amount of unique variance in walking endurance explained by DF strength (incremental R^2 change = 0.01 to 0.18) and PF strength (incremental R^2 change = 0.12 to 0.29) was dependent on the point of entry of each variable into the model. PF spasticity did not make a significant unique contribution to the prediction

of walking endurance (incremental R^2 change = 0.03 to 0.04). In the final model, only PF strength significantly predicted walking endurance ($\beta = 0.464$, $p = 0.012$). Our model explained 17% of the variance in self-perceived limitations in walking ($R^2 = 0.17$, $F(3,38) = 2.65$, $p = 0.063$). The amount of unique variance in self-perceived walking limitations explained by PF strength (incremental R^2 change = 0.04 to 0.14) and DF strength (incremental R^2 change = 0.01 to 0.11) was also dependent on the point of entry of each variable into the model. PF spasticity did not make a significant unique contribution to the prediction of self-perceived walking limitation (incremental R^2 change = 0.02 to 0.03). In the final model, none of the IVs significantly predicted self-perceived limitations in walking.

Plantarflexor spasticity was present in 69% (29/42) of pwMS. Of those with spasticity, 66% (19/29) had bilateral spasticity and 45% (16/29) had the same MAS scores for both limbs. The median (IQR) MaxPFMAS for those with spasticity was 2.0 (1–3), indicating moderate PF spasticity. Figure 1 displays the data for EDSS, ankle strength, and walking measures for the spasticity and no spasticity groups. There were no significant between-group differences for the EDSS (median (IQR) 3.0 (3–5.3) vs. 3.0 (2–5.0), $p > 0.05$), indicating that both groups had similar levels of overall clinical disability. There were no significant differences ($p > 0.05$) between the spasticity and no spasticity groups in MinDFMVIT (0.295 vs. 0.301 Nm/kg, $|d| = 0.05$), MinPFMVIT (0.915 vs. 0.887 Nm/kg, $|d| = 0.09$), T25FWT (6.1 vs. 5.3 s, $|d| = 0.34$), 6MWT (462.7 vs. 478.0 m, $|d| = 0.12$), and MSWS-12 (44.0 vs. 40.5, $|d| = 0.15$), indicating that the spasticity group was similar to the no spasticity group for all measures.

DISCUSSION

Ankle weakness, rather than spasticity, was the more consistent predictor of walking dysfunction when both impairments were measured in our cohort of pwMS. PF weakness was a more consistent predictor of walking dysfunction than DF strength. While PF spasticity uniquely predicted a small amount of the variance in walking speed, PF spasticity was not associated with ankle weakness, walking endurance or self-perceived limitations in walking. PwMS with PF spasticity were not weaker and did not have greater walking dysfunction than pwMS without spasticity. These results suggest that PF weakness negatively impacts walking more than PF spasticity, at least for those with mild disability from MS.

Our results are compatible with reports in persons post-stroke, wherein ankle weakness, rather than PF spasticity, is a major contributing factor to walking dysfunction^{12, 13, 15}. Nevertheless, our results differ from a report in pwMS, where those with PF spasticity were found to have greater mobility impairment than those without PF spasticity⁶. We suggest the discrepancy may be attributable to our study including a formal measure of ankle strength, in addition to the present study having similar levels of disability in the spasticity and no spasticity group. Additional research is needed clarify the ambiguous evidence regarding the impact of PF spasticity on walking function in pwMS.

While ankle weakness is recognized as a key contributor to walking dysfunction^{12, 13, 15, 21, 32, 33}, there is no consensus regarding the relative contribution of DF

and PF weakness to reduced walking speed and endurance. In our cohort of pwMS, PF weakness was the most consistent predictor of walking dysfunction. Our results are consistent with a report in persons post-stroke, where PF weakness, rather than DF weakness, was the largest predictor of walking endurance¹⁵. Others have also reported a strong relationship between PF weakness and reduced walking speed^{21, 22}. Nonetheless, our results are not congruent with recent reports in persons post-stroke where DF strength, rather than PF strength, was the strongest predictor of comfortable walking speed³³ and walking endurance¹³. The impact of PF vs. DF weakness on walking may differ given the relative weakness of each muscle group and the level of clinical disability. In this present study, pwMS had greater relative weakness in the PFs compared to the DFs, when compared to controls (MS vs. WD groups: PF: $d = -0.80$ vs. DF: $d = -0.50$, respectively). This group with mild disability may have had enough DF strength for toe clearance during swing, but insufficient PF strength may have limited walking capacity³⁴ by reducing ankle joint power³⁵.

The proportion of variance explained in our study for the T25FWT (33%) and 6MWT (33%) by PF spasticity and ankle strength is similar the amount of variance explained by knee flexor strength in pwMS for the T25FWT (46%) and Two Minute Walk Test (34%)¹⁸. This raises the question whether one particular muscle group best predicts walking capacity in pwMS. Research is needed to examine the relative contribution of each of the different lower limb muscles to walking dysfunction in pwMS. The fact that the aforementioned models explained less than half of the variance for walking speed and endurance suggests impairments other than PF spasticity and ankle or knee weakness contribute to walking dysfunction in pwMS. Given that MS is a disease characterized by impairments in multiple systems; it is likely that more variance would be explained by models including additional sensorimotor impairments, such as ataxia and sensory loss.

We found that our model only explained 17% of the variability of self-perceived walking limitations as measured by the MSWS-12. This finding is not unexpected because the ankle muscles are only two of many muscles involved in walking and it is unlikely that spasticity and weakness negatively impacts all of the dimensions of walking included in the MSWS-12. Moreover, objective measures do not fully capture the subjective perception of walking problems in pwMS³⁶. It is possible that cognitive, behavioral, emotional, and psychological processes not included in our study are stronger predictors of self-perceived walking difficulty than lower limb muscle weakness³⁷. An understanding of the determinants of self-perceived walking difficulty in pwMS is needed to develop targeted, effective therapies for improving walking from the patient's perspective.

The lack of an association between PF spasticity measured using the MAS and walking dysfunction is not consistent with previous research in pwMS, where self-reported spasticity was associated with self-perceived mobility problems⁷ and impaired spatiotemporal parameters of gait⁸. We propose a few potential explanations for this discrepancy. First, the tools used to assess self-perceived spasticity included descriptors such as pain, spasms, tightness, muscle stiffness³⁸, and jumping of the legs⁷. Thus, symptoms other than spasticity, defined as the velocity-dependent increase in tonic stretch reflexes experienced by a clinician attempting to flex or extend a limb in patients with upper motor neuron

lesions³⁹, may have contributed to the associations reported using these tools. Second, the reports of self-perceived spasticity were not limited to the lower limbs. It is possible that symptoms (e.g. stiffness) in the trunk or upper extremity contributed to the associations between self-perceived spasticity and mobility impairment⁸. Third, the reported relationships between self-perceived spasticity, as measured by the MSSS-88, and spatiotemporal parameters of gait were statistically significant but the magnitude of the relationships were fair ($|r| = 0.40$). These results are congruent with our report of a fair relationship between spasticity and walking dysfunction. Additional research wherein clinically assessed lower limb spasticity, self-perceived spasticity, walking capacity and self-perceived walking ability are documented in the same group of pwMS is needed to fully understand the association between spasticity and walking dysfunction in pwMS.

The MAS is the primary measure of spasticity used in MS clinical practice and clinical trials^{40–42}. We purposefully used this scale to provide information relevant to MS clinical practice and to permit a comparison of our results to those previously published. We acknowledge that the MAS does not distinguish between reflex and non-reflex or passive (e.g., viscoelastic properties of the tissues surrounding a joint) contributions to resistance to passive stretch. The Tardieu Scale⁴³ has been suggested as a more suitable clinical measure of spasticity than the MAS because it involves the assessment of resistance to passive movement at both slow and fast speeds⁴³, thus it appears to adhere more closely to Lance's definition of spasticity³⁹. However, the validity and reliability of the Tardieu Scale have not been established in pwMS. Future research is needed to determine the reliability and validity of the Tardieu Scale in pwMS and to what extent spasticity measured by the Tardieu predicts walking dysfunction in pwMS.

STUDY LIMITATIONS

There are limitations of our study. Our sample size did not allow a secondary analysis to determine if the relationship between PF spasticity, ankle strength and walking dysfunction differs based on the overall level disability¹⁸ or the use oral anti-spasticity medications. We acknowledge that the distribution and limited range of MAS scores in our cohort of ambulatory pwMS may have attenuated the relationship between spasticity and walking function. Because we evaluated spasticity and strength only at the ankle, we are unable to determine whether and to what extent spasticity and weakness of other lower limb muscles contribute to walking dysfunction in pwMS. We did not assess the total range of passive motion at the ankle. It is possible that decreased range of movement due to shortening in the PFs might have impacted the measurement of dorsiflexion strength. Enrollment of pwMS was limited to those with mild to moderate clinical disability. Consequently, our results may not generalize to ambulant pwMS with more pronounced clinical disability (e.g., EDSS = 6.5 or 7.0). We used a sample of convenience for our WD and MS groups, thus limiting the generalizability of our findings.

CONCLUSIONS

Our data demonstrate that there is no relationship between PF spasticity and ankle weakness, and a limited relationship between PF spasticity and walking dysfunction in ambulatory

pwMS with mild clinical disability. Of the impairments measured, PF weakness was the most consistent predictor of the variance in walking capacity and self-perceived limitations of walking dysfunction. Consistent with reports in persons post-stroke^{15, 21, 22}, our results suggest a unique contribution of PF weakness to walking dysfunction in pwMS. Furthermore, our results highlight the importance of evaluating PF strength in this clinical population. Additional research is needed to determine if the relationships between PF spasticity, ankle weakness, and walking dysfunction in pwMS differ based on the overall level of clinical disability, and how other specific lower limb impairments contribute to walking dysfunction in this clinical population.

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LIST OF ABBREVIATIONS

pwMS	persons with multiple sclerosis
PF	plantarflexor
DF	dorsiflexor
MAS	Modified Ashworth Scale
EDSS	Expanded Disability Status Scale
T25FWT	Timed 25-Foot Walk Test
6MWT	Six Minute Walk Test
MSWS-12	12-item Multiple Sclerosis Walking Scale
WD	without disability
MaxPFMAS	maximum plantarflexor Modified Ashworth Scale
MinDFMVIT	minimum dorsiflexor maximum voluntary isometric torque
MinPFMVIT	minimum plantarflexor maximum voluntary isometric torque

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Figure 1.

Individual and median ($\pm$ IQR) values for (A) EDSS, and individual and mean ($\pm$ standard deviation) values for (B) MinDFMVIT, (C), MinPFMVIT, (D) T25FWT, (E) 6MWT, and (F) MSWS-12 for the spasticity (●) and no spasticity (■) groups.

Table 1

Characteristics of participants with multiple sclerosis (MS) and without disability (WD)

	MS	WD
Age, years, mean $\pm$ SD (range)	42 $\pm$ 10 (24–63)	41 $\pm$ 10 (29–60)
Height, cm, mean $\pm$ SD (range)	171 $\pm$ 10 (150–196)	172 $\pm$ 10 (157–190)
Weight, kg, mean $\pm$ SD (range)	78 $\pm$ 19 (53–140)	90 $\pm$ 28 (53–144)
BMI, mean $\pm$ SD (range)	26.7 $\pm$ 5.5 (20.4–42.3)	30.0 $\pm$ 7.1 (21.6–45.6)
Female, n (%)	27 (64)	8 (57)
Disease duration, y, mean $\pm$ SD (range)	7.7 $\pm$ 6.2 (1–20)	NA
EDSS, median (range)	3.0 (0–6)	NA
Race, n (%)		
Caucasian	30 (71)	11 (79)
African-American	12 (29)	2 (14)
Asian	0 (0)	1 (7)
Type of MS (RR/SP/PP), n (%)	35/5/2 (83/12/5)	NA
Use of straight cane during testing, n (%)		NA
T25FWT	7 (17)	
6MWT	9 (21)	
Use of anti-spasticity medication, n (%)	6 (14)	NA
Presence of plantarflexor spasticity, n (%)	29 (69)	0 (0)

MS = multiple sclerosis; WD = without disability; SD = standard deviation; n = number; y = years; EDSS = Expanded Disability Status Scale; RR = relapsing remitting; SP = secondary progressive; PP = primary progressive; T25FWT = Timed 25-Foot Walk Test; 6MWT = Six Minute Walk Test, NA = not applicable.

Table 2

Spasticity, strength and walking measures for the MS and WD groups.

	MS (n = 42)	WD (n = 14)	p value, d
MaxPFMAS, median (IQR)	1.0 (2.0)	0 ± 0 (0)	
MinDFMVIT, Nm/kg, mean ± SD (range)	0.30 ± 0.10 (0.06–0.46)	0.35 ± 0.10 (0.15–0.55)	p = 0.10, d = 0.50
MinPFMVIT, Nm/kg, mean ± SD (range)	0.91 ± 0.33 (0.14–1.71)	1.15 ± 0.27 (0.65–1.51)	p = 0.02, d = 0.80
T25FWT, seconds, mean ± SD (range)	5.9 ± 2.3 (3.7–14.8)	4.1 ± 0.3 (3.6–4.8)	p = 0.0002, d = 1.07
6WMT, m, mean ± SD (range)	466.7 ± 133.9 (157.9–677.0)	634.5 ± 66.5 (548.3–739.4)	p = 0.0001, d = 1.59
MSWS-12, mean ± SD (range)	42.9 ± 22.3 (0–90.5)	NT	N/A

MS = multiple sclerosis; WD = without disability; n = number; d = Cohen's d; SD = standard deviation; MinDFMVIT = minimum dorsiflexor maximum voluntary isometric torque; MinPFMVIT = minimum plantarflexor maximum voluntary isometric torque; MaxPFMAS = maximum plantarflexor Modified Ashworth Scale; IQR: interquartile range; T25FWT = Timed 25-Foot Walk Test; 6WMT = Six Minute Walk Test; MSWS-12: 12-item Multiple Sclerosis Walking Scale.

Table 3

Correlations between plantarflexor spasticity, ankle strength and walking measures for MS group (n = 42)

	MaxPFMAS [^]	MinDFMVIT	MinPFMVIT	T25FWT	6WMT
MinDFMVIT	-0.18	1.0			
MinPFMVIT	-0.10	0.65**			
T25FWT	0.27	-0.25	-0.54**		
6WMT	-0.20	0.42*	0.54**	0.89**	
MSWS-12 [^]	0.11	-0.33*	-0.39*	0.59**	-0.67**

MinDFMVIT = minimum dorsiflexor maximum voluntary isometric torque; MinPFMVIT = minimum plantarflexor maximum voluntary isometric torque; MaxPFMAS = maximum plantarflexor MAS score; T25FWT = Timed 25-Foot walk test; 6WMT = Six Minute Walk Test; MSWS-12 = 12 Item Multiple Sclerosis Walking Scale.

[^] Spearman rank order correlations,

* P < 0.05,

** P < 0.001.

Table 4
Summary of Hierarchical Regression Analyses for variables Predicting Walking (n = 42)

	Independent variable (in order of entry)	Dependent variable		
		Walking Speed (T2FWT) Range: 3.7 to 14.8 s R ² Change (F, p value)	Walking endurance (6MWT) Range: 157.9 to 677.0 m R ² Change (F, p value)	Self-perceived walking limitation (MSWS-12) Range: 0 to 90.5 R ² Change (F, p value)
Model 1	MaxPFMAS	0.08 (F = 3.67, p = 0.062)	0.04 (F = 1.49, p = 0.229)	0.03 (F = 1.08, p = 0.305)
	MinPFMVIT	0.28 (F = 16.82, p = 0.000)	0.28 (F = 16.29, p = 0.000)	0.13 (F = 6.19, p = 0.017)
	MinDFMVIT	0.02 (F = 0.94, p = 0.338)	0.01 (F = 0.36, p = 0.551)	0.01 (F = .606, p = 0.441)
Model 2	MaxPFMAS	0.08 (F = 3.67, p = 0.062)	0.04 (F = 1.49, p = 0.229)	0.03 (F = 1.08, p = 0.305)
	MinDFMVIT	0.06 (F = 2.83, p = 0.101)	0.17 (F = 8.18, p = 0.007)	0.11 (F = 4.76, p = 0.035)
	MinPFMVIT	0.23 (F = 13.97, p = 0.001)	0.12 (F = 6.96, p = 0.012)	0.04 (F = 1.86, p = 0.180)
Model 3	MinPFMVIT	0.29 (F = 16.47, p = 0.000)	0.29 (F = 16.67, p = 0.000)	0.14 (F = 6.74, p = 0.015)
	MinDFMVIT	0.01 (F = 0.78, p = 0.383)	0.01 (F = 0.396, p = 0.533)	0.01 (F = 0.65, p = 0.426)
	MaxPFMAS	0.07 (F = 4.27, p = 0.046)	0.03 (F = 1.43, p = 0.240)	0.02 (F = 0.892, p = 0.351)
Model 4	MinPFMVIT	0.29 (F = 16.47, p = 0.000)	0.29 (F = 16.67, p = 0.000)	0.14 (F = 6.74, p = 0.015)
	MaxPFMAS	0.07 (F = 4.17, p = 0.048)	0.03 (F = 1.49, p = 0.230)	0.02 (F = 0.94, p = 0.338)
	MinDFMVIT	0.02 (F = 0.94, p = 0.338)	0.01 (F = 0.36, p = 0.551)	0.01 (F = 0.61, p = 0.441)
Model 5	MinDFMVIT	0.07 (F = 3.00, p = 0.091)	0.18 (F = 8.49, p = 0.006)	0.11 (F = 5.01, p = 0.031)
	MinPFMVIT	0.24 (F = 13.24, p = 0.001)	0.13 (F = 7.04, p = 0.011)	0.04 (F = 1.93, p = 0.172)
	MaxPFMAS	0.07 (F = 4.27, p = 0.046)	0.03 (F = 1.43, p = 0.240)	0.02 (F = 0.89, p = 0.351)
Model 6	MinDFMVIT	0.07 (F = 3.00, p = 0.091)	0.18 (F = 8.49, p = 0.006)	0.11 (F = 5.01, p = 0.031)
	MaxPFMAS	0.08 (F = 3.49, p = 0.069)	0.03 (F = 1.37, p = 0.249)	0.02 (F = 0.93, p = 0.340)
	MinPFMVIT	0.23 (F = 13.97, p = 0.001)	0.12 (F = 6.96, p = 0.012)	0.04 (F = 1.86, p = 0.180)
Full Model	F ratio ^b	7.619 (3.38)	6.140 (3.38)	2.645 (3.38)
	R ²	0.33, p = 0.000	0.33, p = 0.002	0.17, p = 0.063

T25FWT = Timed 25-Foot walk test; 6MWT = Six Minute Walk Test; MSWS-12 = 12 Item Multiple Sclerosis Walking Scale; MaxPFMAS = maximum plantarflexor MAS score; MinDFMVIT = minimum dorsiflexor maximum voluntary isometric torque; MinPFMVIT = minimum plantarflexor maximum voluntary isometric torque;

^b degrees of freedom in parentheses.