

## RESEARCH ARTICLE

# Spasticity, gait, and balance in patients with multiple sclerosis: A cross-sectional study

Anja Davis Norbye<sup>1,2,3</sup>  | Rune Midgard<sup>2,4</sup> | Gyrd Thrane<sup>5</sup>

<sup>1</sup> Department of Community Medicine, UiT The Arctic University of Norway, Tromsø, Norway

<sup>2</sup> Department of Neurology, Molde Hospital, Møre and Romsdal Health Trust, Molde, Norway

<sup>3</sup> Department of Physiotherapy, University Hospital of North Norway, Tromsø, Norway

<sup>4</sup> Unit for Applied Clinical Research, Norwegian University of Science and Technology, Trondheim, Norway

<sup>5</sup> Department of Health and Care Sciences, UiT The Arctic University of Norway, Tromsø, Norway

**Correspondence**

Anja Davis Norbye, Department of Community Medicine, UiT The Arctic University of Norway, Postbox 6050, Langnes, Tromsø 9037, Norway.  
Email: anja.davis.norbye@uit.no

**Funding information**

The Norwegian Fund for Post-Graduate Training in Physiotherapy

**Abstract**

**Objective:** More than 80% of people with multiple sclerosis (MS) are affected by spasticity. Spasticity is known to reduce quality of life and contribute to additional symptoms, such as pain and reduced mobility, but the association between spasticity, balance, and mobility has not yet been established. Our aim was to examine whether a relationship exists between spasticity in the lower limbs, balance, and gait, as well as to explore the involvement of different muscle groups.

**Methods:** This study employed a cross-sectional design. Thirty patients with MS were included. The Modified Ashworth Scale (MAS) was used to examine spasticity in the ankle plantar flexors, knee extensors, and hip adductors. Balance was measured using the Mini-Balance Evaluation Systems Test, and gait with the 2-Minute Walk Test. The participants were tested once with no additional follow-up. Spearman's correlation, recursive partitioning, and linear regression analyses were used to explore the association.

**Results:** A significant correlation between gait distance and spasticity in the ankle plantar flexors ( $\rho = -.69, p < .001$ ) and knee extensors ( $\rho = -.45, p = .012$ ) was observed. Balance significantly correlated with spasticity in ankle plantar flexors ( $\rho = -.69, p < .001$ ), knee extensors ( $\rho = -.52, p = .003$ ), and hip adductors ( $\rho = -.5, p = .005$ ). The relationship between spasticity in ankle plantar flexors and hip adductors was significant, even from low levels of spasticity, whereas MAS score  $\geq 2$  was clinically correlated with a decrease in gait and balance function. Adjustments for sex, age, or years since diagnosis had only minor impact on the results.

**Conclusions:** This study indicates that spasticity in the lower limbs is clinically significantly associated with mobility in people with MS.

**KEYWORDS**

gait, multiple sclerosis, muscle spasticity, postural balance

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2019 The Authors. Physiotherapy Research International Published by John Wiley & Sons Ltd

## 1 | INTRODUCTION

Multiple sclerosis (MS), the most common disabling neurological illness among young people, most frequently manifests as an initial relapsing–remitting course (Cameron & Wagner, 2011). Globally, approximately 2.5 million people live with the disease. The prevalence is approximately twice as high in women as in men (Thompson, Baranzini, Geurts, Hemmer, & Ciccarelli, 2018). The clinical manifestation largely depends on the topography of the inflammatory lesions in the central nervous system, although the most frequent symptoms and signs observed at disease onset originate from the optic nerve, the brainstem, and the spinal cord. The diagnosis is reached through a combination of history, clinical findings, results from imaging of the central nervous system (e.g., magnetic resonance imaging), and laboratory results, particularly analyses of the cerebrospinal fluid (Thompson et al., 2018).

Disturbances and a decline in motor function and mobility often occur, including gait abnormalities, reduced balance, altered alignment, range of motion, and coordination, as well as spasticity (Cameron & Wagner, 2011). Spasticity, a velocity-dependent increase in muscle tone (Lance, 1980), is commonly observed. Spasticity affects more than 80% of people with MS (Barnes, Kent, Semlyen, & McMullen, 2003; Bethoux & Marrie, 2016; Rizzo, Hadjimichael, Preiningerova, & Vollmer, 2004), with symptoms often appearing approximately 5 years after diagnosis (Vermersch, 2014). Symptoms mainly affect muscles in the lower extremities (Bethoux, 2013; Vermersch, 2014), including triceps surae, hip adductors, and knee extensors (Stokes, 2004, p. 193). Spasticity impacts and tends to exacerbate other symptoms, such as pain (Flachenecker, Henze, & Zettl, 2014; Patti & Vila, 2014), sleeping problems (Bethoux & Marrie, 2016), fatigue, and bladder dysfunction (Zettl, Henze, Essner, & Flachenecker, 2014). Spasticity may predict future falls (Gunn, Creanor, Haas, Marsden, & Freeman, 2013; Nilsagard, Lundholm, Denison, & Gunnarsson, 2009) and is reported to reduce quality of life in several studies (Arroyo, Massana, & Vila, 2013; Svensson, Borg, & Nilsson, 2014; Zettl et al., 2014). The relationship between spasticity and mobility has rarely been studied, despite the high prevalence of spasticity and the documented association with other symptoms of MS. Some studies report a limited association between ankle spasticity and gait (Kremer, Van Dillen, & Wagner, 2014), highlighting muscle weakness as the main factor contributing to impaired mobility (Wagner, Kremer, Van Dillen, & Naismith, 2014). However, Sosnoff, Shin, and Motl (2010) identified a significant association between an elevated Hoffmann's reflex in the soleus muscle and postural sway, providing experimental support for an association between balance function and spasticity. Spasticity in different muscle groups of the lower extremities was only measured in one study (Balantrapu, Sosnoff, Pula, Sandroff, & Motl, 2014) but dichotomised the presence of spasticity. The association between different grades of spasticity in different muscle groups related to gait and balance has, as far as we know, not been established. Our aim was therefore to examine whether (a) a relationship exists between spasticity in the lower limbs, balance, and gait and (b) to explore the involvement of different muscle groups.

## 2 | METHODS

### 2.1 | Design

During a period of 6 months, all patients with MS attending their routine neurological control visits at Molde Hospital Trust were consecutively considered for inclusion in the study. Neurologists considered individuals for inclusion on the basis of the following criteria:

1. a definitive MS diagnosis according to the 2010 McDonalds criteria (Polman et al., 2011);
2. the presence of spasticity in one or more muscles of the lower extremities that was detected by a clinical examination, subjectively reported stiffness in the lower extremities that was interpreted as spasticity by the neurologist, or the use of spasmolytic drugs; and
3. some remaining gait function, specified as a Kurtzke Expanded Disability Status Scale (EDSS) score  $\leq 6.5$  (a score of 6.5 indicates constant bilateral assistance required to walk approximately 20 m without resting; Kurtzke, 1983).

Patients were excluded if any problems with mobility were caused by symptoms other than spasticity, as determined by the neurologist, if diseases other than MS caused the reduction in ambulatory function, if the EDSS score exceeded 6.5, or if they had cognitive difficulties that prevented them from providing informed consent or receiving instructions during testing.

We used a disproportionate selection method in an effort to balance the number of participants with spasticity at each of the five Modified Ashworth Scale (MAS) levels. During the inclusion period, 35 individuals were recruited. The neurologists considered patients on the basis of the inclusion criteria, and the patient's maximal MAS score at inclusion was reported to the project leader. We extended the inclusion period to recruit participants with MAS scores of 0 and 4, but by the end of the inclusion period, none of the participants had a MAS score of 4, despite the stratified selection.

### 2.2 | Procedure

The clinical tests were conducted by four physiotherapists (PTs). A. D. N. conducted the spasticity measurements. The remaining PTs, who were trained in the tests and experienced with the patient population, conducted the mobility measurements. The testers were blinded to the results obtained by the other PTs during testing.

### 2.3 | Measurement tools

We used the MAS, a measure of velocity-dependent resistance on a 6-point scale, where 0 represents no increase in muscle tone and 4 indicates that the affected muscles are rigid in flexion and extension, to measure spasticity. The MAS is considered a convenient tool for a clinical setting and is reported to be useful for clinical assessments of spasticity (Rekand, 2010), is easy to learn and use (Barnes et al., 2003), and has demonstrated

good correlation with self-reported spasticity ( $r = .57$ ; Arroyo et al., 2013). We performed bilateral tests of hip adductors, knee extensors, and ankle plantar flexors (Ghotbi, Ansari, Naghdi, & Hasson, 2011).

During the gait and balance tests, participants were allowed to use any habitual assistance device. We measured gait with the 2-Minute Walk Test (2MWT). This test is suitable for measuring mobility in people with MS, both with mild and more severe disabilities (Baert et al., 2014). The patients were instructed to perform the 2MWT as fast as possible without taking any safety risks, walking 37 m before turning. They were instructed to take breaks if needed, but they would not be encouraged to do so or be encouraged in any way during the test. Patients were instructed to start walking 2 m before the timing started.

We measured balance with the Mini-Balance Evaluation Systems Test (Mini-BESTest), a measurement tool addressing different aspects of dynamic balance using 14 tasks with scores of 0–3 points each and a total score ranging from 0 to 28 points (28 representing the best score possible; Horak, Wrisley, & Frank, 2009). The Mini-BESTest is suitable for measuring balance in individuals with neurological diseases (Franchignoni, Godi, Guglielmetti, Nardone, & Giordano, 2015), and the validated Norwegian version has demonstrated high reliability (Hamre, Botolfsen, Tangen, & Helbostad, 2017).

Information concerning sex, age, years since diagnosis, type of MS, use of spasmolytic medications, and any physiotherapy treatment for MS was collected when the patient arrived for testing.

## 2.4 | Statistical analyses

We computed the sample size on the basis of the expected correlation level. Small or medium correlation coefficients (Cohen, 1977) were considered nonimportant, and the sample size was established to detect a correlation coefficient of at least .5. With an expected correlation coefficient of .5 (Rasova, Martinkova, Vyskotova, & Sedova, 2012), we would reach a power of 80% with 29 participants. The R language for statistical computing Version 3.4.2 was used for statistical analyses (R Core Team, 2017). Categorical variables are presented as frequencies and proportions. The distribution of continuous variables was examined in histograms and quantile-quantile plots. Normally distributed variables are presented as means and standard deviations, whereas nonnormally distributed variables are presented as medians and quartiles.

The highest MAS values for left or right ankle plantar flexors, left or right knee extensors, and left or right hip adductors were pooled into muscle group variables. A maximal spasticity variable, representing the maximal MAS score in any muscle group, was also used for analysis. The bivariate relationship between the spasticity variables and gait/balance was first analysed by calculating Spearman's correlation coefficient,  $\rho$ . Then bivariate recursive partitioning was used to divide the participants into subgroups that explained the impact of spasticity on gait or balance. A conditional interference framework was used to determine the statistical interference of the subgrouping (Hothorn, Hornik, & Zeileis, 2006). Multivariate recursive partitioning was then used to fit a model that included spasticity in all three muscle groups. Age, sex, and years since diagnosis were then included to evaluate the influences of nonmodifiable covariates on

the muscle group model. The relationship between maximal spasticity and balance was also examined with multivariate recursive partitioning, and the impact of covariates was evaluated. The association between maximal spasticity and gait was consistent with the assumption of the regression analysis and was described as a linear function. A multivariate linear regression model was used to evaluate the impacts of the covariates age, sex, and years since diagnosis.

## 2.5 | Ethics

All patients provided written consent before participating in the study. The study was conducted in accordance with the Declaration of Helsinki (World Medical Association, 2013). We submitted the study for review by the Regional Committees for Medical and Health Research Ethics, but the Norwegian Social Science Data (NSD) was considered the relevant institution for approval. The study was approved by NSD (NSD, ID 43393).

## 3 | RESULTS

During the inclusion period of September 2015–January 2016, thirty-five individuals were recruited. Four participants withdrew their consent because they were unable to participate at the scheduled testing times, and one person was excluded from the study due to an MS exacerbation (EDSS score of 8.0). Thus, 30 participants ultimately participated in the entire study, including 21 women and nine men. They were between 24 and 68 years old, with no significant differences in age relating to sex ( $p = .432$ ). Most of the participants had relapsing–remitting MS, and the mean (SD) time since diagnosis was 12 (8) years, although this varied from less than 1 to 26 years. Descriptive characteristics are listed in Table 1. Ten individuals used spasmolytic medications, with baclofen being the most commonly used medication (six individuals), whereas three participants used cannabidiol-tetrahydrocannabinol and one participant received botulinum toxin A treatments. The participants had spasticity scores of 0–3 points on the MAS (Table 2). The median score for the ankles was 1+,

**TABLE 1** Characteristics of the participants

Variable	( <i>n</i> = 30)
Female, <i>n</i> (%)	21 (70)
Male, <i>n</i> (%)	9 (30)
Age, years: mean (SD)	47.3 (12)
MS type, <i>n</i> (%)	
Primary progressive	2 (6.7)
Secondary progressive	5 (16.7)
Relapsing–remitting MS	23 (76.7)
Years since diagnosis, mean (SD)	12 (8)
Used medications to reduce spasticity, <i>n</i> (%)	10 (33.3)
Physiotherapy treatment for MS, <i>n</i> (%)	23(56.7)
Meters walked in the 2MWT, mean (SD)	134 (59.9)
Mini-BESTest scores, mean (SD)	17 (6.9)

Abbreviations: Mini-BESTest, Mini-Balance Evaluation Systems Test; MS, multiple sclerosis; SD, standard deviation; 2MWT, 2-Minute Walk Test.

**TABLE 2** Spasticity measured with Modified Ashworth Scale (MAS)

MAS score	Ankle plantar flexors n (%)	Knee extensors n (%)	Hip adductors n (%)	Maximum MAS score n (%)
0	8 (26)	13 (43)	15 (50)	5 (17)
1	6 (20)	7 (23)	11 (37)	6 (20)
1+	10 (33)	3 (10)	2 (7)	8 (27)
2	6 (20)	4 (13)	2 (7)	8 (27)
3	0 (0)	3 (10)	0 (0)	3 (10)

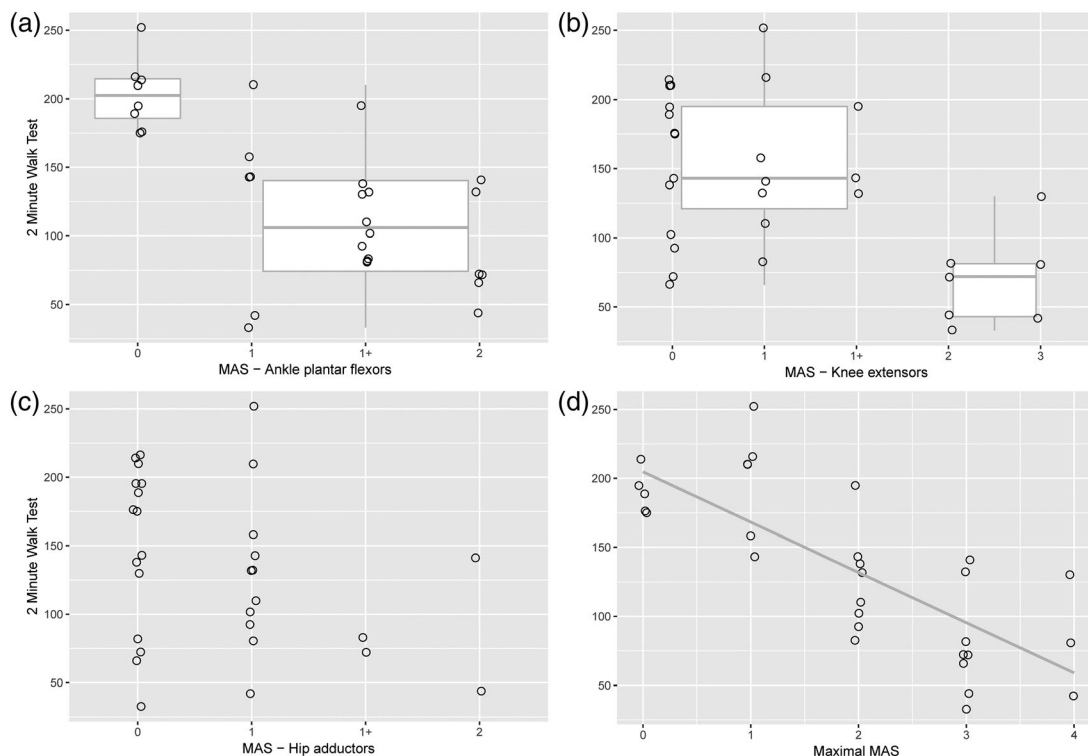
and most of the participants had scores of 0 for the hip adductors and knee extensors.

Seven participants (23%) used their habitual assistance device during testing (i.e., walker and crutches; Table 1). Based on the descriptive results of the 2MWT, participants who did not use assistance devices (23 participants) walked a mean (SD) of 153.1 (52.2) metres, compared with 72.7 (37.3) metres for patients who used their devices (seven participants), representing a significant difference in the functional level ( $p = .001$ ). The balance results were also significantly different between the groups stratified by the use of assistance devices (12.1-point difference; 19.9 points vs. 7.8 points,  $p < .001$ ). When exploring gender-related differences, women walked a mean of 28 (95% [-19.6, 77.3]) metres less than men, however, not a significant difference ( $p = .233$ ). Sex-related differences in the Mini-BESTest scores were not observed ( $p = .911$ ).

The 2MWT ranged from 33 to 252 m, and the association between the 2MWT and spasticity was moderate to strong, as shown in Figure 1 a-d. We observed a moderate correlation between spasticity of the ankle plantar flexors and the 2MWT result ( $\rho = -.69$ ,  $p < .001$ ). The recursive partitioning resulted in two subgroups. The participants without spasticity (MAS = 0) walked a mean (SD) of 203.38 (25.39) metres, whereas participants with a MAS score  $\geq 1$  walked 109.14 (47.45) metres ( $p = .001$ ). Spasticity in the knee extensors was also moderately associated with walking distance ( $\rho = -.45$ ,  $p = .012$ ). A significant difference was determined. The participants with a MAS score  $\leq 1+$  walked a mean (SD) of 154.1 (51.53) metres, whereas participants with a MAS score of 2 or 3 walked 69.1 (33.38) metres ( $p = .025$ ). We did not identify any significant correlation between spasticity in hip adductors and gait ( $\rho = -.30$ ,  $p = .105$ ). The multivariate analysis indicated a combined effect of spasticity in the ankle plantar flexors and knee extensors on the 2MWT result (Figure 3). Three different subgroups were identified. If spasticity was present in the ankle planter flexors, a MAS knee extensor score  $\geq 2$  resulted in a further decrease in walking distance.

A linear relationship between maximal MAS score of the lower extremity and the 2MWT result was observed ( $r = -.77$ ,  $p < .001$ ), as shown in Figure 1d. The linear regression analyses showed a reduction in the walking distance by -36.43 m per 1-point increase in the maximal MAS score. Adjustments for age ( $\beta = -36.11$ ), sex ( $\beta = -38.98$ ), and years since diagnosis ( $\beta = -38.98$ ) had only minor impacts on this result.

The Mini-BESTest total score ranged from 2 to 27 points. The correlation analysis revealed a moderate correlation between spasticity in the ankle plantar flexors and balance, as measured by Mini-BESTest



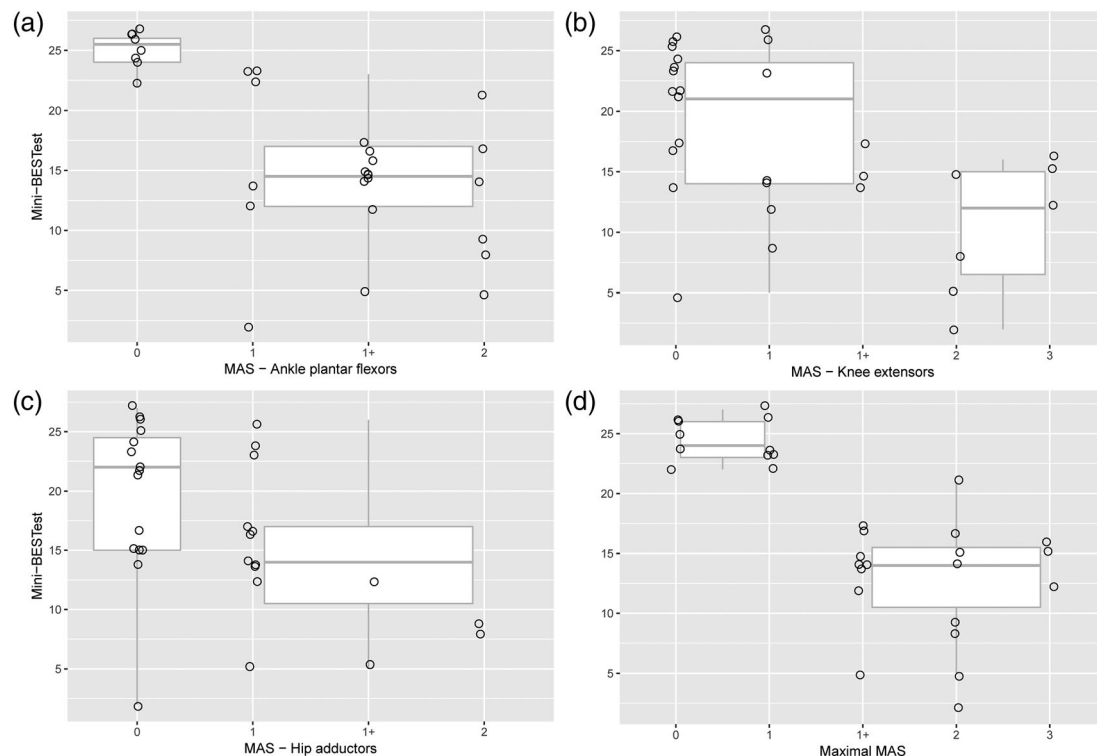
**FIGURE 1** The relationship between spasticity (Modified Ashworth Scale [MAS]) and gait length (2-Minute Walk Test [2MWT]). Circles indicate individual observations. Box plots are divided according to the results from recursive partitioning. The line indicates a linear regression curve

( $\rho = -.69, p < .001$ ) shown in Figure 2a. The recursive partitioning resulted in two subgroups. The participants with a MAS score of 0 had a mean (SD) Mini-BESTest score of 25 (1.6), whereas participants with a MAS score  $\geq 1$  received a Mini-BESTest score of 14.09 (5.71,  $p = .002$ ). The correlation between knee extensor spasticity and Mini-BESTest scores was moderate ( $\rho = -.52, p = .003$ ). Similar to the ankle plantar flexors, two terminal subgroups were identified (Figure 2b). The participants with MAS scores  $\leq 1+$  had a mean (SD) Mini-BESTest score of 19 (6.12), whereas participants with MAS scores  $\geq 2$  received a Mini-BESTest score of 10.43 (5.5,  $p = .022$ ). Spasticity in hip adductors was also related to balance ( $\rho = -.5, p = .005$ ; Figure 2c). A significant mean (SD) difference was observed between participants with a MAS score of 0 and a Mini-BESTest score of 19.6 (6.66), whereas participants with a MAS score  $\geq 1$  received a Mini-BESTest score of 14.4 (6.41,  $p = .043$ ; Figure 2d). The exploratory multivariate recursive partitioning produced three subgroups (Figure 3). An increased tone of the ankle plantar flexors resulted in a reduced balance score. Participants with a MAS ankle plantar flexor score  $\geq 1$  in combination with a MAS knee extensor score  $\geq 2$  had the lowest Mini-BESTest scores. We also identified a significant correlation between Mini-BESTest results and the maximal MAS score (independent of musculature;  $\rho = -.73, p < .001$ ; Figure 2d). A significant mean (SD) difference was observed between participants with a maximal MAS score of 0 or 1, with a mean of 24.36 (1.75), compared with participants with a MAS score of  $\geq 1+$ , with a mean of 12.74 (4.87,  $p < .001$ ). This association did not change when age, sex, or time since diagnosis was included in the model.

## 4 | DISCUSSION

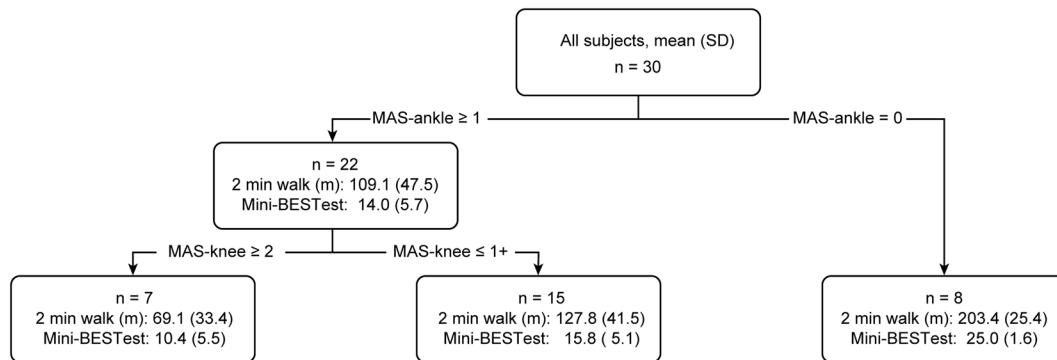
We identified a strong association between spasticity, gait, and balance tested with clinical measurement tools. The maximal spasticity score of the lower extremities moderately correlated with walking distance and balance. For each increase in the level of spasticity, a significant decrease in walking distance was observed, whereas a MAS score of  $\geq 1+$  resulted in significantly decreased balance. When analysing separate muscle groups, only a slight increase in ankle plantar flexor muscle tone (MAS score  $\geq 1$ ) correlated with a decrease in walking distance. An increased knee extensor tone equivalent to a MAS score  $\geq 2$  exhibited the strongest correlations with both walking distance and balance. Spasticity in the hip adductors moderately correlated with balance, whereas no association with walking distance was observed.

The significant correlation between spasticity and gait may indicate that spasticity negatively affects mobility. One explanation for the impact on gait is alterations in presynaptic inhibition and central modulation (Nielsen, Anderson, & Sinkjaer, 2000). According to results from a Danish study, alterations in the stretch reflex threshold in the ankle (Nielsen et al., 2000) activate triceps surae contraction, thus negatively affecting the forward movement of the body over the foot in the early stance phase. Spasticity in the ankle plantar flexors also leads to an early toe-off during the early swing phase, in addition to a suppressed dorsiflexion of the ankle due to a strong activation of the triceps surae musculature (Nielsen et al., 2000; Pau, Coghe, Corona, Marrosu, & Cocco, 2015). As shown in our study, spasticity in knee extensors exerts a strong impact when spasticity is classified



**FIGURE 2** The relationship between spasticity (Modified Ashworth Scale [MAS]) and balance (Mini-Balance Evaluation Systems Test [Mini-BESTest]). Circles indicate individual observations. Box plots are divided according to the results from recursive partitioning





**FIGURE 3** The classification tree from the multivariate recursive partitioning. Recursive partitioning classified participants into dichotomous subgroups on the basis of the exploratory variables. Predictor variables were the Modified Ashworth Scale (MAS) scores for ankle plantar flexors (MAS-ankle) and knee extensors (MAS-knee). Modelling for the two different dependent variables, the 2MWT and Mini-BESTest resulted in equal classification trees. Both analyses are therefore presented in the same figure. Means (standard deviations) for each dependent variable are provided for each subgroup

as moderate or severe. The quadriceps muscles exhibit increased muscular activation during gait (Coghe et al., 2015; Pau et al., 2015), and spasticity in the knee extensors leads to an overall reduction in knee flexion during walking (Pau et al., 2015). In a study reporting treatment effects of cannabidiol-tetrahydrocannabinol (Coghe et al., 2015), the authors note that a reduction in spasticity in the quadriceps musculature was the dominant factor contributing to gait improvement. The clinical significance of knee extensor spasticity is also highlighted in our study. Our results are consistent with those of other studies, implying that spasticity in the ankle musculature disturbs gait in the early stages, whereas proximal muscles have a larger impact on gait in the presence of moderate or severe spasticity. We did not identify significant associations between spasticity in hip adductors and gait, despite previous findings that hip adductors are commonly affected in people with MS (Coghe et al., 2015; Pau et al., 2015). However, only four participants had a spasticity score  $> 1$  in the adductors, which limited further analyses.

In contrast to a recent study concluding that spasticity is not correlated with the risk of falls or represents a contribution to dynamic stability (Peebles, Bruetsch, Lynch, & Huisinga, 2017), we observe a significant correlation between spasticity and the balance variables, although the results were not linear. We chose Mini-BESTest as measurement tool, which examines different aspects of balance, including dynamic balance (Horak et al., 2009). A cut-off of 19 points on the Mini-BESTest has been proposed (Mak & Auyeung, 2013). Using this cut-off, our population displays a high risk of falling. According to another study, the risk of falling increased by 14% for each increase in the MAS score (Nilsagard et al., 2009). The results from our study corroborate the findings in Nilsagard et al. (2009) that spasticity, particularly in the triceps surae and hip adductors, negatively affects balance in subjects even with low levels of spasticity. As shown in Figures 1 and 2, the association between spasticity and balance is greater than the association between spasticity and gait throughout the different muscle groups. Spasticity in the ankle plantar flexors and hip adductors exhibited the same pattern in balance, whereas knee extensors increased the strength of the association in patients

with a MAS score  $\geq 2$ . On the basis of these results, our study contributes to the determination of a clinically significant cut-off for spasticity in different muscle groups in future studies.

To the best of our knowledge, the significant correlation between spasticity in different muscle groups and mobility in our study has not been reported previously. Most studies have investigated the presence of spasticity in the ankle musculature (Balantrapu et al., 2014; Kremer et al., 2014; Sosnoff et al., 2010; Sosnoff, Gappmaier, Frame, & Motl, 2011). Using the Mini-BESTest, spasticity in the ankle plantar flexors and hip adductors negatively influenced balance in participants with a MAS score  $\geq 1$ , with a mean change of more than 10 points in the ankle plantar flexors and 5.2 points in the adductors per increase in MAS score. As a change of 4 points or more reflects a clinical change (Godi et al., 2013), we consider this finding important. Similar to the gait results, spasticity in the knee extensors significantly affected balance when the muscle tone was increased throughout the range of motion (MAS  $\geq 2$ ). When spasticity was evident in several muscle groups (Figure 3), we identified a mean reduction in balance exceeding 5 points. The significant correlation between spasticity in ankle plantar flexors and mobility is potentially explained by alterations in the ability to efficiently use the ankle strategy, as spasticity is thought to affect this mechanism (Sosnoff et al., 2010). The ankle strategy is one of the strategies that is first activated when balance is challenged, and thus, spasticity-induced alterations in muscle activation influence balance in patients even with low levels of increased muscle tone. In mediolateral sway, the hip abductors and adductors are most active (Shumway-Cook & Woollacott, 2012). In people with MS, the increase in postural sway mainly occurs in the mediolateral direction (Sosnoff et al., 2010), which is associated with the risk of falling (Cameron & Lord, 2010). This finding may explain why spasticity in the knee extensors does not significantly impact balance before moderate spasticity is evident.

Several factors may have affected our results. Because we used a convenient sample, the results are prone to selection bias and are not representative of the general population of people with MS. Although we identified a significant correlation between spasticity,

gait, and balance, the cross-sectional design makes the interpretation of the direction of the association difficult. Paresis or weakness in the muscle groups (Wagner et al., 2014), in combination with changes in proprioceptive, vestibular, and visual signals (Brichetto, Piccardo, Pedulla, Battaglia, & Tacchino, 2015), is associated with reduced ambulatory abilities and balance. Although we tried to eliminate these factors by applying defined exclusion criteria, these symptoms were not examined specifically during testing. Thus, we are unable to conclude that the results from our study were not biased by other MS symptoms. In the inclusion criteria, we also excluded participants with a high symptom severity (described as an EDSS score > 6.5), but the EDSS score was not recorded specifically. Because of this, we do not know how the MS severity differed between the participants.

Additionally, 10 individuals in this study used spasmolytic medications, which may have reduced spasticity during testing without necessarily improving the results associated with the clinical mobility variables, as reported in some studies (Nielsen et al., 2000; Orsnes, Sorensen, Larsen, & Ravnborg, 2000), and may have affected the strength of the association. However, we performed a stratified analysis to determine whether spasticity medications altered the results, but the participants who were on medication showed the same trends as the patients who were not taking medication. Participants who were on medication did not diverge from the results of other participants, and thus, this comparison has not been emphasized in the results chapter.

The small sample size is another limitation. Although sufficiently powered to ensure internal validity, the results should be generalized with caution. Notably, significant skewing is observed in the population (70% women); however, the uneven sex distribution in patients with MS is well known, and thus, the results related to sex, in particular, must be interpreted as trends.

Spasticity was measured with the MAS, a measurement tool that has been discussed for its clinical relevance (Arroyo et al., 2013; Rekand, 2010; Sosnoff et al., 2011) and its lack of ability to differentiate the reasons for increased resistance of movement (Johnson, 2002). In other studies, MAS showed good correlations with self-reported spasticity (Arroyo et al., 2013), although its reliability has been questioned (Ghotbi et al., 2011).

#### 4.1 | Implications for physiotherapy practice

Physiotherapy is often viewed as an additional treatment option to pharmacological management, normally focusing on functions affected by spasticity. In one Cochrane review (Amatya, Khan, Mantia, Demetrios, & Wade, 2013), the authors reported the strongest evidence for reduced spasticity when physiotherapy was combined with a pharmacological intervention. Some studies claim that spasticity is beneficial to patients (Newsome et al., 2017; Satkunam, 2003) and should be treated only when imposing restrictions to the individual. As indicated in the present study, even low levels of spasticity may limit function. Based on accumulating evidence, spasticity is a common manifestation in people with MS (Rizzo et al., 2004), occurs early after diagnosis (Patti & Vila, 2014; Vermersch, 2014), increases impairment

throughout the lifespan (Kister et al., 2013), is associated with pain, and exerts a substantial impact on quality of life and daily activities (Flachenecker et al., 2014). People with MS rate walking ability and ambulation as the most important functions, independent of MS severity (Heesen et al., 2008). Despite the conflicting evidence regarding the association between spasticity and gait (Balantrapu et al., 2014; Balantrapu, Sandroff, Sosnoff, & Motl, 2012; Kremer et al., 2014; Peebles et al., 2017; Sosnoff et al., 2011; Wagner et al., 2014), people with MS have reported restricted mobility to be one of the most disturbing symptoms of spasticity (Flachenecker et al., 2014). Spasticity was a predictor of future falls (Nilsagard et al., 2009) and exacerbated overall disability (Flachenecker et al., 2014) in several studies.

In conclusion, our data provide a strong indication for an important relationship between spasticity and gross motor function. Future studies should explore whether spasmolytic medications and physiotherapy treatments aimed at reducing spasticity improve gait and balance function in subjects with MS. Physiotherapists are experienced in evaluating both spasticity and mobility, and an awareness of spasticity in the early stages may help prevent secondary complications associated with the symptom.

#### ACKNOWLEDGEMENTS

We are grateful for the patients participating in the study and for Molde Hospital for facilitating the study. We are especially thankful to the Eline Hoff Austad, Kristine Fredriksen Hjellseth, and Kirsten Eiesland Bjørge who conducted the physical testing.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

#### FUNDING INFORMATION

No financial support was received during the data collection, but we received funding from The Norwegian Fund for Post-Graduate Training in Physiotherapy for publishing the article.

#### ORCID

Anja Davis Norbye  <https://orcid.org/0000-0003-3529-1111>

#### REFERENCES

- Amatya, B., Khan, F., La Mantia, L., Demetrios, M., & Wade, D. T. (2013). Non pharmacological interventions for spasticity in multiple sclerosis. *Cochrane Database of Systematic Reviews*, 2, CD009974. <https://doi.org/10.1002/14651858.CD009974.pub2>
- Arroyo, R., Massana, M., & Vila, C. (2013). Correlation between spasticity and quality of life in patients with multiple sclerosis: The CANDLE study. *International Journal of Neuroscience*, 123, 850–858. <https://doi.org/10.3109/00207454.2013.812084>
- Baert, I., Freeman, J., Smedal, T., Dalgas, U., Romberg, A., Kalron, A., ... Feys, P. (2014). Responsiveness and clinically meaningful improvement, according to disability level, of five walking measures after rehabilitation in multiple sclerosis: A European multicenter study. *Neurorehabilitation and Neural Repair*, 28, 621–631. <https://doi.org/10.1177/1545968314521010>

- Balantrapu, S., Sandroff, B. M., Sosnoff, J. J., & Motl, R. W. (2012). Perceived impact of spasticity is associated with spatial and temporal parameters of gait in multiple sclerosis. *ISRN Neurology*, 2012, 675431. <https://doi.org/10.5402/2012/675431>
- Balantrapu, S., Sosnoff, J. J., Pula, J. H., Sandroff, B. M., & Motl, R. W. (2014). Leg spasticity and ambulation in multiple sclerosis. *Multiple Sclerosis International*, 2014, 649390. <https://doi.org/10.1155/2014/649390>
- Barnes, M. P., Kent, R. M., Semlyen, J. K., & McMullen, K. M. (2003). Spasticity in multiple sclerosis. *Neurorehabilitation and Neural Repair*, 17(1), 66–70. <https://doi.org/10.1177/0888439002250449>
- Bethoux, F. (2013). Gait disorders in multiple sclerosis. *Continuum (Minneapolis, Minn.)*, 19, 1007–1022. <https://doi.org/10.1212/01.CON.0000433286.92596.d5>
- Bethoux, F., & Marrie, R. A. (2016). A cross-sectional study of the impact of spasticity on daily activities in multiple sclerosis. *Patient*, 9, 537–546. <https://doi.org/10.1007/s40271-016-0173-0>
- Brichetto, G., Piccardo, E., Pedulla, L., Battaglia, M. A., & Tacchino, A. (2015). Tailored balance exercises on people with multiple sclerosis: A pilot randomized, controlled study. *Multiple Sclerosis Journal*, 21, 1055–1063. <https://doi.org/10.1177/1352458514557985>
- Cameron, M. H., & Lord, S. (2010). Postural control in multiple sclerosis: Implications for fall prevention. *Current Neurology and Neuroscience Reports*, 10, 407–412. <https://doi.org/10.1007/s11910-010-0128-0>
- Cameron, M. H., & Wagner, J. M. (2011). Gait abnormalities in multiple sclerosis: Pathogenesis, evaluation, and advances in treatment. *Current Neurology and Neuroscience Reports*, 11, 507–515. <https://doi.org/10.1007/s11910-011-0214-y>
- Coghe, G., Pau, M., Corona, F., Frau, J., Loreface, L., Fenu, G., ... Cocco, E. (2015). Walking improvements with nabiximols in patients with multiple sclerosis. *Journal of Neurology*, 262, 2472–2477. <https://doi.org/10.1007/s00415-015-7866-5>
- Cohen, J. (1977). *Statistical power analysis for the behavioral sciences*. Cambridge, MA: Academic Press.
- Flachenecker, P., Henze, T., & Zettl, U. K. (2014). Spasticity in patients with multiple sclerosis—Clinical characteristics, treatment and quality of life. *Acta Neurologica Scandinavica*, 129(3), 154–162. <https://doi.org/10.1111/ane.12202>
- Franchignoni, F., Godi, M., Guglielmetti, S., Nardone, A., & Giordano, A. (2015). Enhancing the usefulness of the Mini-BESTest for measuring dynamic balance: A Rasch validation study. *European Journal of Physical and Rehabilitation Medicine*, 51, 429–437.
- Ghotbi, N., Ansari, N. N., Naghdi, S., & Hasson, S. (2011). Measurement of lower-limb muscle spasticity: Intrarater reliability of modified modified Ashworth scale. *Journal of Rehabilitation Research and Development*, 48(1), 83–88. <https://doi.org/10.1682/JRRD.2010.02.0020>
- Godi, M., Franchignoni, F., Caligari, M., Giordano, A., Turcato, A. M., & Nardone, A. (2013). Comparison of reliability, validity, and responsiveness of the mini-BESTest and Berg balance scale in patients with balance disorders. *Physical Therapy*, 93(2), 158–167. <https://doi.org/10.2522/ptj.20120171>
- Gunn, H., Creanor, S., Haas, B., Marsden, J., & Freeman, J. (2013). Risk factors for falls in multiple sclerosis: An observational study. *Multiple Sclerosis Journal*, 19, 1913–1922. <https://doi.org/10.1177/1352458513488233>
- Hamre, C., Botolfsen, P., Tangen, G. G., & Helbostad, J. L. (2017). Interrater and test-retest reliability and validity of the Norwegian version of the BESTest and mini-BESTest in people with increased risk of falling. *BMC Geriatrics*, 17(1), 92. <https://doi.org/10.1186/s12877-017-0480-x>
- Heesen, C., Bohm, J., Reich, C., Kasper, J., Goebel, M., & Gold, S. M. (2008). Patient perception of bodily functions in multiple sclerosis: Gait and visual function are the most valuable. *Multiple Sclerosis Journal*, 14, 988–991. <https://doi.org/10.1177/1352458508088916>
- Horak, F. B., Wrisley, D. M., & Frank, J. (2009). The Balance Evaluation Systems Test (BESTest) to differentiate balance deficits. *Physical Therapy*, 89, 484–498. <https://doi.org/10.2522/ptj.20080071>
- Hothorn, T., Hornik, K., & Zeileis, A. (2006). Unbiased recursive partitioning: A conditional inference framework. *Journal of Computational and Graphical Statistics*, 15, 651–674. <https://doi.org/10.1198/106186006X133933>
- Johnson, G. R. (2002). Outcome measures of spasticity. *European Journal of Neurology*, 9, 10–16. <https://doi.org/10.1046/j.1468-1331.2002.0090s1010.x>
- Kister, I., Bacon, T. E., Chamot, E., Salter, A. R., Cutter, G. R., Kalina, J. T., & Herbert, J. (2013). Natural history of multiple sclerosis symptoms. *International Journal of MS Care*, 15(3), 146–158. <https://doi.org/10.7224/1537-2073.2012-053>
- Kremer, T. R., Van Dillen, L. R., & Wagner, J. M. (2014). Dynamometer-based measure of spasticity confirms limited association between plantarflexor spasticity and walking function in persons with multiple sclerosis. *Journal of Rehabilitation Research and Development*, 51, 975–984. <https://doi.org/10.1682/JRRD.2013.08.0186>
- Kurtzke, J. F. (1983). Rating neurologic impairment in multiple sclerosis: An Expanded Disability Status Scale (EDSS). *Neurology*, 33, 1444–1452. <https://doi.org/10.1212/WNL.33.11.1444>
- Lance, J. W. (1980). Symposium synopsis. In R. G. Feldman, R. R. Young, & W. P. Koella (Eds.), *Spasticity, disordered motor control* (pp. 485–494). Chicago, IL: Year Book Medical Publishers.
- Mak, M. K., & Auyeung, M. M. (2013). The mini-BESTest can predict parkinsonian recurrent fallers: A 6-month prospective study. *Journal of Rehabilitation Medicine*, 45, 565–571. <https://doi.org/10.2340/16501977-1144>
- Newsome, S. D., Aliotta, P. J., Bainbridge, J., Bennett, S. E., Cutter, G., Fenton, K., ... Jones, D. E. (2017). A framework of care in multiple sclerosis, part 2: Symptomatic care and beyond. *International Journal of MS Care*, 19(1), 42–56. <https://doi.org/10.7224/1537-2073.2016-062>
- Nielsen, J. F., Anderson, J. B., & Sinkjaer, T. (2000). Baclofen increases the soleus stretch reflex threshold in the early swing phase during walking in spastic multiple sclerosis patients. *Multiple Sclerosis Journal*, 6(2), 105–114. <https://doi.org/10.1177/13524585000600209>
- Nilsagard, Y., Lundholm, C., Denison, E., & Gunnarsson, L. G. (2009). Predicting accidental falls in people with multiple sclerosis—A longitudinal study. *Clinical Rehabilitation*, 23, 259–269. <https://doi.org/10.1177/0269215508095087>
- Orsnes, G. B., Sorensen, P. S., Larsen, T. K., & Ravnborg, M. (2000). Effect of baclofen on gait in spastic MS patients. *Acta Neurologica Scandinavica*, 101, 244–248. <https://doi.org/10.1034/j.1600-0404.2000.101004244x/>
- Patti, F., & Vila, C. (2014). Symptoms, prevalence and impact of multiple sclerosis in younger patients: A multinational survey. *Neuroepidemiology*, 42, 211–218. <https://doi.org/10.1159/000360423>
- Pau, M., Coghe, G., Corona, F., Marrosu, M. G., & Cocco, E. (2015). Effect of spasticity on kinematics of gait and muscular activation in people with multiple sclerosis. *Journal of the Neurological Sciences*, 358, 339–344. <https://doi.org/10.1016/j.jns.2015.09.352>
- Peebles, A. T., Bruetsch, A. P., Lynch, S. G., & Huisinga, J. M. (2017). Dynamic balance is related to physiological impairments in persons with multiple sclerosis. *Archives of Physical Medicine and Rehabilitation*, 99, 2030–2037. <https://doi.org/10.1016/j.apmr.2017.11.010>



- Polman, C. H., Reingold, S. C., Banwell, B., Clanet, M., Cohen, J. A., Filippi, M., ... Wolinsky, J. S. (2011). Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Annals of Neurology*, *69*, 292–302. <https://doi.org/10.1002/ana.22366>
- R Core Team. (2017). A language and environment for statistical computing (Version R Version 3.4.2 (2017-09-28) -- "Short Summer"): R foundation for statistical computing. Retrieved from <https://www.R-project.org/>
- Rasova, K., Martinkova, P., Vyskotova, J., & Sedova, M. (2012). Assessment set for evaluation of clinical outcomes in multiple sclerosis: Psychometric properties. *Patient Related Outcome Measures*, *3*, 59–70. <https://doi.org/10.2147/PROM.S32241>
- Rekand, T. (2010). Clinical assessment and management of spasticity: A review. *Acta Neurologica Scandinavica. Supplementum*, *122*(190), 62–66. <https://doi.org/10.1111/j.1600-0404.2010.01378.x>
- Rizzo, M. A., Hadjimichael, O. C., Preiningerova, J., & Vollmer, T. L. (2004). Prevalence and treatment of spasticity reported by multiple sclerosis patients. *Multiple Sclerosis Journal*, *10*, 589–595. <https://doi.org/10.1191/1352458504ms1085oa>
- Satkunam, L. E. (2003). Rehabilitation medicine: 3. Management of adult spasticity. *Canadian Medical Association Journal*, *169*, 1173–1179.
- Shumway-Cook, A., & Woollacott, M. H. (2012). *Motor control—Translating research into clinical practice* (4th ed.). Baltimore, MD: Lippincott Williams & Wilkins.
- Sosnoff, J. J., Gappmaier, E., Frame, A., & Motl, R. W. (2011). Influence of spasticity on mobility and balance in persons with multiple sclerosis. *Journal of Neurologic Physical Therapy*, *35*(3), 129–132. <https://doi.org/10.1097/NPT.0b013e31822a8c40>
- Sosnoff, J. J., Shin, S., & Motl, R. W. (2010). Multiple sclerosis and postural control: The role of spasticity. *Archives of Physical Medicine and Rehabilitation*, *91*(1), 93–99. <https://doi.org/10.1016/j.apmr.2009.09.013>
- Stokes, M. (2004). *Physical management in neurological rehabilitation* (Vol. 2). London: Elsevier Mosby.
- Svensson, J., Borg, S., & Nilsson, P. (2014). Costs and quality of life in multiple sclerosis patients with spasticity. *Acta Neurologica Scandinavica*, *129*(1), 13–20. <https://doi.org/10.1111/ane.12139>
- Thompson, A. J., Baranzini, S. E., Geurts, J., Hemmer, B., & Ciccarelli, O. (2018). Multiple sclerosis. *Lancet*, *391*, 1622–1636. [https://doi.org/10.1016/s0140-6736\(18\)30481-1](https://doi.org/10.1016/s0140-6736(18)30481-1)
- Vermersch, P. (2014). MObility ImproVEment with spasticity in multiple sclerosis in Europe: The MOVE 1 EU study. *Neurodegenerative Disease Management*, *4*, 407–415. <https://doi.org/10.2217/nmt.14.44>
- Wagner, J. M., Kremer, T. R., Van Dillen, L. R., & Naismith, R. T. (2014). Plantarflexor weakness negatively impacts walking in persons with multiple sclerosis more than plantarflexor spasticity. *Archives of Physical Medicine and Rehabilitation*, *95*, 1358–1365. <https://doi.org/10.1016/j.apmr.2014.01.030>
- World Medical Association (2013). World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. *JAMA*, *310*, 2191–2194. <https://doi.org/10.1001/jama.2013.281053>
- Zettl, U. K., Henze, T., Essner, U., & Flachenecker, P. (2014). Burden of disease in multiple sclerosis patients with spasticity in Germany: Mobility improvement study (Move I). *The European Journal of Health Economics*, *15*, 953–966. <https://doi.org/10.1007/s10198-013-0537-5>

**How to cite this article:** Norbye AD, Midgard R, Thrane G. Spasticity, gait, and balance in patients with multiple sclerosis: A cross-sectional study. *Physiother Res Int*. 2019;e1799. <https://doi.org/10.1002/pri.1799>