Higher Lower Limb Strength Asymmetry may be Indicative of Functional Changes in Persons with Multiple Sclerosis

Callie Evanchick, SPT[1], Nicholas Lopez, SPT[1], Elizabeth S. Gromisch, PhD[2-5], Marc Campo, PT, PhD[1], and Heather M. DelMastro, MS[2,3]

(1)Department of Physical Therapy, Mercy University, Dobbs Ferry, NY, USA
(2)Mandell Center for Multiple Sclerosis, Mount Sinai Rehabilitation Hospital, Trinity Health Of New England, Hartford, CT
(3)Department of Rehabilitative Medicine, Frank H. Netter MD School of Medicine at Quinnipiac University, North Haven, CT
(4)Department of Medical Sciences, Frank H. Netter MD School of Medicine at Quinnipiac University, North Haven, CT
(5)Department of Neurology, University of Connecticut School of Medicine, Farmington, CT
Contact information: Heather DelMastro: Heather.DelMastro@trinityhealthofne.org

Trinity Health Of New England | Mandell MS Center
Trinity Health Of New England | Mount Sinai Rehabilitation Hospital
MERCY UNIVERSITY

Background

Research suggests that fall risk, pace of gait, and lower limb asymmetry are among the greatest contributors to falls and fear of falling in persons with MS (PwMS).[1] Lower limb (LL) asymmetry has been associated with decreased stability and increased fear of falling in this patient population.[2] Currently, most research involving MS and strength asymmetry uses 10% as a cutoff to signify a significant difference; however, to the best of our knowledge, there does not appear to be a reason for this selection, that is supported by data.

Objectives

The aim of this study is to determine the percentage of LL strength asymmetry (% asymmetry) in various muscle groups that corresponds to functional changes in PwMS.

Methods

Participants

- A convenience sample of 183 individuals with a diagnosis of MS and no contraindications to exercise.
- Mean (SD) age = 53.0 (19.0) years, BMI = 26.0 (9.8) kg/m2, Disease duration = 12.8 (12.0) years, 5-item Modified Fatigue Impact Scale (MFIS-5) = 10.0 (7.0)
- 78% Female

Study Design

- Secondary analysis from a larger cross-sectional study.[3]
- Data was collected at a one-time visit including demographics (age, gender, BMI) and disease characteristics (disease duration and fatigue: MFIS-5).

Main Outcome Measures:

1. **% asymmetry:** ((stronger limb-weaker limb)/stronger limb x 100) using the isometric peak torque for hip abduction (HA), extension (HE), and flexion (HF), knee extension (KE) and flexion (KF), and ankle plantarflexion (APF) and dorsiflexion (ADF).
2. **Functional level:** scores from the 12-item Multiple Sclerosis Walking Scale (MSWS-12) were used to classify participants as having none (0-24.99), mild (25-49.99), moderate (50-74.99), or severe (75-100) functional impairment.[4]

Statistical Analysis

- Kruskal-Wallis test was performed to compare demographics, disease characteristics, and % asymmetry between functional levels.
- Muscle groups with significant differences ($p < .05$) were further examined using receiver operating characteristic (ROC) curves.
- Areas under the curve (AUCs) were calculated for each significant % asymmetry's accuracy in differentiating between none and severe functional impairment, with optimal cut-off scores determined using the Youden index[5] and the Index of Union **(Table 1)**.[6]
  - The sensitivity and specificity using the 10% cut-off was also calculated for comparative purposes.
- Exploratory binary logistic regression performed to determine which % asymmetry cut-off was the best predictor of none versus severe functional impairment after controlling for covariates **(Table 2)**.

Results

Significant differences were noted between disease severity categories and KE, KF, and ADF. The chosen thresholds performed better than the traditional 10% when predicting impairment category.

Table 1. Lower limb asymmetry cut-offs and their sensitivities and specificities

Muscle Group	Functional Impairment Cutoff %	Sensitivity	Specificity	Sum of Sensitivity and Specificity
KE	20.22%	78.79%	53.85%	1.33
KE	10.00%	80.43%	35.71%	1.16
KF	19.74%	67.19%	92.86%	1.60*
KF	10.00%	86.96%	46.43%	1.33
ADF	14.29%	67.39%	82.14%	1.50*
ADF	10.00%	78.26%	57.14%	1.35

*** A value of ≥1.5 is indicative of a good predictive test.[7]**

In the multiple logistic regression model, only Knee Flexion was significant. Participants who had KF asymmetry greater than 19.7% had odds of severe impairment that were much higher.

Table 2. Logistic regression model for % asymmetry to predict functional impairment

	R^2	Variable	Adjusted Odds Ratio	95% Confidence Interval	*P* value
Step 1	0.64	Age	1.05	0.97-1.13	0.273
		Gender	2.70	0.40-18.38	0.312
		BMI	0.98	0.91-1.07	0.093
		Disease Duration	1.08	0.99-1.19	0.665
		MFIS-5*	1.52	1.22-1.88	<0.001
Step 2	0.88	KF Asymmetry Cut-off*	218.29	2.71-17566.31	0.016
		KE Asymmetry Cut-off	42.92	0.27-6895.55	0.147
		ADF Asymmetry Cut-off	8.14	0.53-126.09	0.134
		Age	1.09	0.92-1.29	0.315
		Gender	9.06	0.32-259.87	0.198
		BMI	0.90	0.74-1.09	0260
		Disease Duration	1.06	0.89-1.26	0.530
		Fatigue*	2.81	1.19-6.64	0.018

*** Denotes $P < .05$**

Discussion

- LL strength asymmetries found in KE, KF, and ADF had a significant impact on functional levels of PwMS.
- The AUC indicated that KE (.679) had poor predictive performance, KF (.826) had good predictive performance, and ADF (.725) had fair predictive performance.[8]
  - KF > ADF > KE
- The sensitivity and specificity sums of KF (1.6) and ADF (1.5) totaled at least 1.5, indicating they were good predictive tests for functional impairment.[7]
- Current literature utilizes an arbitrary 10% cutoff for % asymmetry to indicate functional impairment.
  - However, the results of this study indicate that the real % asymmetry that is indicative of a functional change is higher than 10% in PwMS.
    - KF: 19.74%
    - ADF: 14.29%
    - KE: 20.22%
  - The 10% asymmetry cutoff typically used for these muscle groups does not meet the sensitivity and specificity threshold for being a good predictive test for functional impairment.
- Exploratory regression analysis found that the KF % asymmetry was still predictive of functional impairment after controlling for age, gender, BMI, disease duration, fatigue, as well as ADF and KE asymmetry.

Conclusion

- The amount of muscular asymmetry differentiating between PwMS with no and severe functional changes was higher than the typically used 10% criterion.
- KF asymmetry may be the most predictive of functional change in PwMS.
- The current findings provide clinicians and researchers with the knowledge that a higher threshold of % asymmetry indicates that there may be functional limitations.

Acknowledgements

This study was performed on data collected as part of a larger study supported by an internal Saint Francis BestCare Grant conducted at The Joyce D. and Andrew J. Mandell Center for Comprehensive Multiple Sclerosis Care and Neuroscience Research at the Mount Sinai Rehabilitation Hospital, Trinity Health Of New England, and approved by the Trinity Health Of New England Institutional Review Board. Dr. Gromisch is a Harry Weaver Scholar of the National MS Society.

References

1. Monaghan AS, Huisinga JM, Peterson DS. The application of principal component analysis to characterize gait and its association with falls in multiple sclerosis. Sci Rep. 2021;11(1):12811. Published 2021 Jun 17. doi:10.1038/s41598-021-92353-2
2. Kasser SL, Jacobs JV, Littenberg B, Foley JT, Cardinal BJ, Maddalozzo GF. Exploring physical activity in women with multiple sclerosis: associations with fear of falling and underlying impairments. Am J Phys Med Rehabil. 2014;93(6):461-469. doi:10.1097/PHM.0000000000000049
3. DelMastro HM, Simaitis LB, Gromisch ES, Gomes K, Ruiz JA. Establishment of Regression-Based Normative Isometric Strength Values for Major Lower Limb Muscle Groups in Persons with Multiple Sclerosis. *Multiple sclerosis and related disorders.* 2023:104772.
4. Goldman MD, Ward MD, Motl RW, Jones DE, Pula JH, Cadavid D. Identification and validation of clinically meaningful benchmarks in the 12-item Multiple Sclerosis Walking Scale. Mult Scler. 2017 Sep;23(10):1405-1414. doi: 10.1177/1352458516680749. Epub 2016 Dec 7. PMID: 27903937; PMCID: PMC5411321
5. Youden WJ. Index for rating diagnostic tests. Cancer. 1950;3(1):32-35.
6. Unal I. Defining an Optimal Cut-Point Value in ROC Analysis: An Alternative Approach. Computational and mathematical methods in medicine. 2017;2017:3762651.
7. Power M, Fell G, Wright M. Principles for high-quality, high-value testing. Evid Based Med. 2013;18(1):5-10.
8. Safari S, Baratloo A, Elfil M, Negida A. Evidence based emergency medicine; part 5 receiver operating curve and area under the curve. Emerg (Tehran). 2016;4(2):111-113.