

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Hand Grip Strength as a Predictive Tool for Upper Extremity Functionality, Balance, and Quality of Life in Patients With Multiple Sclerosis

Meral Seferoğlu, MD; Meliha Kasapoğlu Aksoy, MD; and Abdulkadir Tunç, MD

From the Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey (MS, MKA) and the Department of Neurology, Faculty of Medicine, Sakarya University, Sakarya, Turkey (AT). *Correspondence:* Meliha Kasapoğlu Aksoy, MD; *email:* melihakasapoglu@hotmail.com.

Running title: Hand Grip Strength as a Predictive Tool

doi:10.7224/1537-2073.2022-030

© 2024 Consortium of Multiple Sclerosis Centers

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Practice Points

- Hand grip strength is easy to measure with a dynamometer, yet often overlooked in the care of persons with multiple sclerosis.
- In our study, hand grip strength was strongly correlated with measures of upper extremity function, balance, falls efficacy, and quality of life.
- Hand grip strength could be a useful predictor of overall function and quality of life in persons with multiple sclerosis and it is easy to integrate into routine clinical assessments.

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Abstract

Background: Upper extremity strength and function are rarely assessed in routine multiple sclerosis (MS) care. This study aimed to evaluate hand muscle strength and functionality in individuals with MS and investigate correlations with upper extremity function, cognitive status, health-related quality of life (HRQOL), and balance.

Methods: A cross-sectional study was conducted with 45 consecutive individuals with MS between the ages of 18 and 65. Upper limb motor strength was evaluated using a hand grip strength dynamometer. Upper limb functional capacity was assessed using the Nine-Hole Peg Test (9HPT) and the Duruoz Hand Index (DHI). Balance, coordination, and falls were measured with the Berg Balance Scale (BBS), Falls Efficacy Scale (FES), and the 30-Second Chair Stand Test (30CST). Cognitive function was evaluated using the Montreal Cognitive Assessment instrument and the Symbol Digit Modalities Test. Level of HRQOL was assessed using the self-reported 54-item MS Quality of Life-54 questionnaire.

Results: Out of the 45 participants (80% women, mean age 36.6 ± 8.6 years), higher hand grip dynamometer measures were strongly correlated with better DHI, 9HPT, BBS, FES, and 30CST scores. In the regression analysis, a 1-unit increase in dynamometer measures led to a 0.383 increase in overall HRQOL score.

Conclusions: This study demonstrates that increased hand grip strength (HGS) is associated with better hand functionality, balance, and HRQOL in individuals with MS. It provides evidence to support more systematic measurement of HGS in the care of persons with MS. *Int J MS Care*. 2024; XX:XXX-XXX.

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Introduction

Multiple sclerosis (MS) is a central nervous system disease characterized by various neurological disabilities resulting from progressive inflammatory and neurodegenerative processes.¹ People with MS often experience symptoms that significantly impact their quality of life (QOL), including muscle weakness, sensory deficits, and cognitive impairment.²⁻⁴

Approximately 66% of individuals with MS experience upper limb motor impairments, greatly affecting daily activities.⁵ Hand dysfunction, along with fatigue, ambulation, and cognitive decline, has been associated with increased unemployment, which highlights the importance of addressing these deficits in MS.⁶ Despite the disabling effects and negative impact on QOL, little is known about the exact frequency and severity of upper extremity dysfunction in individuals with MS. Additionally, accurately assessing upper limb movements is challenging due to their inherent variability.

Hand grip strength (HGS) is a reliable measurement of upper extremity muscle strength to determine functional capacity. It reflects the force generated from the combined contraction of extrinsic hand muscles.⁷ HGS measurement is recommended as a modality to assess muscle strength and is the simplest method for evaluating muscle functions in clinical practice.⁸ Previous studies have shown that increased HGS is strongly associated with preserved mobility, functional status, higher levels of daily living activities, and decreased disability.⁹⁻¹¹

With an incidence of 40% to 65% in individuals with MS, cognitive impairment is reported to be a predictor of long-term disability. The severity of cognitive decline appears to be related to patients' ages and levels of physical disability, and certain cognitive aspects can predict functional status in MS.¹² Impaired balance is also a disabling symptom that negatively impacts independence and autonomy, leading to falls and injuries. It can be present even in the early stages of the disease course, sometimes even in the absence of physical disability.¹³ People with MS

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

tend to have lower health-related quality of life (HRQOL) levels.⁴ Muscle weakness, balance and gait abnormalities, fatigue, and other functional deficits significantly contribute to their lower HRQOL.^{4,14}

This study aims to evaluate HGS and hand functionality in individuals with MS and investigate their correlations with cognitive status, HRQOL, and balance states in these individuals.

Methods

Participants

This cross-sectional analytical study was conducted in the neurology department of Bursa Yüksek İhtisas Education and Research Hospital (Bursa, Turkey) from February 1, 2020 to May 1, 2020. Ethical approval was obtained from the institutional research committee, and all subjects provided written informed consent.

Physical characteristic data obtained included age, gender, time since diagnosis, and current treatments. Disability was evaluated by a neurologist using the Expanded Disability Status Scale (EDSS).¹⁵ The participants had a confirmed diagnosis of relapsing-remitting MS according to the revised McDonald criteria¹⁶ and an EDSS score between 0 and 5.5. Participants were between the ages of 18 and 65.

Exclusion criteria were current pregnancy, having an MS relapse within the preceding 3 months, sensorial problems not caused by MS, unilateral sensory perception loss, upper motor neuron injury (eg, stroke survivors), history of peripheral neuropathy, and upper limb orthopedic limitations that could interfere with study procedures.

Quantitative Measures

All assessments were performed by the same physician in a quiet, well-illuminated room.

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Upper Limb Functional Capacity: Hand Grip Strength

Upper limb motor analysis was assessed in a seated position with the patient's feet on the ground. The HGS of the dominant hand was measured by the Jamar Plus+ Digital Hand Dynamometer (Sammons Preston). Since the reliability and validity of the Jamar dynamometer has been evaluated as high, it has been considered a gold standard in the assessment of grip strength.¹⁷ Hand dominance was determined by asking the patients which hand they used for writing. The test was performed in a seated position with the shoulder of the tested arm adducted, the elbow flexed at 90°, and the forearm and wrist set in neutral position. Grip strength tests were performed 3 times with 1-minute intervals between each, and the average of the 3 measurements was calculated.¹⁸

The Nine-Hole Peg Test (9HPT) and the Duruoz Hand Index (DHI) were used to evaluate upper limb functional capacity. The 9HPT is a well-known, standardized, quantitative test of upper limb function. It has a strong test-retest reliability for individuals with MS.¹⁹ The test was performed in a seated position with the dominant hand. The chronometer was started as soon as the patient touched the first peg. The chronometer was stopped when the last peg hit the container.

The DHI is an 18-item self-report questionnaire designed to evaluate activity limitations of the hand. It was first developed for individuals with rheumatoid arthritis.²⁰ Questions are grouped in 5 domains: in the kitchen (8), dressing (2), hygiene (2), in the office (2), and other (1). The patient is instructed to answer each question in terms of the level of difficulty they experience when completing various tasks without help from another person or assistive device. Individual items are scored on a 6-point Likert scale where 0 is “without difficulty” and 5 is “impossible.” The 18 individual scores are summed to obtain a composite score. The total score ranges from 0 to 90 with higher scores indicating poorer hand functioning.

Gait and Balance

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

The Berg Balance Scale (BBS), Falls Efficacy Scale (FES), and the 30-Second Chair to Stand Test (30CST) were used to assess balance, coordination, and falls. The BBS has been validated in several populations and cutoff scores have been established to identify the risk of falls and the need for a gait aid for ambulation.^{21,22}

The FES questionnaire has 10 listed activities with responses on a Likert scale from 1, “very confident” at performing the listed activities, to 10, “not confident at all.” The total FES score was obtained from the sum of these 10 items, ranging from 10 to 100.²³

The 30CST was used to evaluate leg strength and endurance. This test was developed to overcome the floor effect that older adults experienced with the 5 to 10 repetitions of the Sit to Stand Test.²⁴

Quality of Life

The self-reported 54-item MS Quality of Life questionnaire (MSQOL-54) supplements the generic 36-Item Short Form Health Survey with 18 disease-specific questions that measure social and cognitive functioning, sexual functioning, pain, energy, health anxiety, and overall quality of life. Aggregate scores are generated for mental HRQOL (MCS-54) and for physical HRQOL (PCS-54). The standardized scores range from 0 to 100 and higher scores indicate better HRQOL.^{25,26}

Cognitive Assessment

The Montreal Cognitive Assessment (MoCA) and the Symbol Digit Modalities Test (SDMT) were used to evaluate participants’ cognitive function. The MoCA is a 30-point test that assesses several cognitive domains, including visuospatial/executive functions, naming, memory, attention, language, abstraction, and orientation.²⁷ The SDMT²⁸ is a digit substitution test that examines attention, visual scanning speed, perceptual speed, and tracking and is very sensitive to various neurological disorders. It has become the most commonly used neuropsychological test of processing speed in MS.²⁹

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Statistical Analyses

Statistical analyses were carried out using the SPSS/PC software (version 23.0). Descriptive statistical methods (frequency, percentage, mean, standard deviation, median, min-max) were used to assess the study data. The Shapiro-Wilk test confirmed that the data showed normal distribution. The independent samples *t* test was used to compare quantitative data according to groups. The relationship between the variables in the patient group was examined by the Pearson correlation. Analysis of categorical data according to groups was performed using the χ^2 test. Stepwise multiple regression analysis was used to evaluate the relationship among factors. Significance level was taken as $P < .05$.

Results

A total of 80 persons with a diagnosis of RRMS for at least 1 year were screened for eligibility. Of the 80, 35 were excluded from the analysis (32 patients did not meet inclusion-exclusion criteria and 3 declined to participate). Of the 45 persons included, 36 were women (80%); the mean age was 36.6 ± 8.6 (range 21-57) years. The mean disease duration was 7.1 ± 6.1 (range 1-23) years. Forty-two (93.3%) patients were using an MS-immunomodulating therapy: 12 glatiramer acetate, 12 interferon, 16 oral therapies (fingolimod, teriflunamid, dimethyl fumarate), and 2 ocrelizumab. The average EDSS for the RRMS group as a whole was 1.9 ± 1.3 (range 0-5.5).

All parameters were evaluated with the Mann-Whitney U test. The median value of the 9HPT repeated was 22.1 (16.8-21.11) for women and 25.6 (19.7-35.1) for men and showed a significant difference according to sex ($P = .027$). The median physical health value was 57.5 (20-100) in women and 90 (35-100) in men, thus, it was significantly higher in men ($P = .048$). There was a significant difference between the sexes in terms of sexual function, with a median value of 66.7 (0-100) for women and 100 (8.3-100) for men ($P = .018$). The satisfaction in sexual function median was 50 (0-100) for women and 100 (0-100) for men ($P = .046$). When the mean value of general QOL was compared by sex,

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

men (72 ± 15) had significantly higher results than women (57.8 ± 18.8) ($P=.041$). Women with MS generated less force (45.6 ± 21) than men (70.5 ± 26.7) as measured by the dynamometer grasp performance, demonstrating a strength difference with a moderate effect size ($P=.04$). Other variables did not differ according to sex ($P>.050$) (See **Table 1**).

Hand grip dynamometer measurements were strongly correlated with DHI ($P=.001$), 9HPT ($P=.018$), BBS ($P=.001$), FES ($P<.001$), and 30CST ($P=.001$) scores, but not with EDSS ($P=.45$) or MoCA test ($P=.251$) scores. Additionally, the SDMT was significantly correlated with 9HPT ($P=.013$), DHI ($P=.006$), BBS ($P=.021$), and 30CST ($P=.003$) scores, but not with grip strength measurements ($P=.109$) (See **Table 2**).

Dynamometer measurements were found to be statistically significant in predicting overall QOL, with each unit increase resulting in an increase in overall QOL score of 0.383 ($P=.001$, $SI=0.104$, $R^2=0.523$ Stepwise Method).

Discussion

The present study was conducted to draw attention to the hand muscle strength and functionality in people with MS and to investigate its association with balance, cognition, and QOL. We found strong correlations between hand grip dynamometer measures and hand functionality tests (DHI, 9HPT), as well as balance measures (BBS, FES, 30CST). Regression analysis revealed that higher dynamometer scores were significantly correlated with better QOL.

Previous studies have shown that upper limb motor function is significantly affected by the level of disability in people with MS.^{30,31} In the Dubuisson et al study, 95% of people with MS considered upper limb function to be more important than lower limb function.³² There are still no standardized, uniform disability scales to evaluate upper limb functionality in people with MS.³⁰ In our study, we used the DHI and 9HPT to assess upper extremity functionality and the Jamar Plus+ Digital Hand Dynamometer to evaluate HGS. Although the HGS test was originally designed for patients undergoing hand surgery, it has been shown to have a strong association with decreased physical fitness and

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

reduced muscle strength.³³ We observed that increased HGS was strongly linked to better upper extremity function and balance but not with cognitive status and disability scores. It was positively correlated with QOL.

As reported in previous studies, people with MS generally exhibit lower HGS due to motor weakness.^{34,35} It has been demonstrated that a change of 5.5kg (12 pounds) or more in hand grip strength and 20% or more in the 9HPT falls beyond the range of day-to-day variability and reliably indicates a true change in functionality for people with MS.^{36,37} Similar to our study, research has also shown that a deficit in hand grip strength negatively impacts QOL and leads to subsequent dependence for those with MS.^{38,39} A study by Aristotelous et al also showed that hand grip strength was not associated with cognitive performance, but was linked to HRQOL, supporting our findings.⁴⁰ While most studies have focused on evaluating lower extremity strength due to its impact on patients with mild disability, our study highlights the growing importance of upper extremity strength in the later stages of MS, especially when patients require walking aids.³⁹ However, we believe that the earlier stages of the disease are more appropriate for evaluating upper limb strength and functionality. Our study also demonstrates that hand function or upper limb functionality constitutes a separate disability area that is distinct from the EDSS, which can significantly affect QOL and merits further investigation in future studies.

Cognitive impairment has been reported in up to 65% of individuals with MS,^{40,41} and in our study, cognitive status was significantly correlated with hand functionality and balance tests, but not with hand muscle strength, similar to the study of Aristotelous et al.⁴⁰ Previous literature suggests that increased functional capacity is linked to better cognition, possibly due to increased blood flow to the brain, improved cardiometabolic health, and reduced chronic inflammation levels.⁴¹ However, conflicting results exist,^{42,43} necessitating further studies with larger MS populations, especially focusing on upper limb function evaluations.

Both the mental and physical components of HRQOL are reported to be negatively affected in people with MS.⁴⁴ Reduced HRQOL was associated with fatigue, depression, and disability in a previous study.⁴⁵ In addition, cognitive decline was shown to negatively affect HRQOL independent of physical disability.⁴⁶ Consistent with previous studies, higher disability scores indicated lower sexual functions, satisfaction with

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

sexual function, overall QOL, and physical health composite scores in our study. Increased HGS and younger age indicated a better QOL, as expected.

Some limitations should be considered when interpreting our results, including the cross-sectional design, which limits conclusions about the direction of the association and precludes any inferences of causality or temporality. The study sample consisted of people with MS, so it may not fully represent the entire MS population. Low sample size and inclusion of only ambulatory persons with an EDSS score of up to 5.5 were other limitations.

Conclusions

This study highlights the importance of hand muscle strength and functionality in individuals with MS and its correlation with their cognitive status, balance, and HRQOL. Enhancing hand functionality and muscle strength can significantly impact independence, daily activities, and QOL for people with MS. Loss prevention and early restoration of hand function should be emphasized before the onset of significant morbidity. Further investigations are necessary to identify the most useful hand functionality or muscle strength test as an outcome measure in clinical trials of neuroprotective or neuroreparative therapies in MS.

Conflict of Interest: The authors do not have any financial or nonfinancial interests directly or indirectly related to the work submitted for publication.

References

1. Dilokthornsakul P, Valuck RJ, Nair KV, Corboy JR, Allen RR, Campbell JD. Multiple sclerosis prevalence in the United States

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

- commercially insured population. *Neurology*. 2016;86(11):1014-1021. doi:10.1212/WNL.0000000000002469
2. Dogru Huzmeli E, Duman T. Somatosensory impairments in patients with multiple sclerosis: association with dynamic postural control and upper extremity motor function. *Somatosens Mot Res*. 2020;37(2):117-124. doi:10.1080/08990220.2020.1753685
 3. Jongen PJ, Ter Horst AT, Brands AM. Cognitive impairment in multiple sclerosis. *Minerva medica*. 2012;103(2):73-96.
 4. Patti F, Cacopardo M, Palermo F, et al. Health-related quality of life and depression in an Italian sample of multiple sclerosis patients. *J Neurol Sci*. 2003;211(1-2):55-62. doi:10.1016/s0022-510x(03)00040-6
 5. Spooren AI, Timmermans AA, Seelen HA. Motor training programs of arm and hand in patients with MS according to different levels of the ICF: a systematic review. *BMC Neurol*. 2012;12:49. doi:10.1186/1471-2377-12-49
 6. Julian LJ, Vella L, Vollmer T, Hadjimichael O, Mohr DC. Employment in multiple sclerosis. Exiting and re-entering the work force. *J Neurol*. 2008;255(9):1354-1360. doi:10.1007/s00415-008-0910-y
 7. Norman K, Stobäus N, Smoliner C, et al. Determinants of hand grip strength, knee extension strength and functional status in cancer patients. *Clin Nutr*. 2010;29(5):586-591. doi:10.1016/j.clnu.2010.02.007
 8. Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. *J Geriatr Phys Ther*. 2008;31(1):3-10. doi:10.1519/00139143-200831010-00002
 9. Velghe A, De Buyser S, Noens L, Demuyneck R, Petrovic M. Hand grip strength as a screening tool for frailty in older patients with haematological malignancies. *Acta Clin Belg*. 2016;71(4):227-230. doi:10.1080/17843286.2016.1162381
 10. Nevill AM, Holder RL. Modelling handgrip strength in the presence of confounding variables: results from the Allied Dunbar National Fitness Survey. *Ergonomics*. 2000;43(10):1547-1558. doi:10.1080/001401300750003970
 11. Mancilla S E, Ramos F S, Morales B P. Fuerza de presión manual según edad, género y condición funcional en adultos mayores Chilenos entre 60 y 91 años [Association between handgrip strength and functional performance in Chilean older people]. *Rev Med Chil*.

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

2016;144(5):598-603. doi:10.4067/S0034-98872016000500007

12. Ruano L, Portaccio E, Goretti B, et al. Age and disability drive cognitive impairment in multiple sclerosis across disease subtypes. *Mult Scler*. 2017;23(9):1258-1267. doi:10.1177/1352458516674367
13. Martin CL, Phillips BA, Kilpatrick TJ, et al. Gait and balance impairment in early multiple sclerosis in the absence of clinical disability. *Mult Scler*. 2006;12(5):620-628. doi:10.1177/1352458506070658
14. Lobentanz IS, Asenbaum S, Vass K, et al. Factors influencing quality of life in multiple sclerosis patients: disability, depressive mood, fatigue and sleep quality. *Acta Neurol Scand*. 2004;110(1):6-13. doi:10.1111/j.1600-0404.2004.00257.x
15. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33(11):1444-1452. doi:10.1212/wnl.33.11.1444
16. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;17(2):162-173. doi:10.1016/S1474-4422(17)30470-2
17. Shechtman O, Gestewitz L, Kimble C. Reliability and validity of the DynEx dynamometer. *J Hand Ther*. 2005;18(3):339-347. doi:10.1197/j.jht.2005.04.002
18. Roberts HC, Denison HJ, Martin HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. *Age Ageing*. 2011;40(4):423-429. doi:10.1093/ageing/afr051
19. Paltamaa J, West H, Sarasoja T, Wikström J, Mälkiä E. Reliability of physical functioning measures in ambulatory subjects with MS. *Physiother Res Int*. 2005;10(2):93-109. doi:10.1002/pri.30
20. Duruöz MT, Cerrahoglu L, Dincer-Turhan Y, Kürsat S. Hand function assessment in patients receiving haemodialysis. *Swiss Med Wkly*. 2003;133(31-32):433-438. doi:10.4414/smw.2003.10216
21. Berg KO, Wood-Dauphinee SL, Williams JI, Maki B. Measuring balance in the elderly: validation of an instrument. *Can J Public*

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Health. 1992;83(suppl 2):S7-S11.

22. Stevenson TJ, Connelly DM, Murray JM, Huggett D, Overend T. Threshold Berg Balance Scale scores for gait-aid use in elderly subjects: a secondary analysis. *Physiother Can*. 2010;62(2):133-140. doi:10.3138/physio.62.2.133
23. Tinetti ME, Mendes de Leon CF, Doucette JT, Baker DI. Fear of falling and fall-related efficacy in relationship to functioning among community-living elders. *J Gerontol*. 1994;49(3):M140-M147. doi:10.1093/geronj/49.3.m140
24. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport*. 1999;70(2):113-119. doi:10.1080/02701367.1999.10608028
25. Vickrey BG, Hays RD, Harooni R, Myers LW, Ellison GW. A health-related quality of life measure for multiple sclerosis. *Qual Life Res*. 1995;4(3):187-206. doi:10.1007/BF02260859
26. Ware JE Jr. SF-36 health survey update. *Spine (Phila Pa 1976)*. 2000;25(24):3130-3139. doi:10.1097/00007632-200012150-00008
27. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53(4):695-699. doi:10.1111/j.1532-5415.2005.53221.x
28. Drake AS, Weinstock-Guttman B, Morrow SA, Hojnacki D, Munschauer FE, Benedict RH. Psychometrics and normative data for the Multiple Sclerosis Functional Composite: replacing the PASAT with the Symbol Digit Modalities Test. *Mult Scler*. 2010;16(2):228-237. doi:10.1177/1352458509354552
29. Costa SL, Genova HM, DeLuca J, Chiaravalloti ND. Information processing speed in multiple sclerosis: past, present, and future. *Mult Scler*. 2017;23(6):772-789. doi:10.1177/1352458516645869
30. Karabudak R, Dahdaleh M, Aljumah M, et al. Functional clinical outcomes in multiple sclerosis: current status and future prospects. *Mult Scler Relat Disord*. 2015;4(3):192-201. doi:10.1016/j.msard.2015.03.004
31. Yozbatiran N, Baskurt F, Baskurt Z, Ozakbas S, Idiman E. Motor assessment of upper extremity function and its relation with fatigue,

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

cognitive function and quality of life in multiple sclerosis patients. *J Neurol Sci.* 2006;246(1-2):117-122. doi:10.1016/j.jns.2006.02.018

32. Dubuisson N, Bauer A, Buckley M, et al. Validation of an environmentally-friendly and affordable cardboard 9-hole peg test. *Mult Scler Relat Disord.* 2017;17:172-176. doi:10.1016/j.msard.2017.08.002
33. Leong DP, Teo KK, Rangarajan S, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet.* 2015;386(9990):266-273. doi:10.1016/S0140-6736(14)62000-6
34. Chen CC, Kasven N, Karpatkin HI, Sylvester A. Hand strength and perceived manual ability among patients with multiple sclerosis. *Arch Phys Med Rehabil.* 2007;88(6):794-797. doi:10.1016/j.apmr.2007.03.010
35. Severijns D, Lamers I, Kerkhofs L, Feys P. Hand grip fatigability in persons with multiple sclerosis according to hand dominance and disease progression. *J Rehabil Med.* 2015;47(2):154-160. doi:10.2340/16501977-1897
36. Schwid SR, Goodman AD, McDermott MP, Bever CF, Cook SD. Quantitative functional measures in MS: what is a reliable change? *Neurology.* 2002;58(8):1294-1296. doi:10.1212/wnl.58.8.1294
37. Rudick RA, Kappos L. Measuring disability in relapsing-remitting MS. *Neurology.* 2010;75(4):296-297. doi:10.1212/WNL.0b013e3181ecf815
38. Krishnan V, Jaric S. Hand function in multiple sclerosis: force coordination in manipulation tasks. *Clin Neurophysiol.* 2008;119(10):2274-2281. doi:10.1016/j.clinph.2008.06.011
39. Schwid SR, Thornton CA, Pandya S, et al. Quantitative assessment of motor fatigue and strength in MS. *Neurology.* 1999;53(4):743-750. doi:10.1212/wnl.53.4.743
40. Aristotelous P, Stefanakis M, Pantzaris M, Pattichis C, Hadjigeorgiou GM, Giannaki CD. Associations between functional capacity, isokinetic leg strength, sleep quality and cognitive function in multiple sclerosis patients: a cross-sectional study. *Postgrad Med.* 2019;131(7):453-460. doi:10.1080/00325481.2019.1662271

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

41. Rao SM, Leo GJ, Bernardin L, Unverzagt F. Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. *Neurology*. 1991;41(5):685-691. doi:10.1212/wnl.41.5.685
42. Baquet L, Hasselmann H, Patra S, et al. Short-term interval aerobic exercise training does not improve memory functioning in relapsing-remitting multiple sclerosis-a randomized controlled trial. *PeerJ*. 2018;6:e6037. doi:10.7717/peerj.6037
43. Zimmer P, Bloch W, Schenk A, et al. High-intensity interval exercise improves cognitive performance and reduces matrix metalloproteinases-2 serum levels in persons with multiple sclerosis: a randomized controlled trial. *Mult Scler*. 2018;24(12):1635-1644. doi:10.1177/1352458517728342
44. Göksel Karatepe A, Kaya T, Günaydn R, Demirhan A, Ce P, Gedizlioğlu M. Quality of life in patients with multiple sclerosis: the impact of depression, fatigue, and disability. *Int J Rehabil Res*. 2011;34(4):290-298. doi:10.1097/MRR.0b013e32834ad479
45. Nourbakhsh B, Julian L, Waubant E. Fatigue and depression predict quality of life in patients with early multiple sclerosis: a longitudinal study. *Eur J Neurol*. 2016;23(9):1482-1486. doi:10.1111/ene.13102
46. Langdon DW. Cognition in multiple sclerosis. *Curr Opin Neurol*. 2011;24(3):244-249. doi:10.1097/WCO.0b013e328346a43b

Table 1. Differences Between Male and Female Participants

A. Test score, median (min-max)

	Female (n=36)	Male (n=9)	U test	P value
30CST	11 (2-30)	12 (6-25)	136	.49
DHI	4 (0-54)	0 (0-35)	140.5	.52
BBS	52.5 (13-56)	56 (22-56)	125.5	.29

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

FES	26.5 (16-60)	21 (18-36)	102	.09
9HPT	24.1 (18.6-44)	28.7 (17.8-35.9)	96	.06
9HPT/R	22.1 (16.8-21.11)	25.6 (19.7-35.1)	84	.027
Physical health	57.5 (20-100)	90 (35-100)	92.5	.048
Role limitations (physical cause)	75 (0-100)	50 (0-100)	152	.77
Role limitations (emotional cause)	66.7 (0-100)	66.7 (0-100)	161	.98
Emotional well-being	52 (28-72)	48 (36-100)	131.5	.38
Cognitive function	55 (0-100)	70 (25-90)	122	.26
Sexual function	66.7 (0-100)	100 (8.3-100)	80	.018
Change in health	50 (25-100)	50 (25-100)	141.5	.54
Satisfaction with sexual function	50 (0-100)	100 (0-100)	94	.046
MSQOL, physical health composite	51.1 (27.4-154.9)	70.8 (32.3-85.1)	108	.13

B. Test score (mean \pm SD)

	Female (n=36)	Male (n=9)	T test	P value
Dynamometer	45.6 \pm 21	70.5 \pm 26.7	-3.002	.004
MoCA	23.1 \pm 4.8	23.4 \pm 2.1	-0.220	.83
SDMT	31.3 \pm 11.4	31.2 \pm 6.2	0.014	.99
MSQOL, pain	57.3 \pm 28.4	66.1 \pm 22.3	0.859	.40

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

MSQOL, energy	43.3 ± 23.1	52.7 ± 14.2	-1.164	.25
MSQOL, health perceptions	50.1 ± 25	57 ± 16.5	-0.782	.44
MSQOL, social function	66.5 ± 24.3	74.2 ± 16.8	-0.893	.38
MSQOL, health distress	58.4 ± 26.2	67.2 ± 24.3	-0.920	.36
MSQOL, overall QOL	57.8 ± 18.8	72 ± 15	-2.104	.04
MSQOL, mental health composite	54.6 ± 18.8	63.3 ± 18.4	-1.249	.22

Note: $P < .05$ was statistically significant.

9HPT, Nine-Hole Peg Test; 9HPT/R, Nine-Hole Peg Test repeated dominant hand; 30CST, 30-Second Chair to Stand Test; BBS, Berg Balance Scale; DHI, Duruoz Hand Index; FES Falls Efficacy Scale; MoCA, Montreal Cognitive Assessment; MSQOL, MS Quality of Life questionnaire; QOL, quality of life; SDMT, Symbol Digit Modalities Test; *T* test, independent samples *t* test; U test, Mann Whitney U test.

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Table 2. Correlation Analysis of Upper Limb Strength, Balance, and Cognition Tests

		Dynamometer	DHI	9HPT/R	9HPT	BBS	30CST	FES	MoCA
DHI	r	-0.467							
	P	.001							
9HPT	r	-0.352	0.487	0.804					
	P	.018	0.001	<0.001					
9HPT/R	r	-0.377	0.482						
	P	.011	0.001						
BBS	r	0.472	-0.746	-0.390	-0.432				
	P	.001	<0.001	0.008	0.003				
30CST	r	0.468	-0.543	-0.555	-0.563	0.698			
	P	.001	<0.001	<0.001	<0.001	<0.001			
FES	r	-0.529	0.378	0.347	0.411	-0.485	-0.376		
	P	<.001	0.010	0.019	0.005	0.001	0.011		
MoCA	r	0.251	-0.239	-0.425	-0.191	0.069	0.167	-0.365	
	P	.096	0.113	0.004	0.210	0.654	0.272	0.014	
SDMT	r	0.242	-0.403	-0.441	-0.367	0.344	0.438	-0.285	0.531
	P	.109	0.006	0.002	0.013	0.021	0.003	0.058	<0.001
EDSS	r	-0.116	0.188	0.248	0.276	-0.324	-0.320	0.151	-0.071
	P	.45	0.22	0.10	0.07	0.03	0.03	0.32	0.64

This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made in the proof stage and before print publication. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Notes: $P < .05$ is statistically significant.

9HPT, Nine-Hole PegTest; 9HPT/R, Nine-Hole PegTest repeated dominant hand; 30CST, 30-Second Chair to Stand Test; BBS, Berg Balance Scale; DHI, Duruoz Hand Index; EDSS, Expanded Disability Status Scale; FES, Falls Efficacy Scale; MoCA, Montreal Cognitive Assessment; P , P value; QOL, quality of life; r , Spearman correlation coefficient; SDMT, Symbol Digit Modalities Test.