Performance and Capacity Measurement of the Lower Extremities in Multiple Sclerosis –How to Approach?

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ABSTRACT

Walking limitations play a key role in the development of disability in multiple sclerosis (MS) patients. Vast majority of patients, even in the very early stages of the disease, experience walking disturbances. Measuring capacity and performance in lower extremities enables us to 1) monitor disease progression; 2) evaluate treatment responses; 3) determine the necessity of new treatment strategies on time. The purpose of this review is

to highlight the importance of regular walking assessments in MS patients, give idea about which measurement tools to choose, and provide insight for future investigations in the light of new technological developments.

Keywords: Lower extremities, performance, capacity, measurement, multiple sclerosis

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INTRODUCTION

Multiple sclerosis (MS) is a chronic, progressive disease of the central nervous system, characterized by inflammation, demyelination and destruction of the motor and sensory axons within the brain and the spinal cord (1). Being one of the leading causes of neurological disability in young adults, MS affects muscles, sensory system, balance and coordination (2, 3). Coupled with emotional stress of being diagnosed as MS, clinical symptoms of MS may result in decreased physical activity, which, together with increased disability, influences exercise capacity (4, 5). Mobility and balance, two basic functions of the lower extremities, are used routinely during daily living activities. Having a chronic systemic disease like MS may lead to muscle inactivity. Additionally, accompanying cardiovascular and pulmonary dysfunctions, systemic inflammation triggering hypoxia and oxidative stress and drugs such as corticosteroids may contribute to muscle disuse (6).

Walking is defined by *The International Classification of Functioning (ICF), Disability, and Health* as “moving along a surface on foot, step by step, so that one foot is always on the ground, such as when strolling, sauntering, walking forwards, backwards, or sideways.” ICF, a multidimensional model, provides a biopsychosocial approach. It is classified into 2 parts: Part 1 - Functioning and Disability - includes Body Functions and Structures and Activities and Participation; Part 2 - Contextual Factors - incorporates Environmental Factors and Personal Factors (7). Approximately 75% of patients with MS suffer from clinically significant walking disturbances which play a key role in disability (8). Furthermore patients attach great importance to walking abilities. A study by Heesen et al. reports that out of 13 dimensions, walking is the most important bodily function amongst both new and long-term diagnosed MS patients (9). There is no defined gait disturbance specific to MS. Distribution of the lesions in the brain and spinal cord may reveal with walking problems. Walking performance

may be affected by certain circumstances such as fatigue, infections, and is likely to fluctuate from day to day, independent of the disease activity (10).

Understanding and Measuring the Capacity of the Lower Extremities in MS Patients

Components of ability to perform daily living activities are capacity (what patients can do), performance (what patients have done), reserve (the difference between the capacity and the performance), and the capacity utilization (how frequent performance is equal to capacity) (11). Walking capacity, muscle power or endurance capacity, functional capacity, exercise capacity, physical capacity, aerobic capacity, mitochondrial capacity, skeletal muscle oxidative capacity are some of the measurements, also used in MS patients, that enable us to assess lower extremity capacity. It is important to note, however, that gender, age, body weight, height, neurological signs and symptoms such as postural control, ataxia, spasticity, motor and sensory functions and muscle oxidative stress may also affect the walking capacity in MS patients (12). Body composition, lower extremity torque, and muscle quality are the other factors affecting the lower extremities capacity and performance. Muscle mass, composition, metabolism, aerobic capacity, insulin resistance, fat infiltration, fibrosis and neural activation affect muscle quality and function during ageing (13).

Dual Energy X-Ray Absorptiometry (DXA) developed by different manufacturers may measure body composition in terms of fat and fat-free mass (14–16). DXA may also calculate muscle quality (muscle specific torque) as the ratio of right thigh total torque to lean muscle mass. Better muscle quality means more efficiently working muscle (17). Another technique of body composition measurement is air-displacement

plethysmography such as BOD POD - a new air displacement method for the determination of human body composition (18).

There is evidence suggesting that individuals with MS are weaker than controls with similar age and body mass. A study by Lambert et al. compared muscle strength and muscle fatigue of the knee extensors and flexors in individuals with multiple sclerosis (MS) and non-MS control subjects and concluded that strength of knee extensors and flexors in MS patients are weaker than the control group (19). Motl et al. examined the association between the rates of accelerometer activity counts and energy expenditure during walking in persons with multiple sclerosis (MS) versus controls and calibrated the output of accelerometers for computing time spent in light, moderate, and vigorous physical activity. The results indicated that persons with MS had greater energy expenditure during treadmill walking, and the cut-points for light, moderate, and vigorous physical activity were lower in persons with MS than in controls (20). Muscle strength, determined by muscle cross section area, type of muscle fiber, neural control (including total recruitment of motor units), and velocity of power reaches its maximum level during 25–35 years in healthy people. Because lower extremities are used less than upper extremities in daily living activities in the elderly, ageing affects lower extremities more than upper extremities. Muscle power declines at a rate of 12–14% per decade in people over 50 years of age (21, 22). Lower extremity muscle strength decreases at a rate of 1–4% per year after age 50. Studies evaluating muscle mitochondrial capacity with near-infrared spectroscopy suggest a decrease in mitochondrial capacity by 40% in MS patients compared to the control group (23).

Technological advances such as biosensors make it possible to measure physiologic and kinetic parameters. Wearable biosensors like accelerometers and pedometers have great potential for assessing walking abilities and can be used for monitoring disability in people with MS (24–26). MS patients have been found to be 35% less active than healthy people according to measurements done by triaxial accelerometer. Higher body fat percentage is present in MS patients than healthy people (27). A study by Wens et al. reported that MS has negative impact on skeletal muscle fibre cross sectional area, muscle strength and muscle mass of the lower limbs of mildly affected MS patients (28).

Why is Performance Measurement of the Lower Extremities Important in MS?

Which Measurement Tools Should be Used?

Monitoring mobility dysfunction in MS is important because identifying subclinical gait and balance abnormalities, even in the presence of stable Expanded Disability Status Scale (EDSS), makes it possible to evaluate treatment strategies and creates a physiotherapy opportunity for the patient. EDSS, a MS-specific measure tool, heavily evaluates mobility dysfunction, and depends on ambulation. Evidence of mild gait and postural control impairments even for MS patients with minimal neurological signs on clinical examination has been provided by laboratory-based movement analysis. Reduced speed and stride length have been described in MS patients with only mild neurologic signs and no functional limitations (29). Monitoring of walking abilities during MS course is warranted due to the presence of both axonal injury and gait abnormalities in the very early stages of MS. Martin et al. evaluated the gait and balance performance of minimally impaired MS patients (EDSS 0–2.5) with no clinical evidence of gait disturbance and compared their performance to an age- and gender-matched control group. People with recently diagnosed MS who displayed mild neurological signs, walked with reduced speed and stride length, had limited ankle motion, altered ankle muscle recruitment, and reduced balance performance compared to age- and gender- matched control subjects (30).

Interest in economic evaluation of MS is increasing. Treatment for MS targets avoiding temporary disability caused by relapses and more importantly, delaying the progression to more permanent disability. Delaying or preventing patients' progression to more severe disease will ensure economic savings. According to a Europe-wide study by Kobelt and associates aiming to establish the cost of MS at different levels of disease severity; the proportion of patients in early retirement because of MS ranged from 33% to 45%, all types of costs concerning medical and non-medical resources increased with worsening disease, the total mean annual costs per patient were estimated at € 18 000 for mild disease (EDSS <4.0), € 36 500 for moderate disease (EDSS 4.0–6.5) and €62 000 for severe disease (EDSS >7.0) (31).

All aforementioned studies clearly indicate the need for regular assessment of walking performance. Raising question is which measurement tools should be used? Ideal measurement tools should be disease-specific, feasible and practical, and should reflect both clinician's and patient's perspectives. Instruments are classified as clinician-assessed rating scales and performance tests, and patient self-report questionnaires. Among the rating scales Kurtzke EDSS is the gold standard for determining disability levels and disability progression in MS patients. Walking is established between the score 4.5 and 7.5 with the assessment based on maximum walking distance and the need to use any assistant device. Although the value of EDSS is well known, it may have certain limitations. For example, it relies on a detailed neurologic examination performed by a clinician. Albrecht et al. measured the maximum walking distance and walking time on four consecutive days in twenty-nine patients with clinically stable MS who could walk unaided 100 up to 500 m. Results showed that a day-to-day variability of maximum walking distance, which corresponds to changes up to 1.5 points in the EDSS. The authors concluded that scoring of MS patients should not be based on one single measurement of the maximum walking distance and the more reliable parameter seems to be the mean walking speed rather than the distance (32). In addition to traditional clinical scales such as EDSS, the National MS Society's Clinical Outcomes Assessment Task Force proposed a multidimensional clinical outcome measure titled MS Functional Composite (MSFC). MSFC measures three key clinical dimensions of MS - leg function/ambulation (Timed 25-Foot Walk), arm/hand function (Nine-Hole Peg Test), and cognitive function (Paced Auditory Serial Addition Test) (33).

The Timed 25-Foot Walk (T25FW) is a practical and validated instrument which correlates well with both the EDSS and patients' perspectives (34, 35). The patient is asked to walk 25 feet (8 m) as quick as possible, but safely. Subjects are allowed to use assistive devices if necessary. After reviewing different instruments, Bethoux et al. declared that among all available tools, T25FW (observed performance) and the 12-Item Multiple Sclerosis Walking Scale (patient-reported) appear to provide complementary assessment of a patients' walking limitations (36). Additionally, Consortium of Multiple Sclerosis Centers agree T25FW, Timed Up and Go test (TUG), Dynamic Gait Index (DGI), 6-Minute Walk (6MW), and self-reported 12-item Multiple Sclerosis Walking Scale (MSWS-12) should be included when assessing walking performance (37). During TUG, the patient is observed and timed while he rises from an arm chair, walks 3 meters, turns, walks back, and sits down again. TUG test is easy to administer and measures balance and fall risk (38).

Dynamic Gait Index is an eight-item assessment tool assessing gait, balance and fall risk. Patient is asked to walk, change in gait speed, do horizontal and vertical head turns while walking, turn, step over and around obstacles, walk up and down the stairs (39).

6-Minute Walk Test is used to measure the maximum distance that a person can walk in six minutes. It gives opinion about exercise endurance. Patients with severe disability and fatigue may experience difficulty while

performing the test. Thus, 2-Minute Walk test may be an alternative (40).

The MSWS-12 was designed to measure the impact of MS on walking ability. It is consisted of 12 questions and Likert type answers. The MSWS-12 is a reliable and valid patient-based instrument measuring the impact of MS on walking (41).

A review by Caset et al. reports that physical activity is commonly expressed as activity counts and step counts per day and uni-axial accelerometers and pedometers are the most popular physical activity measurement tools used in the current MS literature. The accelerometers can be worn on the side of the waist of the leg, ankle, wrist. Pedometers can be worn on the hip (42).

Rehabilitation Programs to Improve the Walking Performance in MS Patients

Increase in body temperature during exercise has historically been acknowledged to have negative impact on disability in MS patients leading to concerns with regard to exercise prescription for MS patients. However, increasing interest on the link between exercise and MS has challenged this approach since 2000. Muscle strength of thigh has an important influence on the walking capacity in MS patients (43). Endurance power of knee extensor muscles and isometric knee flexor muscle power have also been shown to affect walking capacity of MS patients with moderate walking disabilities. That's why exercises aiming increase in muscle strength should be included in rehabilitation programs of MS patients (44). A study by Valet et al. reports perceived fatigue and physical fitness in mildly disabled MS patients are closely related to low and intermediate aerobic capacity, mobility, walking capacity, depression, and neuromuscular fatigability. Focusing on improving these parameters may help in management of fatigue (45). Additionally, it is reported that aerobic training can improve aerobic capacity in MS patients to an extend that will ensure secondary health benefits (46). There is evidence suggesting low-to-moderate and also high intensity cardiovascular exercise combined with resistance training improves exercise tolerance, muscle strength, functional capacity and health-related quality of life in MS patients (47-51). A meta-analysis of 21 studies focusing on the impact of technology based (internet, telephone, combination) physical rehabilitation conducted with MS patients suggests the use of technological equipment results in the improvement of physical activity in MS. (52). A study by Filli et al. reports that by using three dimensional gait analysis systems gait disturbances in a cohort of mildly-to moderately-affected patients with MS are typified by decreased knee and ankle flexion, reduced dynamic stability and increased variability of movements. This information may help to inform rehabilitative gait training in patients and to develop deficit-specific and patient-tailored exercise programs (53).

CONCLUSION

Studies exploring the factors affecting the lower extremity performance and capacity in MS are accumulating in the literature. Thus efforts in understanding and measuring the capacity and performance are becoming an important challenge in MS patients. The ones which include both the patient's and the clinician's perspectives are the most recommended measurement batteries. Additionally, combining the clinical and patient-reported evaluations with continuous monitoring via new technology, like wearable biosensors, provide useful information for intervention in planning treatment strategies, particularly physiotherapy. Yet, available evidence suggests exercise should be an integral part of programs to be implemented for MS patients and should be prescribed more often. Further studies using new technology to investigate performance and capacity are essential to shed light on MS mobility.

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