Journal of the Neurological Sciences 382 (2017) 131–136

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Performed and perceived walking ability in relation to the Expanded Disability Status Scale in persons with multiple sclerosis

D. Langeskov-Christensen[a], P. Feys[b], I. Baert[b], M. Riemenschneider[a], E. Stenager[c,d], U. Dalgas[a,*]

[a] Section of Sport Science, Department of Public Health, Aarhus University, Aarhus, Denmark
[b] REVAL, BIOMED-Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt University, Hasselt, Belgium
[c] Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark
[d] MS-Clinic of Southern Jutland (Sønderborg, Esbjerg, Kolding), Department of Neurology, Sønderborg, Denmark

ARTICLE INFO

Keywords:
Multiple sclerosis
EDSS
Walking impairment
Walking measures
6MWT
MSWS-12

ABSTRACT

Background: The severity of walking impairment in persons with multiple sclerosis (pwMS) at different levels on the expanded disability status scale (EDSS) is unclear. Furthermore, it is unclear if the EDSS is differently related to performed- and perceived walking capacity tests.

Aims: To quantify walking impairment and perceived impact of MS on walking according to EDSS scores and to examine the relations between these parameters in pwMS.

Methods: EDSS was collected by neurologists and walking was assessed by the timed 25 ft walk test (T25FWT), two minute walk test (2MWT), six minute walk test (6MWT) and the 12-item MS walking scale (MSWS-12) in 474 PwMS with mild (EDSS 1–4: n = 200) to moderate (EDSS 4.5–6.5: n = 274) MS. Magnitude of walking impairment was calculated and related to EDSS.

Results: Compared to predicted values in healthy controls, walking speed was reduced by 41.5 ± 25.8% in the 6MWT for the total MS group and by 21.8 ± 20.2% and 55.8 ± 19.1% in the mild and moderate MS subgroups, respectively. The EDSS score showed the strongest relationship to the 2MWT and the 6MWT in the total MS group ($r = -0.76$, $p < 0.0001$), to the MSWS-12 score in the mild MS group ($r = 0.56$, $p < 0.0001$), and to the 2MWT in the moderate MS group ($r = -0.50$, $p < 0.0001$).

Conclusion: In pwMS (EDSS scores 1–6.5), walking speed is on average reduced by ~40% when compared to predicted values in healthy controls, and impairments are already present at early disease stages, suggesting early initiation of rehabilitation. The 2MWT and 6MWT show the strongest relationship to EDSS, but the MSWS-12 identify impairments more gradually at low EDSS scores.

1. Introduction

Multiple sclerosis (MS) is a demyelinating, inflammatory and neurodegenerative disorder of the central nervous system (CNS) that is characterized by progressive neurologic impairment [1]. Ambulatory dysfunction is a common and well-recognized feature of the disease [2] with MS patients perceiving walking as the most valued bodily function independent of disease duration [3]. In persons with MS (pwMS) decreased walking capacity relates to reduced health-related quality of life [4]. Compared to healthy persons, it has been shown that most pwMS walk slower during longer walking tests (e.g. 6 minute walk test, 6MWT) [5–7]. However, only few and small studies have precisely quantified the magnitude of reduced walking speed or distance in PwMS at different disease stages and compared these with reference values from sex and age matched healthy controls [6–8]. Such a quantification can give insight to the actual reduction in walking capacity throughout the different disease stages, and this has to be investigated and confirmed by a large sample study [6,7]. Furthermore, it is unclear to which extent walking speed is compromised at low disability levels, although changes in muscle coordination and gait kinematics has been documented [9–11]. This could help to clarify the necessity for early rehabilitation interventions aiming at maintaining walking abilities.

The expanded disability status scale (EDSS) of Kurtzke [12] is the most widely used instrument to describe the clinical severity in MS. The EDSS score is based on neurological examination and reflects the functional system scores (pyramidal, cerebellar, brain stem, sensory, bowel and bladder, visual, cerebral and other), which may be related to walking capacity, since walking performance is affected by loss of muscle strength, cerebellar damage, ataxia, sensory loss, visual

* Corresponding author at: Section of Sport Science, Dep. of Public Health, Aarhus University, Dalgas Avenue 4, 8000 Aarhus C, Denmark.
E-mail address: dalgas@ph.au.dk (U. Dalgas).

http://dx.doi.org/10.1016/j.jns.2017.09.049
Received 20 June 2017; Received in revised form 6 September 2017; Accepted 30 September 2017
Available online 03 October 2017
0022-510X/

impairment, and cognitive impairment in PwMS [5]. However, previous studies reporting on the relationship between the EDSS score and various walking measures, in terms of the timed 25 foot walk test (T25FWT) [13–17], the 2 min walk test (2MWT) [18], the 6 min walk test (6MWT) [7,16–22], and the 12-item MS walking scale (MSWS-12) [7,16,17,23–26], show heterogeneous results ranging from no to strong correlations. Only few studies [16,17] simultaneously examined the relation between the EDSS score and multiple walking measures, and these studies suggest that the objective 6MWT is most closely related to the EDSS score. However, these studies are either preliminary [16], or are limited in the range of included EDSS scores [17]. Therefore, the relations between different walking measures and the EDSS score still remain to be investigated in a large and representative sample of pwMS. A better understanding of the relationship between EDSS score and different walking measures as well as the magnitude of walking impairments, can help clinicians in the assessment of walking capacity and in optimizing rehabilitation interventions for pwMS.

Consequently, the purposes of this study were 1) to quantify the magnitude of reduction in walking speed and perceived impact of MS on walking at various EDSS levels by applying predicted reference values from healthy persons and 2) to examine to which extent several walking measures, including performed and perceived outcome measures, are related to the EDSS. We hypothesized that 1) walking impairment would be present already at disease onset, and that walking impairments are more pronounced at higher EDSS scores, and 2) that the 6MWT and MSWS-12 would relate better to the EDSS than the T25FWT.

2. Methods

The current study presents data from two cross-sectional multicentre studies performed within the European Rehabilitation in MS network for best practice and research in MS rehabilitation (www.eurims.org). Detailed description of methodology and study design has been reported elsewhere [27–29] and is only summarized below.

2.1. Subjects

A convenience sample of 503 MS patients was recruited at inpatient and outpatient rehabilitation and research centers in Europe (n = 18), Israel (n = 1) and the USA (n = 1). The included subjects had a definite diagnosis of MS and an EDSS ≤ 6.5. The subjects had not experienced an exacerbation in the month prior to testing, and had no other medical conditions that interfered with walking. All participants gave written informed consent. The study was conducted in accordance with the declaration of Helsinki and approved by the Human Ethics Committee of the leading University of Hasselt as well as by the local ethical committees of the participating centers.

2.2. Experimental design, outcome measures and procedure

A cross-sectional multicentre study design was applied. The EDSS score was collected by neurologists from the participating sites [12]. The outcome measures in this study were short (T25FWT) and long (2MWT, 6MWT) walking capacity tests, patient reported walking ability (MSWS-12) and disability level (EDSS). Subjects were permitted to use habitual assistive devices during testing. All sites utilized the same standardized instruction booklet. The MSFC guidelines [30] were applied for the T25FWT, meaning that subjects were instructed 'to walk at fastest but safe speed' over a 25 ft/7.62 m course using a static start. Subjects also completed the 2MWT and 6MWT 'at fastest speed'. They were instructed to cover as much distance as possible, albeit safely, according to the script of Goldman et al. [7]. Participants walked back and forth in a 30-metre hallway turning around cones at each end, and were notified, without further encouragement, about each expired minute. Total distance (m) was registered, and was also expressed as walking speed (m/s). The 2MWT represented either the distance covered after the first 2 min in the 6MWT or the distance walked in an independent 2MWT, which has been shown not to influence the result of the test [18]. The transformed MSWS-12 score (0 − 100) was used as a patient-reported measure of the impact of MS on walking [26].

2.3. Data processing

The subjects were classified as having mild MS if they had an ≤ 4.0 and moderate MS if they had an EDSS ≥ 4.5 and ≤ 6.5. This criterion has been used in previous studies as it discriminates relatively mild ambulatory dysfunction (self-sufficient and able to walk without aid for 500 m) and moderate to severe ambulatory dysfunctions [9,27,29,31]. The percent of predicted walking speed in the 2MWT and 6MWT compared to healthy subjects was calculated based on reference values for healthy persons with formulas published by Selman et al. [32] (2MWTpredicted = 252.583 − 1.165 ∗ age + 19.987 ∗ gender, where gender = 1 if male subject and gender = 0 if female subject) and Enright et al. [33] ($6MWTpredicted_{men}$ = 7.57 ∗ height, cm − 5.02 ∗ age − 1.76 ∗ weight, kg − 309 m; $6MWTpredicted_{women}$ = 2.11 ∗ height,cm − 2.29 ∗ weight, kg − 5.78 ∗ age + 667 m).

No good evidence-based reference values could be found for the T25FWT. Subjects were excluded from the analyses if they 1) had an EDSS score below 1 or over 6.5 due to small sample sizes in these subgroups (n = 1 and n = 4, respectively), 2) took > 30 s to complete the T25FWT (n = 12), 3) or if data on crucial variables were missing (EDSS: n = 1, height: n = 3, 6MWT: n = 4, MSWS-12: n = 4). From the total sample of 503 subjects this left 474 subjects for analyses.

2.4. Statistical analysis

The statistical analysis was performed in Stata version 11.2 and used a 5% limit of significance. The variables that were modelled as continuous were assumed to follow a normal distribution and subsequently the characteristics of the two MS-subgroups were compared by Student's unpaired *t*-test or Welch's *t*-test where appropriate for continuous variables and the Chi-squared test for categorical variables. To determine which walking measures had the strongest linear relations to the EDSS score at different disability levels, Pearson correlation coefficients were calculated between EDSS scores and walking measure variables. Pitman's test, which calculates the Pearson correlation between the sum and the difference of the residuals from two linear regressions, was applied in order to determine the ranking of correlations. Linear regressions between walking variables and EDSS scores were used to determine the relationship between level of EDSS scores and walking measure outcomes. Post-hoc, we analyzed which items in the MSWS-12 that were driving the correlations between this walking measure and the EDSS by calculating Pearson correlation coefficients between the individual items in the MSWS-12 questionnaire and the EDSS.

3. Results

3.1. Patient characteristics

The characteristics of the total, mild and moderate MS groups are presented in Table 1. The persons with moderate MS were older, had longer disease duration, and had more primary progressive ($p < 0.001$) and secondary progressive patients ($p < 0.001$) when compared to those with mild MS.

3.2. Walking capacity according to EDSS

Walking speed was reduced to 61.3 ± 25.4% and 58.5 ± 25.8% of the predicted walking speed of healthy persons, in the total sample of pwMS in the 2MWT and 6MWT, respectively (see Table 1). The