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Within-day variability on short and long walking tests in persons with multiple sclerosis☆

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ABSTRACT

Objective: To compare within-day variability of short (10 m walking test at usual and fastest speed; 10MWT) and long (2 and 6-minute walking test; 2MWT/6MWT) tests in persons with multiple sclerosis.
Design: Observational study.
Setting: MS rehabilitation and research centers in Europe and US within RIMS (European network for best practice and research in MS rehabilitation).
Subjects: Ambulatory persons with MS (Expanded Disability Status Scale 0–6.5).
Intervention: Subjects of different centers performed walking tests at 3 time points during a single day.
Main measures: 10MWT, 2MWT and 6MWT at fastest speed and 10MWT at usual speed.
Ninety-five percent limits of agreement were computed using a random effects model with individual pwMS as random effect. Following this model, retest scores are with 95% certainty within these limits of baseline scores.
Results: In 102 subjects, within-day variability was constant in absolute units for the 10MWT, 2MWT and 6MWT at fastest speed (+/−0.26, 0.16 and 0.15 m/s respectively, corresponding to +/−19.2 m and +/−54 m for the 2MWT and 6MWT) independent on the severity of ambulatory dysfunction. This implies a greater relative variability with increasing disability level, often above 20% depending on the applied test. The relative within-day variability of the 10MWT at usual speed was +/−31% independent of ambulatory function.
Conclusions: Absolute values of within-day variability on walking tests at fastest speed were independent of disability level and greater with short compared to long walking tests. Relative within-day variability remained overall constant when measured at usual speed.

1. Introduction

Walking is important for persons with multiple sclerosis. Walking assessment received increased interest given recent trials in exercise therapy, rehabilitation and symptomatic treatment, in particular extended-release dalfampridine [1,2]. Also longitudinal monitoring of progression in persons with MS, including trials of disease modifying treatment, requires more reliable and sensitive ambulation outcome measures than the neurological Expanded Disability Status Scale [3,4]. In this regard, the timed 25 foot walk test as part of the MS Functional Composite Score is commonly used [5].

In rehabilitation, a heterogeneity of walking outcome measures are applied, also including longer walking tests such as the 2 and 6 minute walking test. The latter tests were recommended as superior outcome

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measures as not limited by a floor effect while also encompassing endurance, fatigability and cardiorespiratory fitness [6,7]. Although short and long walking tests are strongly correlated [8–11], relative errors when estimating the 6 minute walking test outcome based on short walking tests were about 10% in mildly and 15% in moderately affected persons with multiple sclerosis compared to only 5–6% in both groups when based on the 2 minute walking test [10]. Moreover, both longer walking tests were advocated to better reflect habitual walking performance in the community setting than short walking tests, particularly in more disabled MS patients [12].

The interpretation of changes in walking capacity test performance requires knowledge on test–retest reliability, validity, and responsiveness of the measure. Regarding test–retest reliability, both within- and between-day variability have been reported to be ~20% for the timed 25 foot walk test [13–15], which some consider as clinically meaningful based on comparison with longitudinal changes in both patient- and clinician reported anchors [8,16–18]. However, one must be cautious as results were reported for (small) samples with variable ambulatory dysfunction. There are indications that test–retest reliability may depend on disability level, as documented for the 10 m walking test [19,20], more pronounced for usual compared to fastest speed [19–21]. For longer walking tests, one study reported in persons with multiple sclerosis on between-day variability on the 6 minute walking test (standard error of mean of 35 m) [26], while Goldman et al. [6] demonstrated high ICC's for three repeated performances of the 6MWT with 1 hour rest in-between, with most patients having an EDSS up to 4.

There are no studies yet reporting on test–retest reliability of the 2 minute walking test, or directly comparing test–retest reliability between short and long test formats.

This multi-center study investigated within-day variability of short and long walking tests in persons with multiple sclerosis, who performed the 10 meter (self-selected and fastest speed), 2 and 6 minute walking test three times on one single day, with a 3-hour time interval. It was hypothesized that test format and disability level would influence magnitude of within-day variability.

2. Methods

This study included persons with multiple sclerosis with an EDSS score ≤6.5 [4], indicating an ability to walk at least 20 m independently with or without the use of assistive devices. Subjects participated to a larger multi-center study, which was initiated within the European RIMS network of MS Centers (www.euRIMS.org) and approved by the leading ethical committee of Hasselt University (Belgium) and local committees. Effect of time of day on walking capacity and perceived energy level was reported previously [22].

Walking capacity testing was systematically performed at 3 predefined time intervals during a single day, that is between 9–10 AM, 12–1 PM and 3–4 PM. Short walking tests consisted of two formats of the 10 meter walk test. Subjects were once instructed 'to walk at usual comfortable speed', while the other trial had to be executed 'at fastest safe speed'. Timing with a handheld stopwatch was done over the middle 10 m of a 14-meter walkway to avoid measuring acceleration and deceleration. Short walking test formats were randomly administered and separated by a 1-minute rest interval. After a 5 minute rest, subjects performed long walking tests (6 and 2 minute walking test, with the latter representing the distance covered during the first 2 min, and thus being an integral part of the 6MWT). Subjects were instructed 'to walk at fastest speed and to cover as much distance as possible', according to the script of Goldman et al. [6] Participants walked back and forth in a 30-meter hallway turning around cones, and were each minute notified, without further encouragement. Distances walked at 2 and 6 min were registered. Participants were permitted to use their habitual assistive devices during all tests, and were tested by the same investigator across time of day. In-between measurements, subjects performed their habitual activities ranging from therapies to outside city walking or resting, which were documented in a diary.

Data from each walking test were analyzed using a mixed effect model with trial number as a fixed effect and individual patients as a random effect, thus taking into account the expected positive correlation between the test results of a same subject. Following this model, observed scores on retest should be the same as baseline, within a range determined by the measurement variability expressed by 95% prediction intervals or limits of agreement.

All data were expressed as walking speed (m/s), allowing direct comparisons between short and long walking tests. Data from the 10 meter walk test at usual speed were log-transformed in order to meet the requirements for an analysis based on a normal distribution. Afterwards, prediction intervals on the original scale of measurement were obtained by exponentiation of the upper and lower bounds of the prediction intervals on the log scale. Finally, limits of agreement for the different walking tests were compared by modifying the mixed effects model.

The reported prediction intervals are based on all three measurements (9–10 AM, 12–1 PM, and 3–4 PM) for each patient, while for the graphical presentation, the first two measurements only are shown. Figures are, however, similar for the other comparisons (1 vs 3, 2 vs 3).

To illustrate the impact of disability level on the magnitude of within-day variability for different walking tests, ambulation groups were formed based on the usual walking speed classification system of Lord [23]. The patient group walking slower than 0.82 m/s during the 10 meter walk test was categorized as severe ambulatory dysfunction, while groups walking faster than 0.82 and 1.14 m/s were labeled as having moderate and mild ambulatory dysfunction respectively. For each subgroup, a new calculation of the 95% prediction intervals were done for all walking tests applying the abovementioned mixed effects model.

3. Results

102 persons from 8 centers in 5 countries participated in this study (see acknowledgment and reference [22] for details). Descriptive characteristics are provided in Table 1. For the walking test scores, the mean of the three measurements is reported, revealing a wide distribution of gait dysfunction in the sample.

Variability of short and long walking tests performed at maximal speed, expressed in absolute units, was relatively constant across the entire study population. Consequently, 95% prediction intervals, also expressed in absolute values, were independent of patient's ambulation status (see Fig. 1A–B–C with the limits of agreement displayed as dashed lines).

Expected performance for the 10 meter walk test at fastest speed, on retest, varied between the subjects' baseline performance by ±0.26 m/s. Expected gait speed values for the 2 and 6 minute walking test on retest

Table 1
Subject characteristics, including walk test scores.

	Subjects (n = 102)
Gender (m/f)	37/65
Age (years)	49 ± 9 (25–69)
Disease duration (years)	11 ± 7 (1–30)
Type of MS (RR/SP/PP)	53/31/18
EDSS	4.3 ± 1.6 (0–6.5)
Use of a walking aid (*n*)	47
6MWT (m/s)	1.04 ± 0.44 (0.09–1.92)
2MWT (m/s)	1.07 ± 0.44 (0.14–1.93)
10MWT, fastest speed (m/s)	1.34 ± 0.52 (0.14–2.4)
10MWT, usual speed (m/s)	1.04 ± 0.38 (0.11–1.79)

Values are mean ± SD (range), or number of subjects.
RR, relapsing–remitting; SP, secondary progressive; and PP, primary.