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Correlates of the Timed 25 Foot Walk in a Multiple Sclerosis Outpatient Rehabilitation Clinic

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Abstract

The Timed 25 Foot Walk (T25FW), a test of maximum walking speed on a short distance, is commonly used to monitor ambulation status and to assess treatment outcomes in MS. The main goal of this study was to determine how walking speed on the T25FW correlates with other clinician-reported and patient-reported measures in an outpatient MS rehabilitation clinic. We analyzed cross-sectional data systematically collected during a physiatry evaluation for the management of spasticity and walking limitations. In addition to demographic variables and the Expanded Disability Status Scale (EDSS), measures of body functions [lower extremity manual muscle testing (LE MMT), lower extremity Modified Ashworth Scale (LE MAS), Fatigue Severity Scale (FSS), leg pain], and measures of activity and quality of life [reported frequency of falls, Incapacity Status Scale (ISS), Rivermead Mobility Index (RMI), EQ-5D health questionnaire, and Patient Health Questionnaire-9 items (PHQ-9)] were administered. A multivariate regression analysis was conducted. 199 patients were included in the analysis (age 49.41(9.89) years, disease duration 15.40 (10.22) years, EDSS score 5.6 (1.2), and T25FW speed 70.93(44.13) cm/s). Both EDSS and LE MMT were significantly correlated with T25FW speed (R square 0.692, $p<0.001$). After adjusting for EDSS and LE MMT, lower T25FW speed was associated with higher ISS scores (R square=0.316, $p<0.001$), lower RMI scores (R square=0.540, $p<0.001$), and higher frequency of falls. EQ-5D and PHQ-9 were not significantly associated with T25FW speed. Our findings support the clinical relevance of the T25FW in the rehabilitation of patients with MS.

Keywords

Multiple Sclerosis; Rehabilitation; Walking Speed; Mobility

Introduction

Multiple Sclerosis (MS) is a chronic autoimmune disease of the central nervous system causing demyelination and axonal injury, and resulting in a wide range of symptoms. A

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majority of persons with MS (PwMS) become increasingly disabled throughout the duration of the disease (Ebers, 2001).

Walking limitations constitute one of the most common and one of the most visible consequences of MS. Walking difficulties affect up to 75% of PwMS at some point in the course of their disease (Hobart *et al.*, 2001). Further, published evidence demonstrates the importance of lower extremity function for PwMS (Heesen *et al.*, 2008), and the negative consequences of decreased walking ability on patients' functional status, quality of life, and employment (Paltamaa *et al.*, 2007; LaRocca *et al.*, 2011, Edgley *et al.*, 1991). Walking is included in the Brief ICF Core Set for MS (Coenen *et al.*, 2011).

The Timed 25 Foot Walk (T25FW), a component of the Multiple Sclerosis Functional Composite (MSFC), assesses a patient's ability to walk 25 feet "as quickly as possible, but safely" (Polman and Rudick, 2010). Due to its psychometric qualities and ease of administration, the T25FW is the most commonly used standardized test of walking performance in MS patients, both in the clinic and in clinical research (Bethoux and Bennett, 2011). However, the relationship between walking speed on the T25FW and other measures of disability and quality of life has not been fully established (Learmonth *et al.*, 2012).

There is growing interest in the systematic collection of standardized data in the context of routine clinical care, for the purpose of practice assessment, quality improvement, and reimbursement (Blumenthal and Tavenner, 2010). These datasets offer an opportunity to further validate outcome measures on large clinical populations.

The purpose of this study is to assess the relationship between walking speed on the T25FW and pertinent clinician- and patient-reported data from a large clinical registry, in MS patients referred to an outpatient MS rehabilitation clinic.

Methods

This study is a cross-sectional analysis of data systematically collected during initial physiatry evaluations for the management of spasticity and walking limitations in an MS rehabilitation clinic. The data was stored in the Knowledge Program (KP) IRB-approved clinical registry. The KP is an institution-wide initiative to promote the systematic collection, during routine clinical encounters, of clinical information into the electronic medical record (EMR), and to allow access to the data for research and clinical purposes (Katzan *et al.*, 2011). The chart review was approved by our Institutional Review Board.

Subjects

All patients with a diagnosis of MS established by their treating neurologist based on published diagnostic criteria (Polman *et al.*, 2011) who underwent a physiatry evaluation between 1/1/01 and 5/31/12, were considered for inclusion. Patients for whom performance on the T25FW was not documented were excluded from the analysis.

Data Collected

Data was collected during routine patient visits. Self-report questionnaires were completed by the patient on a computer immediately before the visit. Clinician-collected data was obtained during the visit based on interview and physical examination.

Data collected on all patients in the KP, regardless of diagnosis, include demographic parameters, ambulation status (no assistive device, unilateral support, bilateral support, or non-ambulatory), and two generic outcome measures:

- ○ The EQ-5D™ health questionnaire, a health-related quality of life (HR-QOL) measure which covers five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The scale also includes an index that measures health state from 0 to 100, 100 being the best health state (EuroQol Group, 1990). The psychometric properties of the EQ-5D™ were summarized in a recent literature review (Kuspinar and Mayo, 2014).
- ○ Patient Health Questionnaire-9 (PHQ-9), a 9-item depression inventory where each item is rated from 0 to 3, with higher scores reflecting more severe depressive symptoms. The total score ranges from 0 to 27 (Kroenke *et al.,* 2001). The PHQ-9 was found to be an adequate measure of depressive symptoms in MS, with acceptable inter-item reliability and convergent or discriminant validity. (Amtmann *et al.*, 2014)

Data specific to our clinic was chosen by the clinicians based on their prevalence and clinical relevance:

Self-report data:

- ○ Fatigue Severity Scale (FSS), a 9-item scale that measures the severity of fatigue and its effect on a person's activities and lifestyle (Krupp *et al.,* 1989). The FSS has robust psychometric properties, including sensitivity to worsening due to disease progression or improvement with treatment. (Krupp *et al.*, 2010)
- ○ Rivermead Mobility Index (RMI), a 15 item Questionnaire with progressing difficulty relating to daily mobility. 14 of the items are self-report. Scored 0-15, lower scores indicate decreased mobility in a patient (Collen *et al.,* 1991). The RMI exhibited concurrent validity with measures of ambulation and sensitivity to the effects of rehabilitation in patients with MS. (Vaney *et al.*, 1996)

Data collected by the clinician during the interview:

- ○ Disease duration (time elapsed between the first occurrence of neurologic symptoms and the visit)
- ○ Current disease course (relapsing remitting, secondary progressive, primary progressive, progressive relapsing)
- ○ Patient-reported leg pain using a generic pain numeric rating scale from 1 to 10, 10 being the worst possible pain. (Turk *et al.*, 1993)

○ Reported frequency of falls over the past year (none, less than once per month, more than once per month, more than once per week, daily). This questionnaire was developed for use in our clinic and has not been yet validated.

○ Incapacity Status Scale (ISS), A 15 item questionnaire assessing incapacity of a patient. Patients are asked to rate their difficulty with daily tasks from 0-4. Total score ranges 0-60, with a higher score indicating more severe impairment. Data on the validity and reliability of the ISS was gathered with initial scale development (LaRocca *et al.,* 1984). A recent study showed that the ISS correlates with both the physical and the mental composite scores of the SF-36 in individuals with MS. (Gavelova *et al.*, 2015)

Data collected during the physical examination:

○ Timed 25 Foot Walk (T25FW): the T25FW was performed once during the visit and walking speed in cm/s was calculated (T25FW speed).

○ Manual Muscle Testing (MMT): Muscle strength was assessed in the lower extremities (LE MMT: hip flexors, knee extensors, knee flexors, and ankle dorsiflexors),. Strength output was rated on a 0-5 scale where 0 denotes no muscle contraction and 5 represents normal strength (Wadsworth *et al.,* 1987).

○ Modified Ashworth Scale (MAS) (Bohannon & Smith, 1987): resistance to passive movement was assessed in the lower extremities (LE MAS: hip adductors, knee extensors, knee flexors, and ankle plantarflexors), and in the upper extremities (UE MAS: shoulder adductors, elbow flexors/extensors, wrist flexors/extensors, and finger flexors.) A score between 0 and 4 was allocated for each muscle group tested, with 0 indicating no increase in muscle tone and 4 indicating rigid in flexion or extension (Pandyan *et al.,* 1999).

○ Expanded Disability Status Scale (EDSS): the EDSS is widely used to assess neurologic disability from MS. Scores range from 0 to10 with higher scores indicating greater disability. Scores between 4.0 and 8.0 are primarily based on ambulation (Kurtzke, 1983).

○ One item of the RMI: The patient's ability to stand unsupported for 10 seconds was observed by the clinician.

Statistical Analysis

Categorical variables were summarized using frequency and percent. Continuous variables were summarized using mean and standard deviation. To determine how demographic and disease characteristics, as well as impairments, correlate with T25FW speed, a multivariate linear regression analysis was performed. Stepwise variable selection was used to obtain a final model. Variables considered in the analysis included: Age, Gender, EDSS, Disease Duration, Average UE strength, Average LE strength, Average UE spasticity, Average LE spasticity, Fatigue severity scale (FSS), and Patient reported leg pain score. Variables with $p<0.05$ were included in the final model. For each of EQ5D, ISS score, RMI score, and PHQ9 score, a multivariate regression analysis was performed to assess the relationship between T25FW speed and that outcome after adjusting for EDSS and factors significantly

associated with T25FW speed. For fall status, a cumulative logistic regression model (Proportional Odds Model) was used to assess its relationship with T25FW speed after adjusting for EDSS and factors significantly associated with T25FW speed. P value < .05 was considered statistically significant. All analyses were performed using SAS 9.2(Cary, NC)

Results

Out of a total of 450 patients who underwent an evaluation during the pre-defined time period, 199 were included in the analysis. The characteristics of our patient sample are presented in Table 1, and clinical data are summarized in Table 2.

Both EDSS and LE MMT scores were significantly correlated with T25FW speed (Table 3). After adjusting for EDSS and LEMMT, lower T25FW speed was associated with higher ISS scores, lower RMI scores, and higher frequency of falls. EQ-5D and PHQ-9 were not significantly associated with T25FW speed (Table 4).

Discussion

Our cross-sectional analysis of a large sample of MS patients, referred to a rehabilitation clinic for the management of spasticity and walking limitations, showed a strong correlation between walking speed on the T25FW, and both EDSS scores and lower extremity strength. After adjusting for EDSS and muscle strength, measures of mobility (RMI) and functional limitations (ISS) were associated with walking speed, but not measures of depression (PHQ-9) or quality of life (EQ-5D).

The characteristics of our patient sample are consistent with a rehabilitation setting, with an average disease duration of 15 years, a secondary progressive disease course in 44% of individuals (yet the disease course was relapsing-remitting in 41%), and approximately 70% using an assistive device for walking. A mean time of 15.7 years from disease onset to a Disability Status Scale score of 6 (requiring an aid for walking) has been reported in a population-based study (Scalfari *et al.,* 2014). Sex ratio and ethnicity data are consistent with the general MS population, and are not expected to be affected by the higher level of disability.

Correlations between EDSS and performance on the T25FW were reported in published validation studies of the MSFC. Rudick et al. observed that, of all of the components of the MSFC, the T25FW exhibited the strongest correlation with the EDSS (Rudick *et al.*, 2002). Further, Kalkers et al. found that, in 240 MS patients with a wide range of disability, the T25FW correlated independently with the EDSS across levels of disability and types of MS course, with the strongest associations observed among patients with severe disability and those with primary progressive MS (Kalkers *et al.,* 2000). Due to the nature of our practice, our patients' level of disability was in the higher range (average EDSS score between 5 and 6), which corresponds to the range of EDSS scores most affected by ambulation performance. Patients with primary progressive MS represented only 11% of our sample. In a multiple linear regression analysis, EDSS exhibited the strongest correlation with walking speed on the T25FW.

Even though many neurological impairments have an impact on walking, strength has been most consistently associated with walking speed. Our finding of a strong correlation between muscle strength on manual muscle testing and walking speed on the T25FW is consistent with findings from studies using more sophisticated instrumented strength measurements. In comparison with our subjects, most of those studies were focused on MS patients with a lower level of disability. Thoumie et al. observed a strong correlation between walking speed and peak hamstring torque in 20 individuals with MS and EDSS score lower than 6.0 (Thoumie *et al.,* 2002). Muscle strength parameters were correlated with performance on the T25FW in 35 MS patients with EDSS score from 2.0 to 4.0. In a longitudinal study of 136 MS patients with a wide range of EDSS scores, Zackowski et al. determined changes in the time to perform the T25FW associated with a 1 lb decrease in hip flexor or ankle dorsiflexor strength (Zackowski *et al.,* 2015). Significant differences in performance on a variety of walking and balance tests (including the T25FW) were reported in ambulatory MS patients with lower extremity spasticity based on the MAS, compared to patients without spasticity (Sosnoff *et al.,* 2011). However, muscle strength was not measured in this study, even though it is a significant confounding factor since the spasticity is generally associated with paresis. The absence of association between spasticity and walking performance in our study may also be explained by the low average severity of spasticity with a narrow standard deviation in the sample.

The observation of strong associations between walking speed on the T25FW and the RMI, a measure of mobility, in the setting of an outpatient MS rehabilitation clinic, is a novel finding. Walking is only one component (albeit a major component) of mobility. We did not find published reports of correlations between walking speed on the T25FW and the RMI. Vaney et al. reported a strong correlation between walking speed on the 10-meter walk test (at self-selected speed) and RMI scores, in 200 patients admitted to an inpatient rehabilitation unit (Vaney *et al.,* 1996). After the patients were divided into 2 groups (“normal” and “slow” walking speed), the correlation remained strong only in the slow speed group, which is more comparable to our sample. The authors also found that the RMI was more sensitive than the EDSS or preferred walking speed on the 10-meter walk test in detecting functional changes after rehabilitation in MS patients, and recommended combined use of the RMI and walking speed to measure the outcomes of interventions. Since our analysis was cross-sectional, we did not address the issue of sensitivity to change.

Similarly, we found no reports of association between the ISS and walking speed on the T25FW. The ISS is strongly correlated with the EDSS, but we adjusted for EDSS scores in our analysis (Gavelova *et al.,* 2015). Validation studies of the ISS reveal that the scores are strongly influenced by mobility, even though only 2 out of 16 items (Stairs and Ambulation) are directly linked to walking. A Principal Component Analysis of the ISS identified 3 factors: Mobility, Activities of Daily Living, and Bowel and Bladder (Syndulko *et al.,* 1996). Another study identified mobility and self-care as the main factors associated with the ISS total score (La Rocca *et al.,* 1984). Thus, it is not surprising that a measure of walking speed correlates with the ISS.

We found a weak association between T25FW speed and self-reported frequency of falls. Associations between walking speed and falls are not frequently reported in the literature. In

the study by Nogueira et al. mentioned previously, recurrent falls were correlated with walking speed on the 10-meter walk test (Pearson r 0.445, p< 0.01) (Nogueira *et al.,* 2013). Cattaneo et al. reported significantly higher scores on the Ambulation Index, a measure of walking impairment in MS where the score takes into account the T25FW time, in MS patients who reported 2 or more falls in the past 2 months, compared to those who reported less than 2 falls (Cattaneo *et al.,* 2002). However, in a study aiming at identifying measures of balance, gait, and strength that predict falls (prospectively reported over a 1-year period) in women with MS, walking velocity as measured on the GAITRite electronic walkway was not identified as a significant predictor (Kasser *et al.,* 2011). Given the known limitations associated with self-reported falls, and the fact that we did not assess other variables commonly identified as risk factors for falling, this finding must be interpreted with caution.

Depression and HR-QOL measures were not associated with T25FW walking speed in our sample. Literature focusing on depression in MS reports no association between performance on walking performance tests and the severity of depressive symptoms, although one recent study showed that PHQ-9 scores may be associated with disability worsening as defined by a 20% worsening on the T25FW (Gottberg *et al.,* 2007; Miller *et al.,* 2015). The lack of correlation between T25FW speed and EQ-5D is more surprising, particularly when considering the fact that 3 out of the 5 items of the EQ-5D pertain to mobility. Ambulation and mobility limitations were reported by MS patients as affecting their QOL (which was not assessed with standardized questionnaires) in a large population-based survey (La Rocca, 2011). In another survey of over 3,000 individuals with MS in the North American Research Committee on Multiple Sclerosis (NARCOMS) registry, those who reported an impact of MS on walking speed also reported poorer quality of life on a variety of measures, including the EQ-5D (Kohn *et al.,* 2014). These associations remained significant but were weaker after adjustment for demographic, disease-related, and symptom-related variables. The apparent contradiction between these reports and our findings may be attributed to the fact that there was no direct measurement of walking speed in these studies, and the fact that they included patients with a wide range of disability, as opposed to a clinic-based sample in our study.

We acknowledge methodological limitations to our study. We studied a specific group of MS patients, therefore our results cannot be generalized to the entire MS population. Further, since we included patients with various types of disease course, the results cannot be generalized to a specific MS subtype. We only performed a cross-sectional assessment, and as a consequence we cannot comment on the value of the T25FW in the prospective monitoring of patients undergoing rehabilitation interventions. The tools for measuring HR-QOL and depression were not specifically developed for and validated in the MS population. As stated above, our ability to detect an association between walking performance and spasticity was limited due to the low level and range of lower extremity spastic hypertonia in our sample.

In summary, we found that walking speed on the T25FW was associated with variables relevant to physical functioning (mostly lower extremity function) in a large sample of MS patients with walking limitations referred to an outpatient rehabilitation clinic, but not with measures of depression or quality of life. Our findings suggest that the T25FW, which is

easy and quick to administer, is a useful tool, which should be systematically administered in a rehabilitation setting, but complemented with self-report measures of perceived health status and emotional status. Further studies are needed, particularly prospective evaluations of the responsiveness of the T25FW to rehabilitation interventions compared to other outcome measures.

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Table 1

Patient sample characteristics (n=199)

Age	49.41±9.89 years
Sex	132 (66.3) female
Ethnicity	171(85.9) Caucasian, 17(8.5) African-American, 11(5.5) Unknown
Disease duration	15.40±10.22 years
Clinical course	88(44.2) Secondary Progressive, 82(41.2) Relapsing-Remitting, 22(11.1) Primary Progressive, 6(3.0) Progressive Relapsing, 1(0.50) Other
Ambulation status	60(30.2) no assistive device, 52(26.1) unilateral support, 86(43.2) bilateral support, 1(0.50) non-ambulatory(bilateral support for T25FW)

Values presented as Mean ± SD or N (%). No missing data.

Table 2

Clinical parameters (n=199)

T25FWSpeed (cm/s)	70.93±44.13
LE MMT* (0-5)	3.95±0.82
LE MAS (0-4)	0.89±0.71
EDSS	5.64±1.20
ISS (0-60)	18.57±7.15
Fall frequency	30(15.1) none, 84(42.2) < once per month, 48(24.1) > once per month, 32(16.1) > once per week, 5(2.5) daily
FSS* (0-100)	50.89±11.04
EQ5D_Index* (0-1)	0.63±0.18
EQ5D_HealthState* (0-100)	57.98±19.91
PHQ9* (0-27)	7.95±6.33
Leg pain* (0-4)	2.72±1.16
RMI* (0-15)	9.76±3.20

Values presented as Mean ± SD or N (%). T25FW: Timed 25 Foot Walk, LE MMT: Lower Extremity Manual Muscle Testing, LE MAS: Lower Extremity Modified Ashworth Scale, EDSS: Expanded Disability Status Scale, ISS: Incapacity Status Scale, FSS: Fatigue Severity Scale, EQ5D: European Quality of Life, PHQ9: Patient Health Questionnaire-9, RMI: Rivermead Mobility Index

*Missing values: LE MMT=2, FSS =12, EQ5D index =16, EQ5D health state=92, PHQ-9 =46, leg pain =11, RMI =14.

Table 3

Factors associated with T25FW speed (N=197, R square = 0.692)

Parameter	Coefficient	Standard Error	p
EDSS	−16.78	1.79	<.001
LE MMT*	3.70	0.38	<.001

*Square transformed. EDSS: Expanded Disability Status Scale, LE MMT: Lower Extremity Manual Muscle Testing

Table 4

Multivariate regression analysis of relationship between selected variables and T25FW speed after adjusting for EDSS and LE MMT.

ISS (N=197, R square=0.316)				
Parameter		**Coefficient**	**Standard Error**	**p**
T25FWSpeed		−0.07	0.02	<.001
EDSS		0.85	0.52	0.10
LE MMT*		−0.05	0.11	0.64
RMI (N=183, R square=0.540)				
Parameter		Coefficient	Standard Error	p
T25FWSpeed		0.04	0.01	<.001
EDSS		−0.25	0.20	0.21
LE MMT*		0.07	0.04	0.097
Fall frequency (N=197, Nagelkerke's Pseudo R square=0.053)				
Variable	**Odds Ratio**	**95% Lower CI**	**95% Upper CI**	**P**
T25FWSpeed	1.01	1.00	1.02	0.048
EDSS	0.84	0.61	1.15	0.28
LE MMT*	0.92	0.86	0.99	0.024
PHQ9 (N=151, R square=0.029)				
Parameter		**Estimate**	**Standard Error**	**p**
T25FWSpeed		−0.04	0.02	0.10
EDSS		−0.58	0.69	0.41
LE MMT*		0.27	0.13	0.047
EQ5D (N=181, R square=0.026)				
Parameter		**Coefficient**	**Standard Error**	**p**
T25FWSpeed		0.0006	0.0006	0.31
EDSS		−0.0145	0.0159	0.36
LE MMT*		−0.0040	0.0034	0.24

*Square transformed. T25FW: Timed 25 Foot Walk, UE MMT: Upper Extremity Manual Muscle Testing, LE MMT: Lower Extremity Manual Muscle Testing, UE MAS: Upper Extremity Modified Ashworth Scale, LE MAS: Lower Extremity Modified Ashworth Scale, EDSS: Expanded Disability Status Scale, ISS: Incapacity Status Scale, FSS: Fatigue Severity Scale, EQ5D: European Quality of Life, PHQ9: Patient Health Questionnaire-9, RMI: Rivermead Mobility Index