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## ARTIGO ORIGINAL

### Functional gait assessment in patients with relapsing-remitting Multiple Sclerosis and relation to the risk of falls

#### *Avaliação funcional da marcha em pacientes com esclerose múltipla recorrente-remitente e relação com o risco de quedas*

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## Resumo

**Objetivo:** Demonstrar as avaliações funcionais e sua correlação nos padrões de marcha de pacientes com Esclerose Múltipla, utilizando um método não invasivo por meio do *Timed Up and Go*, teste de Tinetti, teste de caminhada de 25 pés e escala de *Expanded Disability Status Scale* (EDSS). **Métodos:** Foram avaliados 40 pacientes com Esclerose Múltipla, usando *Timed Up and Go*, teste de Tinetti, teste de caminhada de 25 pés e escala de EDSS. **Resultados:** No presente estudo, observamos correlações moderadas a altas entre EDSS e *Timed Up and Go*, teste de Tinetti e teste de caminhada de 25 pés ( $p < 0,0001$ ). Os pacientes relataram tempos de execução mais longos para os testes *Timed Up and Go* e *25-Foot Walk* e menores escores no teste de Tinetti. Encontramos uma correlação direta entre a duração da doença, a escala EDSS, o tempo de execução *Timed Up and Go*, o tempo de execução de *25-Foot Walk* e o escore do teste de Tinetti ( $p < 0,0001$ ). **Conclusão:** avaliações adequadas de risco de marcha e queda são importantes para evitar complicações relacionadas à Esclerose Múltipla.

**Palavras-chave:** esclerose múltipla, avaliação da marcha, EDSS, risco de quedas.

## Abstract

**Objective:** To demonstrate correlation functional evaluations of gait on the patients with Multiple sclerosis, using a noninvasive method by means of *Timed Up and Go*, Tinetti test, 25-Foot Walk test and *Expanded Disability Status Scale* (EDSS). **Methods:** We evaluated 40 patients with Multiple sclerosis using *Timed Up and Go*, Tinetti test, 25-Foot Walk test and EDSS scale. **Results:** In present study, we have observed moderate to high correlations between EDSS and *Timed Up and Go*, Tinetti test and 25-Foot Walk test ( $p < 0.0001$ ). The patients reported longer execution times for *Timed Up and Go* and 25-Foot Walk tests and lower scores on the Tinetti test. We found a direct correlation between illness duration, EDSS scale, *Timed Up and Go* execution time, 25-Foot Walk execution time and Tinetti test score ( $p < 0.0001$ ). **Conclusion:** Proper gait and fall risk evaluations are important in order to avoid complications that are related to Multiple sclerosis.

**Key-words:** multiple sclerosis, gait evaluation, EDSS, risk of falls.

## Introduction

Multiple Sclerosis (MS) is a chronic immune disease of the central nervous system, in which an inflammatory and degenerative process of white and gray matter occurs [1]. MS is one of the most common neurological diseases affecting gait in young adults, with approximately 2.3

million people globally living with some form of MS. It is a degenerative condition of the central nervous system in which inflammation causes demyelination, disrupting neurological conduction [2].

The impact of MS varies widely, ranging from mild to severely disabling as the disease progresses. It has several clinical manifestations including, but not limited to, sensory disturbance, weakness, ataxia, muscle spasticity, and cognitive difficulties [3]. Different subtypes of the condition significantly increase the variety and timing of symptoms in a condition that is already extremely diverse in its effect on each individual. Of note, MS is a chronic, lifelong condition, and most people who are diagnosed with MS are 20 to 40 years old [2,4]. Among disabilities, gait disorders are the most frequent since proprioceptive, pyramidal tracts and the cerebellum are frequently affected [5]. During gait patterns, various aspects can be affected, for example, the speed, the length of the step, the maximum distance, the quality of the movements and the ability to maintain balance [5-8].

The motor skills involvement, especially gait disturbances, are relevant in studies involving MS patients since walking is a domain of fundamental neurobiological and muscular association for life. In view of the above, MS may cause deficiencies in mobility tasks [9]. In addition, Kelleher *et al.* [3] demonstrate that gait impairment is the main target, which becomes a priority in studies that target rehabilitation in people diagnosed with MS since 85% of study participants reported gait changes as their main complaint. The impairment in sensory function and mobility is a frequent and disabling consequence of MS that may lead to greater deficits [10], for instance, muscular atrophy and increased risk of falls traumas [9,11]. Thus, the balance-gait relationship through functional evaluations of Tinetti test (TT), Time Up and Go (TUG) test and Timed 25-Foot Walk (T25FW) are frequently used as indicators of the motor incapacity progression [12]. A cross-sectional study corroborates that gait speed acts as a spatiotemporal measure of greater sensitivity to disease severity [10,12,13].

Inevitably, interventions for MS include drug therapy as well as the joint action of rehabilitation activities and constant assessment through walking domain scales [14,15]. Therefore, we used TT, TUG, T25FW and EDSS scale in order to evaluate and direct the therapeutic protocol for MS patients. However, a complementation is necessary, with diagnosis based on a thorough medical history associated with clinical and laboratory examination [16]. According to clinical evolution, MS has specific classifications: remitting-relapsing (MS-RR), primary progressive (MS-PP), primary progressive with episode (MS-PP with episode) and secondary progressive (MS-SP) [4,17]. The most common classification is MS-RR, accounting for 85% of all newly diagnosed cases. MS-SP form is a natural evolution of the first one. In approximately 50% of cases, after 10 years of the initial form diagnosis (MS-RR) a conversion to the MS-SP form happens [18]. As for MS-PP and MS-PP with the episode, they add up to 10%-15% in all cases [16]. Accordingly, the present study examined the relation between the TT, TUG, T25FW and EDSS scale as a cognitive behavior evaluation and gait performance, of the few non-pharmaceutical therapies that maintain or improve the ability to walk and size the potential risk of falls in MS patients [19].

## Material and methods

### *Participants*

Transversal study with MS-RR patients attended at Hospital Antônio Pedro of Fluminense Federal University (HUAP/UFF), Rio de Janeiro, between May 2013 and July 2015. The present study evaluated 40 patients with MS-RR (11 men and 29 women, average age =  $41.5 \pm 11.0$  years). We selected participants aged over 18 years, with a diagnosis of MS-RR, Expanded Disability Status Scale (EDSS) lower than 6.5. Exclusion criteria were comorbid conditions that could cause changes in the tests such as orthopedic (arthrosis, ligament injuries), rheumatological (rheumatoid arthritis), cardiological (heart failure) and neurological diseases (i.e., Parkinson's disease). Additionally, recent episodes (last three months), cognitive deficit preventing the understanding of tests and people's refusal to sign an FPIC were used as exclusion criteria. Finally, all subjects signed the Free and Informed Consent Form. This study research project was submitted to the Ethics Committee of the Medical School of the Fluminense Federal University, approved under the registration no. 12300413.2.0000.5243.

### *Experimental procedure*

Functional Activity Evaluation: Two neurologists evaluated the neurological involvement by the EDSS scale, as well as three tests that evaluate patients functionality: TT, TUG and T25FW [19,20]. We instructed all patients to avoid any activity that could cause muscle fatigue, for instance, long walks or stairs in which the energy expenditure is higher [21]. In order to complement the results about the functional disability of patients, the results were classified by using EDSS [22], whose score refers to the functions involvement. The scale ranges from 0 to 10 [20].

TT has been used to evaluate balance and gait abnormalities. A score above 24 points means low fall risk, between 19 and 24 points means moderate risk and lower than 19 points means low risk. The maximum score is 28 points [20].

T25FW is a quantitative measure of lower extremity function described by Fischer et al. [23]. The time required to walk 25 feet was measured to evaluate the functional activity of the patients. The reliability of this test has previously been confirmed. The test was repeated three times, with 5-minute rest intervals to prevent fatigue. The time required to complete the test was measured using a standard chronometer, and the lowest time was considered [20,24].

TUG Test is a valid and reliable test to evaluate functional activity in patients with MS and is based on the time required to complete a complex activity. Validity and test-to-test reliability have been proved in previous studies. The procedure is as follows: the patient must get up from a sitting position in a standard chair, advance for 3 m, return to the chair, and sit down again. The test was repeated three times, with 5-minute rest intervals to prevent fatigue. The time required to complete the test was measured using a standard chronometer, and the lowest time was considered [25].

### *Statistical analysis*

We described the variables using means (standard deviation [SD]) for continuous variables. We use Pearson's Correlation for calculate to detect the relationship between the TT, TUG, T25FW and EDSS variables, and with the objective of relating to risk of falls. We used the descriptive statistics in tables to show contingency, calculation of averages, standard deviations and results of the group. Statistical significance was considered in the case of  $p < 0.05$ . All analyses were performed with the SPSS software for Windows version 320 20.0.

## **Results**

The results of the EDSS showed scores between 0 and 6.5 with an average of  $3.02 \pm 2.16$  for patients with MS. In view of this question, with the statistical analysis already mentioned, variables of TT, TUG and T25FW test were correlated. All tests are correlated with each other and with moderate to strong relationships ( $p < 0.001$ ) (Table I). Only the TT relationship with all others is inversely proportional, that is, the greater the TT score, the shorter the TUG and T25FW execution times will be. In addition, as for the relationship between TUG and T25FW it is directly proportional, the greater the value of TUG, the greater the value of T25FW. In summary, correlation of EDSS was also calculated with other tests and it showed that TUG, T25FW. In addition, T25FW replication has significant positive relationship with EDSS; in the case of TT, the correlation is negative (Table I).

With the final data about functional activity evaluation, we calculated the average of the result of TT, TUG and T25FW (table II). For each patient, risk types were assigned based on TUG and another on TT. The total average of these test were referred to as general fall risks (Table III). EDSS and T25FW averages for each type of risk were also included. The risks were classified as mild, moderate and severe (Table III).

**Table I – Pearson's Correlation for detect the relation between the TUG test, TT, T25FW and EDSS variables.**

		Timed Up and Go	Tinetti	T25FW	T25FW Replication	EDSS	Time of disease	Episodes of fall
<b>TUG (seconds)</b>	PC	1	-0.609	0.922	0.915	0.669	0.310	-0.006
	p-value		0.0001	0.0001	0.0001	0.0001	0.070	0.983
	N	40	40	40	40	40	35	17
<b>Tinetti</b>	PC	-0.609	1	-0.621	-0.575	-0.732	-0.430	-0.015
	p-value	0.0001		0.0001	0.0001	0.0001	0.0101	0.953
	N	40	40	40	40	40	35	17
<b>T25FW (seconds)</b>	PC	0.922	-0.621	1	0.992	0.639	0.365	0.426
	p-value	0.0001	0.0001		0.0001	0.0001	0.031	0.088
	N	40	40	40	40	40	35	17
<b>T25FW Replication (seconds)</b>	PC	0.915	-0.575	0.992	1	0.589	0.065	0.036
	p-value	0.0001	0.0001	0.0001		0.0001	0.031	0.027
	N	40	40	40	40	40	35	17
<b>EDSS</b>	PC	0.669	-0.732	0.639	0.089	1	0.042	0.053
	p-value	0.0001	0.0001	0.0001	0.0001		0.044	0.039
	N	40	40	40	40	40	35	17
<b>Time of Disease</b>	PC	0.010	-0.030	0.065	0.065	0.042	1	0.751
	p-value	0.070	0.010	0.031	0.031	0.044		0.001
	N	35	35	35	35	35	35	17
<b>Episodes of fall</b>	PC	-0.006	-0.015	0.026	0.036	0.053	0.751	1
	p-value	0.983	0.953	0.088	0.027	0.039	0.001	
	N	17	17	17	17	17	17	17

PC = Pearson's Correlation

**Table II - Mean of the Patient Group results: TUG test, Tinetti, T25FW and EDSS variables.**

	Timed Up and Go*	Tinetti	T25FW*	T25FW Replication*
Mean± S.D	15.5±10.9	21.8±4.9	9.6±7.9	9.8±9.1
<b>Patients</b> Minimum	6.18	11	4.00	4.00
Maximum	69.87	28	42.40	47.68

**Table III – Mean data with Risk analysis of fall in MS patients.**

General Risk	EDSS	TUG (seconds)	Tinetti	T25FW (seconds)	T25FW Replication (seconds)	Time of disease (seconds)	Episodes of fall	
<b>Mild</b>	N	20	20	20	20	20	19	
	Mean ± S.D	1.5±0.8	9.8±1.5	25.8±1.5	6.1±1.3	6.1±1.3	8.2±7.6	2.5±1.1
	Minimum	0.00	6.18	22	4.00	4.00	0	1
	Maximum	3.00	13.26	28	10.00	10.00	25	5
<b>Moderate</b>	N	12	12	12	12	12	11	
	Mean ± S.D	3.4±1.8	14.6±2.04	19.6±3.6	8.2±2.9	7.7±2.9	13.7±7.6	2.5±1.0
	Minimum	1.00	12.43	11	5.00	5.00	0	2
	Maximum	6.00	18.87	24	14.00	15.00	22	4
<b>Severe</b>	N	8	8	8	8	8	5	
	Mean ± S.D	6.3±0.4	30.9±16.9	15.0±1.5	20.4±12.6	21.9±15.2	16.4±10.8	
	Minimum	5.50	17.00	13	9.08	8.80	4	
	Maximum	6.50	69.87	17	42.40	47.68	28	
<b>Total</b>	N	40	40	40	40	40	35	
	Mean ± S.D	3.02±2.5	15.5±10.9	21.8±4.9	9.6±7.9	9.8±9.1	11.09±8.5	2.5±1.06
	Minimum	0.00	6.18	11	4.00	4.00	0	1
Maximum	6.50	69.87	28	42.40	47.68	28	5	

## Discussion

This study include a sample of patients with Multiple Sclerosis remitting-relapsing to examine the relationship of neurological involvement by the EDSS scale, as well as three tests that evaluate patients' functionality: TT, TGU, T25FW with changes in gait and association with the risk of falls. The results will be discussed on the basis of this paradigm.

Overall, our findings show that quantitative measures by the TT, TGU and 25FW detect specific deficiencies in MS patients, and these relate to global measures of disability and ambulation. The functional measures analysis has shown a decline in the strength of muscle control during gait, which may be associated with the increase in fatigue that is more frequent in patients with multiple sclerosis remitting-relapsing. The mean scores for the TT, TGU, T25FW and EDSS scale suggest a greater tendency for changes in light sensory perception embedded in motor skills [19,26,27]. Thus, it is essential to emphasize that the Report of the Quality Standards Subcommittee of the American Academy of Neurology establishes a level of recommendation for all patients in a neurological doctor's office with risk factors identified as gait and balance disorders, the use of walking assistance, weakness of limbs, or sensory loss. The report recommends that patients with these risk factors are evaluated for fall risk.

Accordingly, altered gait is a major problem for many MS individuals because it limits their participation in regular activities, decreases their ability to participate in physical exercise, and increases the episode of falls and injuries [6,28,29]. Interestingly, our variables correlated with the EDSS cognitive ability test demonstrate limited mobility as well as the overall health impact of MS patients. Therefore, being identified as the main determining factor for physical and social limitations [10]. Through this study, it was possible to analyze several secondary variables as the relation between the number of episodes, the illness duration and the age of patients with risk. It was found thereby that the illness duration is at the limit of significance, giving the impression the greater the illness duration, the greater the execution time in TT, TGU and T25FW. This shows that even "stable" patients, i.e. no new lesions on MRI, suffer functional decline regardless.

The factors TT, TGU, T25FW and EDSS scale were correlated, traditionally accurate measures to determine the distance covered over a period of time through protocols standardized [15]. It acts as evaluative anchors of gait domain, a possible means of rehabilitation, as well as measuring potential risks of falls for patients. Several studies were used to evaluate the prediction failure. In one of them, Mazumder *et al.* [30] reported on fall prediction, which evaluated 54 patients with EDSS scores of 6 or lower. It used the Twelve Item MS Walking Scale (MSWS-12), T25FW, computerized balance assessment and the fall FES-1 questionnaire as a methodology. The results showed thirty-seven (71%) individuals fell at least once in the six-month period according to FES-1. AUC measurement, a statistical method of summary information of a series of measures in individuals, was used to predict falls in the following 6 months. In this evaluation model, the methods are potentially accurate, since the evaluations are supported in statistical norms from diverse clinical and physiological data of the patient [2,5,6]. In exemplification of the questioning, despite the natural variability among the patients, the gait may be a personal trait rather than an impact of the fatigue induced by the neurological disease. Therefore, changes in gait characteristics over a given period of time may be measured by the joint action of the TT, TGU and T25FW, in order to draw clinical conclusions and remove the variability between subjects.

We similarly report that mobility limitations measured by the performance of TT, TGU and T25FW correspond to changes in employment and functional independence, and propose that MS individuals are more likely to be functionally impaired. The results assume that mobility deficits correspond to changes in functional gait use and MS progression related disability. Comparing the parameters of TT, TGU and T25FW, we observed significant differences when correlating the major gait effects and cognition-related.

In relation to the previous questions, we interpret this as connection deficiencies in the neuronal inputs of sensorimotor integration promoted by the neurological disease, since they have a greater impact on the patient daily life. The results show that MS patients showed scores related to decreased motor control and had a high variation of gait cycle length in the tests. It is also observed that the EDSS components of the cognitive evaluation scale related to the functional evaluation tests corroborate with the literature that the cognitive domain has a relation with the sensorimotor integration level in gait activity. In view of this, it is important that rehabilitation therapists understand the nature of gait dysfunction in MS people and the effect of interventions that target gait symptoms. In short, cognitive behavior assessment and gait

performance favor physical rehabilitation, which is one of the few non-pharmaceutical therapies to maintain or improve the ability to walk and size the potential risk of falls in MS patients [20,24,25].

#### *Study limitations*

Despite the finding of correlations between the gait evaluation tests, the cognitive decline test and the risk of falls episode, the present study has some limitations. At first, the results come from a small sample of convenience. Second, the study design did not include a corresponding control group to consider the extent of these results beyond the current sample. Another point is that the risk of falls was measured in a population in which memory deficits are common since it requires caution in interpreting the results. However, it is important to note that our findings provide some support that leads to the understanding of the cognitive decline relation and gait changes as possible markers of falls episodes in patients with neurological diseases.

#### **Conclusion**

Tests and functional evaluations of lower limbs were able to trace possible fall risk and/or gait disorder. Thus, it was possible not only to correlate test variables with EDSS with fall risk, but also compare TT, TGU and T25FW in patients with MS. The study observations suggest that a decrease in walking resistance, in addition to being associated with a higher risk of falls. Our findings, although with some limitations, support the monitoring of future falls in MS patients. In this context, future research is needed to understand the consistency of fall risk factors across the disability spectrum in MS patients, and thus to determine a model of interventions designed to reduce and prevent falls. In summary, we highlight that these tests are fast, easy to perform, low cost and present high sensitivity which helps optimize outpatient care.

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