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Impact of disease duration on functional status of patients with spinocerebellar ataxia type 2

Repercussões do tempo de evolução sobre o perfil funcional de pacientes com ataxia espinocerebelar do tipo 2

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ABSTRACT

Objective: To correlate disease duration in spinocerebellar ataxia type 2 (SCA2) with disease severity, balance and functionality. **Method:** Sixteen SCA2 patients were analyzed for: disease duration, disease severity (SARA score), balance (Berg balance scale score) and functionality (FIM and Lawton scores). **Results:** Greater severity was correlated with worse functionality (Lawton: r = -0.0561, FIM: r = -0.6402) and balance (r = -0.7188). Longer disease duration was correlated with greater severity (p = 0.0002) and reduced functionality (FIM: p = 0.005; Lawton: p = 0.0402) and balance (p = 0.0036). A year increase in disease duration corresponded to a 0.8-point increase on the SARA scale, a 1.38-point decrease in FIM score, a 2.30-point decrease on the Berg balance scale and a 0.45-point decrease on the Lawton scale. **Conclusion:** Longer disease duration in this series of SCA2 patients was correlated with greater disease severity, worse balance and greater functional dependency.

Keywords: spinocerebellar ataxias; severity of illness index; postural balance.

RESUMO

Objetivo: Correlacionar com o tempo de evolução da doença em pacientes com ataxia espinocerebelar do tipo 2 (SCA2) com a gravidade, equilíbrio e funcionalidade. **Método:** Foram considerados dados de 16 indivíduos: tempo de evolução, nível de gravidade (SARA) e escores de equilíbrio (BERG) e funcionalidade (MIF e LAWTON). **Resultados:** A maior gravidade esteve relacionada aos piores escores de funcionalidade (LAWTON: r = -0,0561, MIF: r = -0,6402) e de equilíbrio (r = -0,7188). O maior tempo de evolução esteve relacionado à maior gravidade (p = 0,0002) e menor funcionalidade (MIF: p = 0,005; Lawton (p = 0,0402) e equilíbrio (p = 0,0036) sendo que para o aumento de um ano no tempo de evolução, espera-se um aumento de 0,8 pontos no escore da SARA, e decréscimo de 1,38 pontos na MIF, 2,30, na Berg e 0,45 na Lawton. **Conclusão:** O tempo de evolução dos sintomas está associado a maior gravidade da doença, pior equilíbrio e maior dependência funcional em pacientes comSCA2.

Palavras-chave: ataxia espinocerebelar; índice de gravidade da doença; equilíbrio postural.

Spinocerebellar ataxias (SCAs) are a large, complex group of neurodegenerative diseases characterized by progressive cerebellar ataxia with oculomotor abnormalities, dysarthria, pyramidal and extrapyramidal signs, pigmentary retinopathy, peripheral neuropathy and cognitive dysfunction, among other manifestations[1,2]. More than 40 types of SCA have been identified to date, including SCA type 2 (SCA2), which is caused by a CAG trinucleotide repeat expansion on chromosome 12q23-24.1[1].

The third most common form of SCA in Brazil is SCA2. Symptoms typically begin in the third decade of life and are associated with worse disease prognosis when they appear early[1].

Clinical manifestations of the disease include action and rest tremor, polyneuropathy, upper motor neuron impairment and parkinsonism, which may predominate in some cases[3]. A balance deficit is one of the most characteristic signs of SCA and one of the main factors directly affecting posture and functionality[4]. Increased disease severity implies greater impairment of postural balance and functionality, and increased risk of falls[4,5].

An annual increase in the Scale for the Assessment and Rating of Ataxia (SARA) score of between 1.40 and 1.49 has been reported in patients with SCA2[6,7], but progression

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of functional loss and loss of balance have not yet been extensively described.

The aim of this study was, therefore, to assess functionality and balance in individuals with SCA2 and to correlate these with disease severity and duration.

METHODS

This was a retrospective, descriptive, cross-sectional study and was approved by the Committee for Ethics in Research at the Hospital de Clínicas, Federal University of Paraná (HC-UFPR) (CAAE: 48399915.7.0000.0096, ref. no.: 1.280.919).

The study sample was non-probabilistic and comprised men and women who were being followed up at the ataxia outpatient unit in the movement disorders unit at the Hospital de Clínicas, Federal University of Paraná.

Inclusion criteria were: being at least 18 years old; having a clinical diagnosis of SCA2; having a positive genetic test for SCA2 or having a family member who had a positive genetic test for SCA2; and taking coenzyme Q10 (100–500 mg/day) regularly. Individuals who had any musculoskeletal disorders that could affect their balance or functionality or who had other concomitant neurological disease (non-ataxic manifestations) were excluded.

Sixteen patients who had been diagnosed with SCA2 and had complete medical records were included in the study.

The following information was collected: age, gender, diagnosis, age of onset of ataxic symptoms, disease duration, disease severity, balance and functional-independence scores, and number of CAG repeats.

Balance was assessed on the Berg balance scale, which has 14 items and a maximum score of 56. Scores of less than 46 indicate a high risk for falls[8].

Functional independence was assessed using the Functional Independence Measure (FIM), which assesses motor and cognitive domains. Scores vary from 18 to 126, and a high score indicates good functional independence.

The FIM measures disability in patients with functional limitations due to various causes and quantifies their need for assistance when performing motor and cognitive tasks associated with activities of daily living. The validated Brazilian version was published in 2004. The instrument is used in interviews with the patient and/or the patient's care-giver. In this study, it was only used with the patient[9].

Independence for instrumental activities of daily living was assessed on the Lawton scale[10], which consists of seven items and has a total score ranging from 7 (dependence on others to help carry out activities) to 21 (complete independence). The Lawton scale is an appropriate instrument to assess abilities that are considered more complex than the basic activities of daily living, such as shopping, doing housework and using transportation, and is useful for identifying a person's functional ability at a given time and how this improves or deteriorates over time[11]. The severity of ataxia was assessed on the SARA scale.

All the scales used in this study were translated into Portuguese and validated for Brazil[12,13,14,15].

Statistical analysis

The descriptive analysis was based on the mean and standard deviation of the scores for severity, balance, instrumental activities of daily living and functionality. Correlations between parametric data were investigated using the Pearson correlation coefficient and Biostat® 5.0 for Windows. The Shapiro-Wilk test was used to test for normality. Analysis of variance, applied to regression, was used to test for a relationship between disease duration and severity, functionality and balance.

The scale of magnitudes for effect statistics proposed by Hopkins was used to interpret the correlation coefficients: < 0.1 = trivial; 0.1 to 0.29 = small; 0.30 to 0.49 = moderate; 0.50 to 0.69 = large; 0.70 to 0.90 = very large; > 0.90 = nearly perfect. A level of significance of $p < 0.05$ was used.

RESULTS

Of the 16 patients evaluated, 75% (n = 12) were male. Mean age was 45.43 ± 10.41 years, and mean age at onset of symptoms was 35 ± 8.72 years. Mean disease duration was 9.12 ± 4.61 years, mean disease severity (SARA score) 11.4 ± 4.65, mean balance score on the Berg scale 37.25 ± 15.61, mean FIM score 115.37 ± 9.64 and mean score on the Lawton scale 17.25 ± 4.09. Disease duration, SARA, Lawton, FIM and Berg scores and number of CAG repeats for each patient are shown in Table 1.

There was a strong negative correlation between scores on the SARA and Lawton scales (r = -0.0561), a strong negative correlation between SARA scores and FIM scores (r = -0.6402), a strong negative correlation between SARA scores and Berg scores (r = -0.7188), a strong positive correlation between Lawton scores and FIM scores (r = 0.8963), a strong negative correlation between Lawton scores and Berg scores (r = -0.8340) and an almost perfect correlation between FIM scores and Berg scores (r = 0.9674). The results of the correlation tests between the SARA, Berg, FIM and Lawton scores are shown in Table 2.

Linear regression revealed a significant relationship between disease duration and the SARA score ($p = 0.0002$), FIM score ($p = 0.0051$), Berg balance score ($p = 0.0036$) and Lawton score ($p = 0.0402$). These results are shown in the Figure and interpreted in Table 3.

DISCUSSION

This study of 16 SCA2 patients revealed significantly impaired functionality and balance. Disease severity was correlated with worse functionality and balance scores, and

Table 1. Disease duration and functional independence, disease severity and balance scores for each patients.

Patient	Gender	Current age	Disease duration (years)	SARA	Lawton	FIM	Berg	CAG repeats
1	F	36	2	4.5	21	125	54	22/52
2	M	30	3	9	21	124	48	20/39
3	M	36	3	3	21	126	56	-
4	F	46	4	9	21	123	54	21/38
5	M	46	5	10	18	121	47	16/48
6	M	45	8	7	9	108	32	22/40
7	M	65	10	7.5	21	118	47	23/54
8	M	40	10	12	21	122	47	20/48
9	M	40	10	13	14	104	16	22/58
10	M	54	11	13	15	109	32	22/48
11	M	49	11	12.5	21	126	46	-
12	M	44	11	18	17	118	23	20/37
13	M	42	12	12.5	17	115	40	20/46
14	F	55	13	18.5	11	100	9	22/37
15	M	33	15	18	12	96	5	-
16	F	66	18	15	16	111	28	22/56

F: female; M: male; SARA: total SARA (Scale for the Assessment and Rating of Ataxia; FIM: Functional Independence Measure) score; Berg: total score on the Berg scale; FIM: total score on the Functional Independence Measure scale; Lawton: total score on the Lawton independence for instrumental activities of daily living (ADL) scale.

Table 2. Correlation between SARA, Berg, FIM and Lawton scores, $p > 0.05$*.

Variable	SARA	Berg	FIM	Lawton
SARA	1			
Berg	(r) = -0.7188* (p) = 0.0017	1		
FIM	(r) = -0.6402* (p) = 0.0075	(r) = 0.9674* (p) = < 0.0001	1	
Lawton	(r) = -0.5061* (p) = 0.0454	(r) = -0.8340* (p) = < 0.0001	(r) = -0.8963* (p) = < 0.0001	1

SARA: Scale for the Assessment and Rating of Ataxia; FIM: Functional Independence Measure

greater disease duration was correlated with greater severity, worse balance and greater functional impairment.

Mean age at onset of symptoms in the study series was 35 years, in agreement with the literature, in which the age of onset is reported to be between the third and fifth decades of life[16]. The main symptoms of ataxia are a balance deficit and worsening gait. The disease initially affects the legs, but as it progresses the symptoms extend to the trunk and arms[2].

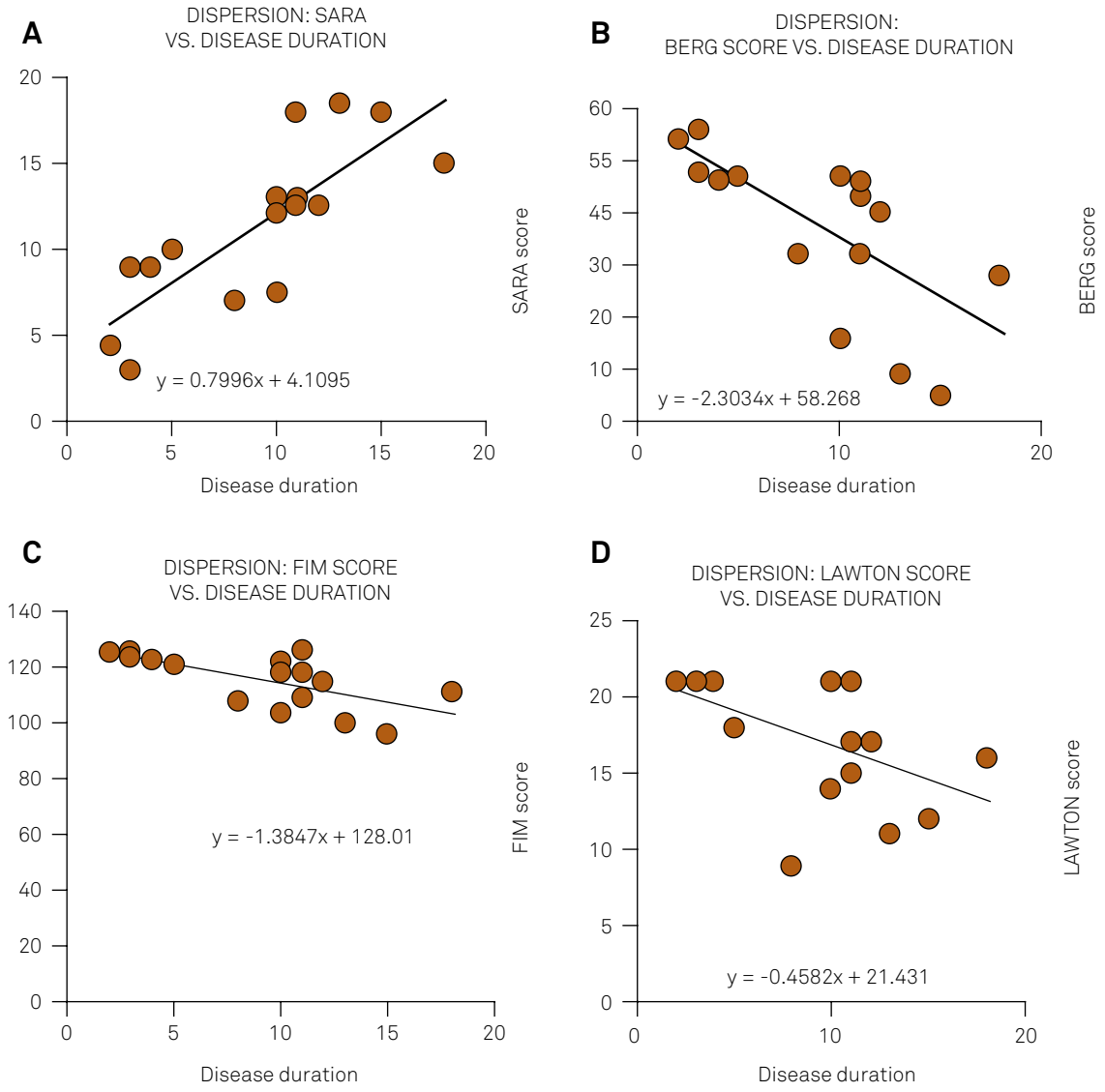
The mean Berg score was 37.25 ± 15.61, and minimum and maximum scores were 5 and 56. The Berg test is objective and can identify an increased propensity for falls. Although a lower score on this scale is associated with a greater risk of falls, the relationship is not linear: between 56 and 54, a one-point decrease on the Berg scale is associated with a 3% to 4% increase in the risk of falls, but between 54 and 46, a one-point decrease on the scale is associated with a 6% to 8% increase. Below 36 there is an almost 100% risk of falls. Hence, changes in the Berg score can lead to very different forecasts for the probability of falls[8]. It is reasonable to conclude, therefore, that the risk of falls for the patients in this study is close to 100%.

The cerebellum plays a crucial role in the control of movement, locomotion and postural stability. Cerebellar degeneration in individuals with SCA2 can therefore affect postural control. It has also been suggested that postural instability is one of the main signs of SCA2 and leads to balance deficits and, consequently, limitations on the individual's ability to perform activities of daily living[17].

The ability to maintain balance is an integral part of gross motor skills, and poor balance and inadequate posture result in difficulties performing activities of daily living[18]. In this series, the main functional difficulties involved locomotion (walking, moving around in a wheel chair and going up and down stairs). The implications for mobility are profound: more than 50% of patients with inherited neurological diseases report having incurred injuries as a result of falls, leading to morbidity and reduced quality of life. In addition, repeated falls instill intense fear of falling, so that patients restrict their activities and become less independent, limiting their ability to perform physical activities, which in turn affects their posture and gait control[19].

In a study that assessed balance and functionality in 44 patients with SCA, Aizawa et al.[20] concluded that individuals with SCA have significant balance impairment and an increased risk of falls and that this affects their ability to perform certain activities, such as self-care, transfers, locomotion and instrumental activities of daily living. They also concluded that the more severe the ataxia, the greater the balance and functional impairment, corroborating the results of the present study.

Torrani et al.[21], in a study that investigated whether there was a correlation between functional independence and balance in



SARA: Scale for the Assessment and Rating of Ataxia; FIM: Functional Independence Measure

Figure. Relationship between disease duration and (A) disease severity (SARA), (B) balance (Berg) and (C) functionality (FIM and Lawton).

Table 3. Interpretation of the results of the linear regression analysis.

Variable	Interpretation
Disease duration vs. SARA	A 0.7996-point increase in SARA score can be expected for a year increase in disease duration
Disease duration vs. FIM	A 1.38-point decrease in FIM score can be expected for a year increase in disease duration
Disease duration vs. Berg	A 2.3034-point decrease in Berg score can be expected for a year increase in disease duration
Disease duration vs. Lawton	A 0.4582-point decrease in Lawton score can be expected for a year increase in disease duration

SARA: Scale for the Assessment and Rating of Ataxia; FIM: Functional Independence Measure.

patients with SCA, concluded that the correlation between functional performance and balance was significant. They found that the greater the score on the Berg scale, the greater the FIM score. Again, their findings corroborate the results of this study.

The relationship between the scores on the FIM and Lawton scales shows clearly that a change in an individual's functionality directly affects his ability to perform instrumental activities of daily living, reflecting the major impact that certain diseases can have on patients' lives. Independence in basic activities of daily living, such as self-care and transferring, as well as in more complex, or instrumental, activities, such as preparing meals and using transportation, are important markers of functionality. Functionality, in turn, is dependent on balance, which was assessed here with the BERG balance scale. The instruments for assessing functional ability and balance used in this study not only allow the patient's need for

care and his/her degree of independence to be quantified, but also can be markers of disease progression over time, as observed here. The cross-sectional nature of this study can be considered a limitation, as longitudinal analyses with these instruments could provide information on progression of functional disability in individual tasks.[22]

LeónCarrión et al.[23], in a study involving patients with neurological sequelae following traumatic brain injury, reported a reduction in incapacity after an intensive multidisciplinary therapy program. They observed improvements of over 70% in functional, cognitive, emotional and behavioral deficits.

In a study by Lana et al.[24] of patients with Parkinson's disease, dimensions related to physical aspects of the disease adversely affected patients' quality of life and limited their activities. As quality of life was not assessed in the present study, further studies focusing on this issue in patients with SCA should be carried out.

Multicenter studies with a greater number of subjects diagnosed with SCA2 should also be carried out, as well as studies using other instruments to assess functionality in these patients and the repercussions of non-cerebellar manifestations, such as spasticity, neuropathy and extrapyramidal signs, on functionality and balance.

In conclusion, disease duration in this series of SCA2 patients was correlated with greater disease severity, worse balance and greater functional dependency.

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