Poster M277

Content Validity of the Friedreich's Ataxia Rating Scale – Activities of Daily Living (FARS-ADL) for Use in Patients With Spinocerebellar Ataxia (SCA)

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CONCLUSIONS

1. Findings from semi-structured interviews with patients and healthcare professionals (HCPs) support the Friedreich's Ataxia Rating Scale – Activities of Daily Living (FARS-ADL) as appropriately constructed for use in individuals with spinocerebellar ataxia (SCA) due to its relevance, clarity, ease of use, and clinical meaningfulness
2. Suggestions offered by HCPs to improve the FARS-ADL included clarifying response options and providing instructions for specific items

BACKGROUND and METHODS

Background

- SCAs are a dominantly inherited, heterogeneous group of rare disorders that cause progressive neurodegeneration of the cerebellum and spinal cord[1]
  - In addition to impairing physical functioning in patients, symptoms of cerebellar dysfunction impact the ability of patients with SCA to conduct activities of daily living[2]
  - Increased reliance on caregivers and impacts to patient quality of life have been observed[2,3]
- The FARS-ADL, a subscale of the validated FARS,[4,5] is a highly used outcome measure that provides an assessment of day-to-day abilities in patients with Friedreich ataxia[6]
  - The instrument consists of 9 items: speech, swallowing, cutting food and handling utensils, dressing, personal hygiene, falling, walking, quality of sitting position, and bladder function[6]
  - Items are rated on a scale from 0 to 4; lower scores represent normal function, and higher scores represent greater functional disability[6]
- The FARS-ADL has been used in several SCA studies,[7-9] including as a secondary outcome measure in a phase 3 study evaluating the efficacy of troriluzole for the treatment of ataxia symptoms in participants with SCA (NCT03701399)[10]
  - Data supporting the content validity of the FARS-ADL in assessing SCA progression, based on patient and HCP perspectives, need to be established

Objective

- To establish the content validity of the FARS-ADL in SCA by understanding (1) disease symptoms and impacts from the perspectives of individuals with SCA and HCPs, (2) its clarity and ease of use among HCPs, and (3) its ability to capture clinically meaningful changes

Methods

- Qualitative interviews were conducted with individuals with SCA in the US and HCPs who treat patients with SCA in the US and Europe; their perspectives on the content validity of the FARS-ADL were assessed
  - Eligibility criteria included diagnosis of SCA of any type and age 18 to 75 years; individuals with SCA must have been recruited via clinician referral or self-referral from a patient advocacy organization (National Ataxia Foundation)
    - Interviews with individuals with SCA were conducted between October and December 2022
  - Enrolled HCPs were recruited from centers of excellence in treating ataxias and related cerebellar disorders and had extensive experience with a range of clinical outcome assessments for patients with SCA
    - Interviews with US HCPs were conducted between July and September 2022, and those with European HCPs were conducted between June and August 2023
- The interview consisted of 2 steps: concept elicitation (with all participants) and cognitive debriefing (with HCPs only, as the FARS-ADL is a clinician-rated scale)
  - Concept elicitation (open discussion, followed by clinician-advised probes) entailed querying participants on the most common SCA signs, symptoms, and impacts
    - The probes were designed to further explore additional SCA symptoms that HCPs regarded as most common
    - Findings from the concept elicitation interviews were used to generate the reported concepts that impact daily functioning
  - Cognitive debriefing was employed to evaluate the understandability, relevance, and comprehensiveness of the FARS-ADL through mapping of identified concepts
  - Perspectives on the relationship between changes in FARS-ADL scores and SCA progression were explored
  - Interviews were recorded, transcribed, coded, and analyzed by the ATLAS.TI software, following established methods

RESULTS

Participant Demographics and Characteristics

Individuals With SCA

- In total, 7 individuals with SCA1 or 3 (SCA1/3; SCA3 [n=6] and SCA1 [n=1]) from the US participated in the interviews
- The mean age of individuals with SCA was 51 years; the mean age at SCA diagnosis was 44 years
- All individuals with SCA were diagnosed via genetic testing, with most (n=6) also mentioning a family history of SCA (**Table 1**)

Table 1. Summary of Demographics and Clinical Characteristics of Individuals With SCA1/3

Demographics	Individuals With SCA, n (%) (N=7)
Age, mean (range), years	51 (34–65)
Sex, n (%)	
Male	4 (57.1)
Female	3 (42.9)
Ethnicity, n (%)	
Asian	2 (28.6)
White	4 (57.1)
Black or African American	1 (14.3)
Education level, n (%)	
High school	2 (28.6)
Bachelor's degree	2 (28.6)
Graduate degree	3 (42.9)
Work status, n (%)	
Working full time	5 (71.4)
Retired	1 (14.3)
Disability benefit	1 (14.3)
SCA diagnosis, n (%)	
SCA3	6 (85.7)
SCA1	1 (14.3)
Age at diagnosis, mean (range), years	44 (31–56)
Diagnosis type (not mutually exclusive), n (%)	
Genetic testing	7 (100.0)
Family history[a]	6 (85.7)
Clinical/medical/other diagnosis[a]	5 (71.4)
Severity of SCA, n (%)	
Stage 0 (no gait/walking difficulties)	1 (14.3)
Stage 1 (gait difficulties but can walk)	0
Between stage 1 (gait difficulties but can walk) and stage 2 (cannot walk without permanent use of a walking aid/help)	4 (57.1)
Stage 2 (cannot walk without permanent use of a walking aid/help)	1 (14.3)
Stage 3 (confinement to wheelchair)	1 (14.3)

SCA, spinocerebellar ataxia.
[a] All individuals with a family history and/or a clinical/medical/other diagnosis also indicated a diagnosis via genetic testing.

HCPs

- Eight HCPs from the US (n=5) and Europe (n=3) were included
- More than half of the HCPs (62.5%) specialized in neurology; the remaining specialized in neurology and movement disorders. HCPs reported the number of patients with SCA that they treated during the course of their career, which ranged from 80 to "thousands" (**Table 2**)

Table 2. Summary of HCP Characteristics

Demographics	HCPs, n (%) (N=8)
Sex	
Male	5 (62.5)
Female	3 (37.5)
Specialty/profession	
Neurology	5 (62.5)
Neurology and movement disorders	3 (37.5)
Patients with SCA treated over career course	
50 to 100	3 (37.5)
101 to 200	1 (12.5)
201 to 500	1 (12.5)
"Hundreds"	2 (25.0)
"Thousands"	1 (12.5)

HCP, healthcare professional; SCA, spinocerebellar ataxia.

SCA Signs, Symptoms, and Impact on Daily Function

Perspectives From Individuals With SCA

- All of the items in the FARS-ADL were discussed with patients in the concept elicitation interviews, considering a combination of spontaneous and probed discussions (**Figure 1**)
- 8 of the 9 items of the FARS-ADL were discussed by more than half the patients. Cutting food and handling utensils was discussed by 2/7 patients
- The FARS-ADL items most frequently reported spontaneously were walking/gait abnormalities (n=7/7), falling (n=6/7), impaired speech (n=4/7), and swallowing difficulties (n=3/7)
- When including probed discussion, impaired speech was discussed by all individuals (n=7/7)

Walking/Gait

"Difficulties with gait and walking [are] definitely number one…every single step you take not to fall, which is frustrating because your knees buckle back…and then that might cause balance issues…"

"… gait and walking [are] the most important…well, if you can't walk, it's very frustrating, especially on your regular surfaces. People have to make accommodations for you, and you can't keep up with anyone…"

Falling

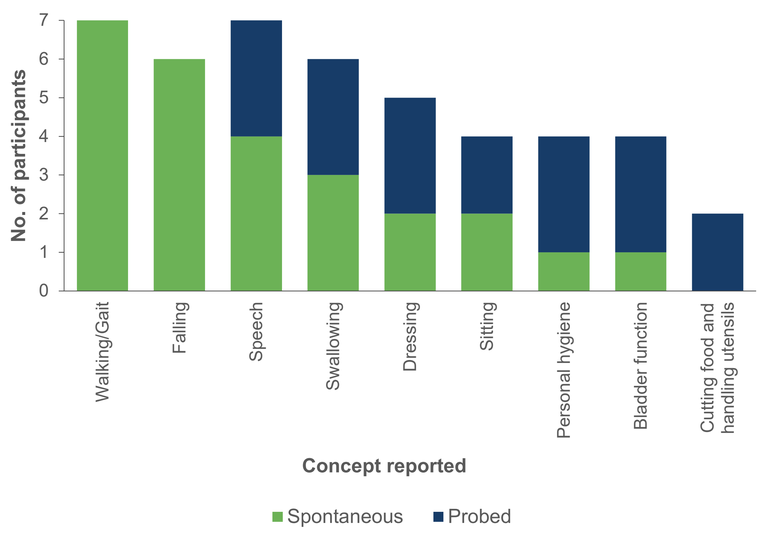
"Falling down, sometimes all the way to the ground, would be [the second most important]. It's really the same thing…falling down hurts and it's just not pleasant, especially when you don't know when it's going to happen"

Speech

"People currently understand what I'm saying, but I fear for the day when they don't"

"Because the number one thing for me is to be able to speak"

Figure 1. Overarching Concepts Identified in Interviews With Individuals With SCA



SCA, spinocerebellar ataxia.

- When asked to discuss the most bothersome and important symptoms, gait, speech, and falling were mentioned

Most bothersome symptom

"The fact that I have my gait [and] my balance issue, because with that, walking from point A to point B, and that's the most important thing that I need to do…to get out and do things"

Most affected ADL

"I guess doing daily activities…I still do them, but they're more difficult like cooking or doing laundry"

Most important or meaningful symptom related to impact on ADL

"My balance…getting from point A to point B, being able to get around the house or wherever I want to go…I hold onto things and just walk freely, that being more meaningful"

Perspectives From HCPs

- The 5 most impactful concepts that affected the daily life of individuals with SCA, as spontaneously reported by HCPs, were walking (n=8/8), speech (n=8/8), fine motor accuracy (n=5/8), balance (n=5/8), and social or work impact (n=5/8)
- All HCPs described speech/communication impairments and use of assistive devices to walk, which are both FARS-ADL items, as impacts of key importance when describing SCA disease severity and progression in clinical practice

Clinical Impression of the FARS-ADL Among HCPs

- HCPs reported that the FARS-ADL is useful for assessing individuals with SCA in clinical practice

"I've been using the FARS-ADL for quite some time, particularly in research settings, and I think it provides useful information, and it's quite easy to go through your items to score in conversation with the patient or the study participant…of the ADL scales I have been using, this is the one I like most in the context of ataxia research"

"It nicely captures (…) those different domains of living [that] are affected by ataxia"

"The scale is useful because FA usually is a more complex disease than SCA in the dominant forms of ataxia"

"I think what I like about it is it's pretty thorough and covers a variety of different things that people do in day-to-day life that would not necessarily be discussed by the patient or documented in any other way…and that's a good assessment of activities of daily living"

"I like the instrument because it's like a more patient-reported outcome, so that's more relevant to their lives. So, if you can see whether it's really impacting their life…"

Clarity and Understanding of the FARS-ADL Among HCPs

- HCPs reported that the FARS-ADL was clear and easy to use
- HCPs generally found most of the response options to be clear; however, ratings provided were between 60% and 100%, depending on the item
  - Suggestions for improvements included the need for methods to assess speech that consider a person's accent; clarification of response options for dressing, falling, walking, and bladder function items due to difficulty in distinguishing adjacent response options; and clarification of sitting instructions since sitting was often not seen as a problem
- Most HCPs found it possible to generate a correct and valid assessment in patients with SCA; all of them reported rarely using the 0.5-score increment
  - They stated that the categories within the FARS-ADL were distinct enough

Clinically Meaningful Changes or Stability in FARS-ADL Scores Based on HCP Perspectives

Meaningful Stability in FARS-ADL Scores

- Stability on any item and/or total score over 1 year was considered clinically meaningful by most HCPs (n=5/8); others indicated that a longer period was needed, depending on the natural history of the respective SCA

"Because we expect these patients to get worse over time, the fact that if someone doesn't get worse over time, that's actually a huge deal"

"No change…would be meaningful from year to year…so if they stabilized and didn't have any change, that would be meaningful"

"Just considering that in the natural history of the disease you will have approximately (a 2-point change) over 1 year"

Meaningful Change in FARS-ADL Scores

- A 1- to 3-point range for worsening or improvements in the total score was considered meaningful (median values: 2-point worsening and 1-point improvement)
  - The HCPs reported that the type of items that worsened or improved could have implications on clinical meaningfulness

"I would be very sure, a worsening by 2 points is meaningful; for one… and it depends a little bit on the per-item level"

"Let's say they had 18 points off, they score 2 points off on everything, and they improve 1 point on one of the subscales…that 1-point improvement would be meaningful to the patient…it is going to be very item specific"

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DISCLOSURES

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