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**Background**

Spinobulbar muscular atrophy (SBMA), also known as Kennedy’s disease, is a rare X-linked hereditary disorder caused by expansion of the CAG trinucleotide repeat in exon 1 of the androgen receptor gene. It is classified as a lower motor neuron disease but exhibits a complex clinical presentation due to the widespread expression and pleiotropic effects of the androgen receptor. SBMA typically presents between the ages of 30 and 50, with progressive weakness predominantly affecting the lower limbs and a characteristically slow disease progression. The heterogeneity of clinical symptoms (1) and the gradual course of the disease have made identification and validation of biomarkers and outcome measures particularly difficult. SBMA Functional Rating Scale (SBMAFRS) and 6-minute-walk test (6MWT) are currently considered the most sensitive measures to monitor disease progression (2).

**Aim, Patients and Methods**

This was a single-center, longitudinal study aimed at identifying clinically meaningful changes in the SBMAFRS score and the 6-minute walk test (6MWT) using a patient-centered approach. The study was conducted at the Motor Neuron Disease Clinic, Department of Neurosciences, University Hospital of Padua. From January 2023 to December 2024, 31 walking patients with a genetically confirmed diagnosis of SBMA were enrolled. Each patient underwent two follow-up visits approximately one year apart (baseline and T1). For each patient, demographic data, SBMAFRS total and subscores (bulbar, upper and lower limbs, trunk, breath), and also 6MWT values were collected at both time points. Patients were divided to subjectively assess their clinical progression since the previous visit, classifying it as stationary, slightly worsened, or significantly worsened. Statistical analysis included Kruskal-Wallis to assess whether significant differences existed in the variable deltas among groups; Spearman correlation converting "subjective clinical" into numeric variable; and ordinal logistic regression. All statistical analyses were performed using R (version 4.3.2). P values < 0.05 were considered significant.

**Results**

At baseline, the mean age was 57.3 ± 9.6 years, and disease onset occurred at an average age of 42.5 ± 10.2 years. **Figure 1** provides an overview of SBMAFRS and 6MWT changes from baseline to the T1 visit, stratified by patients’ subjective clinical impression (clinical groups). The Kruskal-Wallis test did not reveal a significant association between clinical groups and Δ6MWT, whereas the Spearman correlation showed a significant inverse relationship (rho = -0.53, p = 0.01979). Linear Regression confirmed this significant association among groups (p = 0.0469). For the percentage change in 6MWT (see **Figure 2**), all tests showed significant correlations: Kruskal-Wallis (p = 0.0186), Spearman (rho = 0.6497, p = 0.0026), and Linear Regression (p = 0.0066).

Regarding ΔSBMAFRS and % ΔSBMAFRS, either the Kruskal-Wallis and the Spearman test failed to find significant correlations with clinical groups. However, the sub-item “Breathing” (see **Figure 3**) showed significant differences when comparing “severely worsened” patients to the other clinical groups (Spearman p = 0.0048; Linear Regression p = 0.0009).

**Conclusions**

Over one year, an average 6MWT reduction of 6% and 16% was associated with a slight or severe impact, respectively, on patients’ perception of disease progression. Regarding SBMAFRS, further studies considering larger patient cohorts are required.

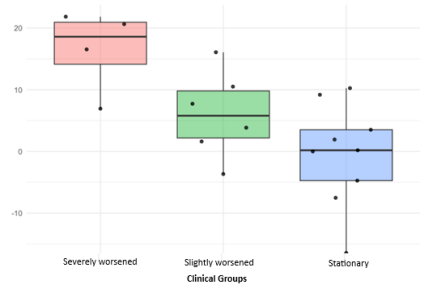
**Figure 1.** Descriptive statistics of the change in 6MWT and SBMA from baseline to T1

Clinical Group	Average ΔSBMAFRS	Median ΔSBMAFRS	IQR ΔSBMAFRS
Severely worsened	-1.86	-2.00	-3.5 - -0.5
Slightly worsened	-1.90	-1.00	-2 - -1
Stationary	-0.87	-1.00	-1.5 - 0

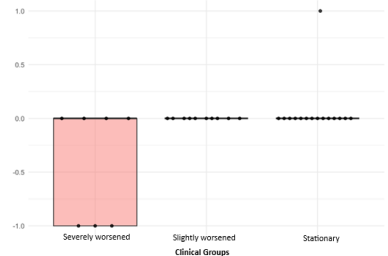
Clinical Group	Average % Δ6MWT	Median % Δ6MWT	IQR % Δ6MWT
Severely worsened	16.4842863	18.5851768	14.13 - 20.34
Slightly worsened	6.0153005	5.7833710	2.17 - 9.81
Stationary	-0.4053635	0.1858736	-4.74 - 3.51

Clinical Group	Average Δ6MWT	Median Δ6MWT	IQR Δ6MWT
Severely worsened	-37.50	-32	-44.25 - -25.25
Slightly worsened	-24.33	-16	-41.25 - -10.25
Stationary	4.00	-1	-10 - 27

**Figure 2.** Percentage reduction in the 6-minute walk test (6MWT) from baseline to T1



**Figure 3.** ΔSBMAFRS-Breathing compared between baseline and T1



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