

# Short-term assessment of progression, muscle involvement asymmetry, and clinical correlates in Amyotrophic Lateral Sclerosis

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## Background

To date, no curative treatment is available for Amyotrophic lateral sclerosis (ALS), which is characterized by a particularly rapid progression compared to other neurodegenerative diseases [1]. This accelerated course presents a challenge for the selection of relevant clinical outcomes that can accurately reflect the short-term natural history of the neuromuscular system in patients with ALS.

## Aims

This study aimed to characterize the functional motor progression of ALS over a six-week period by identifying the most sensitive clinical measures of change, evaluating muscle strength asymmetry, and analyzing the correlations between muscle strength, functional performance, and standardized clinical scales.

## Methods

**Participants** : 10 patients with ALS, aged 18-70 years, ambulatory with or without assistive device and without cognitive impairment

**Study design** : Patients were followed over six weeks during three assessment visits spaced three weeks apart

**Outcome measures** :

**Lower Limb muscle strength** using dynamometry

**Walking and balance tests** : 6-Minute Walk test (6MWT), 10-Meter Walk Test (10mWT), Timed Up and Go test (TUG), Berg Balance Scale (BBS)

**Respiratory function** : Forced vital capacity (FVC) using spirometry

**Standardized clinical scales** : ALS Functional Rating Scale - Revised (ALSFRS-R), ALS Assessment questionnaire – 40 items (ALSAQ-40), Fatigue severity scale (FSS), Modified fatigue Impact scale (MFIS), Hospital Anxiety and Depression scale (HADS)



Three assessment visits (V1, V2, V3) including dynamometry, functional tests, spirometry and clinical scales

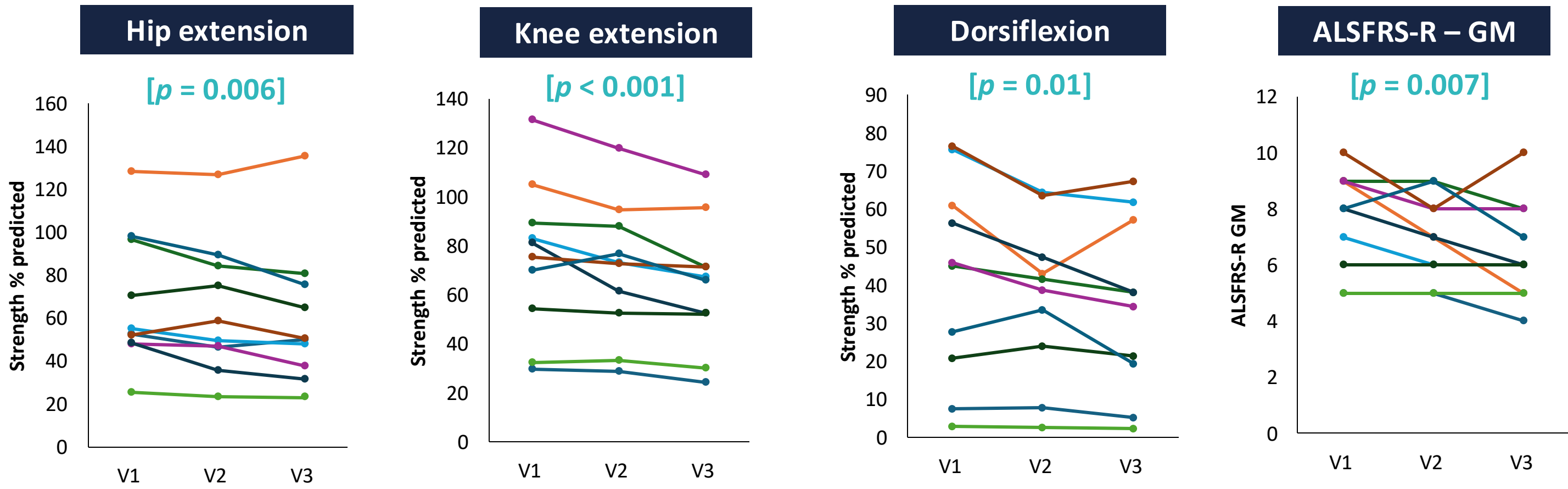


Evaluation of knee and hip flexors and extensors using an isokinetic dynamometer (Biodex System 4 Pro, Biodex Medical Systems, Shirley, NY, USA) (A–B), and ankle dorsiflexors and plantar flexors using a dedicated ankle dynamometer (MyoAnkle) (C–D). Photos displayed with patient consent.

## Results

### Change over 6 weeks

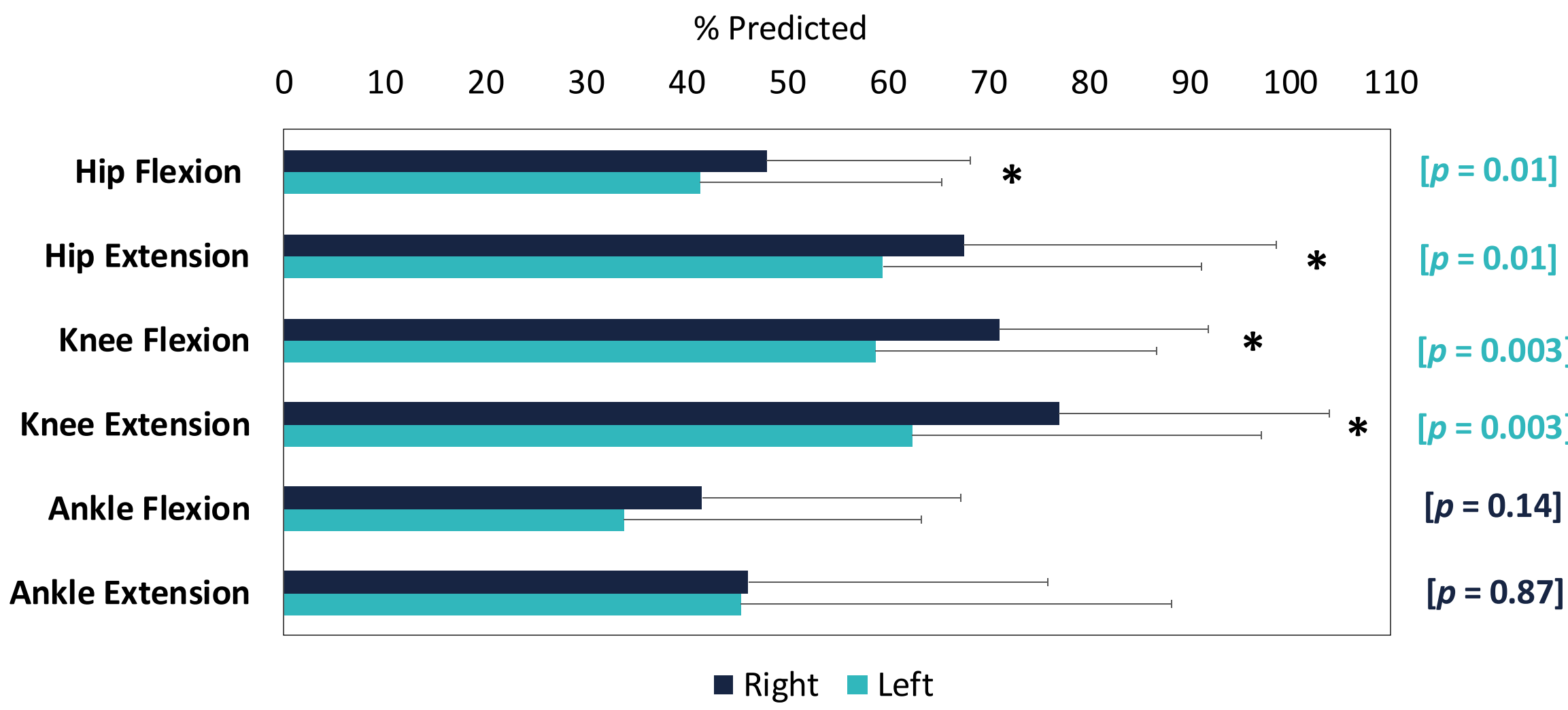
All motor outcomes measures showed a general trend towards deterioration



Data were analyzed using the Friedman test ( $p < 0.05$  for significance). Only outcomes showing a significant change over time are presented. ALSFRS-R – GM : Gross Motor subscore of the ALSFRS-R

### Muscle involvement asymmetry

Muscle weakness was generally asymmetrical. Strength in hip and knee flexion and extension was significantly greater on the right side



Data were analyzed using the Wilcoxon matched-pairs signed rank test ( $p < 0.05$  for significance). Muscle strength values were expressed as a percentage of predicted strength, based on predictive equations [2,3].

### Clinical correlates

#### Correlations between muscle strength and functional outcomes

	Hip Flexion	Hip Extension	Knee Flexion	Knee Extension	Dorsiflexion	Plantarflexion
ALSFRS-R - T				0.36		
ALSFRS-R - B			-0.38		-0.54	-0.51
ALSFRS-R - FM						-0.39
ALSFRS-R - GM	0.50		0.63	0.71	0.60	0.65
ALSFRS-R - R						
6MWT	0.45		0.63	0.64	0.41	0.37
10mWT			0.58	0.54	0.38	
TUG			-0.51	-0.55		
BBS		0.41	0.37	0.36		0.65

#### Correlations between muscle strength and clinical scales

	Hip Flexion	Hip Extension	Knee Flexion	Knee Extension	Dorsiflexion	Plantarflexion
ALSAQ-40 - T		-0.44				
ALSAQ-40 - M	-0.63		-0.47	-0.47		-0.47
ALSAQ-40 - ADL						
ALSAQ-40 - ED						0.60
ALSAQ-40 - Com					0.57	
ALSAQ-40 - ER						
FSS	-0.63	-0.46	-0.64	-0.51		
MFIS - T	0.66	0.38	0.53	0.55		
MFIS - P	0.65		0.67	0.62		0.41
MFIS - C	0.43					
MFIS - PS	0.74	0.37	0.60	0.67	0.43	
HADS - A	-0.51		-0.59	-0.60	-0.65	-0.52
HADS - D	-0.45					

#### Correlations between functional outcomes and clinical scales

	ALSFRS-R - T	ALSFRS-R - B	ALSFRS-R - FM	ALSFRS-R - GM	ALSFRS-R - R	6MWT	10mWT	TUG	BBS
ALSAQ-40 - T	-0.69			-0.50		-0.80	-0.75	0.79	-0.62
ALSAQ-40 - M	-0.55			-0.71		-0.77	-0.70	0.62	-0.63
ALSAQ-40 - ADL	-0.82		-0.64	-0.46		-0.80	-0.75	0.80	
ALSAQ-40 - ED		-0.51			-0.463				
ALSAQ-40 - Com		-0.60	-0.52						
ALSAQ-40 - ER	-0.54			-0.54		-0.58	-0.50	0.57	-0.53
FSS	-0.45			-0.59		-0.77	-0.69	0.67	-0.61
MFIS - T	0.37			0.39		0.58		-0.46	
MFIS - P	0.46						0.68		0.42
MFIS - C		-0.41							
MFIS - PS	0.37			0.48		0.58	0.45	-0.45	
HADS - A				-0.70		-0.51			-0.55
HADS - D									

Correlations were analyzed using Spearman's rank correlation test ( $p < 0.05$  for significance). Only significant correlations are displayed. The 6MWT was expressed as a percentage of predicted values [4]. ALSAQ-40 subscores include T: total, M: Mobility, ADL: Activities of Daily Living, Eat: Eating and Drinking, Com: Communication, and ER: Emotional Reactions. ALSFRS-R subscores include T: total, B: Bulbar, FM: Fine Motor, GM: Gross Motor, and R: Respiratory. HADS subscores include A: Anxiety, D: Depression. MFIS subscores include T: Total, P: Physical, C: Cognitive, and PS: Psychosocial.

## Conclusion

Within only six weeks, a clear deterioration in motor performance was observed, emphasizing the rapid functional decline in ALS. Persistent strength asymmetry and the high sensitivity of muscle strength, particularly knee extension, support the use of targeted motor and functional outcomes for short-term follow-up and clinical trials.

## References

[1] Tzeplaff L. et al., Cells, 2023; 12:1523. [2] Hogrel J.Y. et al., Arch Phys Med Rehabil, 2007; 88(10):1289-97. [3] Moraux A. et al., BMC Musculoskelet Disord, 2013; 14:104. [4] Enright P.L., Sherrill D.L., American Journal of Respiratory and Critical Care Medicine, 1998; 158(5 Pt 1): 1384–1387.

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