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Muscle changes in amyotrophic lateral sclerosis: A longitudinal ultrasonography study

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ABSTRACT

Objective: We performed a longitudinal study to assess structural muscle changes in amyotrophic lateral sclerosis (ALS) using ultrasonography.
Methods: During a follow-up of 6 months, ultrasonography parameters (muscle thickness, echo intensity and fasciculations) were obtained from 6 muscle groups in 31 ALS patients, together with strength and scores on the revised ALS functional rating scale (ALSFRS-r).
Results: At baseline, we found an increased echo intensity and decreased thickness, and these parameters correlated with lower strength. Moreover, ultrasound abnormalities were also detected in muscles with preserved strength. Longitudinal changes in echo intensity, muscle thickness and fasciculations showed large variations between patients. Rates of change in ultrasound parameters did not correlate with changes in ALSFRS-r or strength.
Conclusion: In patients with ALS ultrasound abnormalities can be found in muscles with preserved strength. The pattern of ultrasonographic muscle changes in ALS is highly variable and shows no evident correlation with functional measures.
Significance: Ultrasonography is not suitable to monitor disease progression in ALS.

1. Introduction

Amyotrophic lateral sclerosis (ALS) characteristically presents as a focal disease, with a combination of upper and lower motor neuron symptoms restricted to one body region (Ravits et al., 2007). Symptoms then spread to other regions, ultimately leading to death with a median survival time of 28 months after symptom onset (Zoccolella et al., 2008). The phenotype of ALS is highly heterogeneous due to marked differences in region of onset, the relative mix of upper and lower motor neuron involvement and the rate of disease progression (Ravits and La Spada, 2009).

Muscle ultrasonography is an easily accessible, inexpensive and painless method to detect structural muscle changes caused by neuromuscular diseases (Pillen et al., 2008). Affected muscles show a diminished muscle thickness and appear whiter (i.e. have an increased echo intensity) (Pillen et al., 2008). Previously, we have shown that already in the diagnostic phase of ALS, ultrasonography reveals marked abnormalities, such as diminished thickness, increased echo intensity and fasciculations (Arts et al., 2008). The objective of the present longitudinal study was to visualize ALS related muscle changes during a follow up period of 6 months. Furthermore, we compared ultrasonography to manual muscle testing and the revised ALS functional rating scale (ALSFRS-r) to assess the validity of ultrasonography to monitor disease progression in ALS.

2. Methods

2.1. Subjects

We included 31 patients, in the following categories: possible ALS ($n = 7$), probable ALS laboratory-supported ($n = 13$), probable ALS ($n = 9$) or definite ALS ($n = 2$) according to the revised El Escorial Criteria (Brooks et al., 2000). We planned to evaluate each patient five times with an interval of six weeks. The local ethical committee approved the study and all patients gave written informed consent.

2.2. ALSFRS-r and muscle strength

The ALSFRS-r was used to quantify activities of daily living (Cedarbaum et al., 1999). It consists of 12 items with scores ranging from 0 to 4, with a maximum achievable score of 48 (0 = total disability, 48 = normal).

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Table 1
Baseline characteristics.

	<3 Measurements	⩾3 Measurements	*P*-value
	n = 9	*n* = 22	
Males (n) (%)	3 (33.3%)	16 (72.7%)	0.044
Weight (kg)	75,2 ± 8.6 (64–86)	77.9 ± 11.6 (53–93)	0.537
Age (year)	57,6 ± 13.8 (37–77)	61.5 ± 11.8 (40–79)	0.434
Disease onset – diagnosis, months	11,0 ± 6.9 (5–26)	15.0 ± 9.1 (3–39)	0.596
Diagnosis – ultrasonography, months	8,3 ± 6.6 (1–20)	7.0 ± 5.7 (2–18)	0.248
Disease onset (n) (%)			0.236
Bulbar	2 (22.2%)	0	
Thoracic	0	1 (4.5%)	
Upper limbs	4 (44.4%)	8 (36.4%)	
Lower limbs	3 (33.3%)	11 (50%)	
Upper and lower limbs	0	2 (9.1%)	
Strength (max 100)	75.7 ± 11.2 (59–89)	88.0 ± 10.1 (57–99)	0.008
ALSFRS-r (max 48)	31.1 ± 6.5 (22–42)	37.1 ± 6.3 (18–46)	0.025

Data are presented as means ± SD (range).

Muscle strength of 10 different muscle groups was manually tested, and scored with the modified scale of the Medical Research Council (9-grade; MRC 5 = 5.00; MRC 5− = 4.67; MRC 4+ = 4.33; MRC 4 = 4.00; MRC 4− = 3.67; MRC 3 = 3.00; MRC 2 = 2.00; MRC 1 = 1.00; MRC 0 = 0.00) (Medical Research Council, 1976). The muscle tested were neck flexors, neck extensors, and neck rotators, elbow flexors, wrist extensors and flexors, finger extensors and flexors, hip flexors, knee extensors and foot dorsiflexors on both sides. The total sum score was calculated, with a maximum achievable score of 100.

2.3. Ultrasonography

Using a standard protocol (Arts et al., 2008; Arts et al., 2010b), ultrasound scans were made of the following muscles or muscle groups on both sides: sternocleidomastoid (representing the bulbar region), biceps brachii including the underlying brachialis muscle, forearm flexor group, forearm extensor group (cervical region), quadriceps femoris and tibialis anterior (lumbosacral region). All scans were made in the transverse plane with a standard transducer location corresponding to the muscle belly (Supplementary Table S1). For each muscle, three consecutive measurements were taken in order to minimize variation in echo intensity. Due to malfunction of the ultrasound device, we had to use a second apparatus. Measurements were performed using either a Philips IU22 with a 5–17 MHz linear broadband transducer or a HP Sonos 2000 phased-array real-time scanner with a 7.5-MHz transducer. Consecutive measurements in a single patient were done using the same ultrasound device. The system settings and conversion procedure to combine results of the two devices have been described elsewhere (Pillen et al., 2009b).

2.3.1. Measurement of muscle thickness and echo intensity

Muscle thickness was measured with electronic calipers placed at standardized locations (Supplementary Table S1). The ultrasound images were stored for further evaluation offline. Using cus-

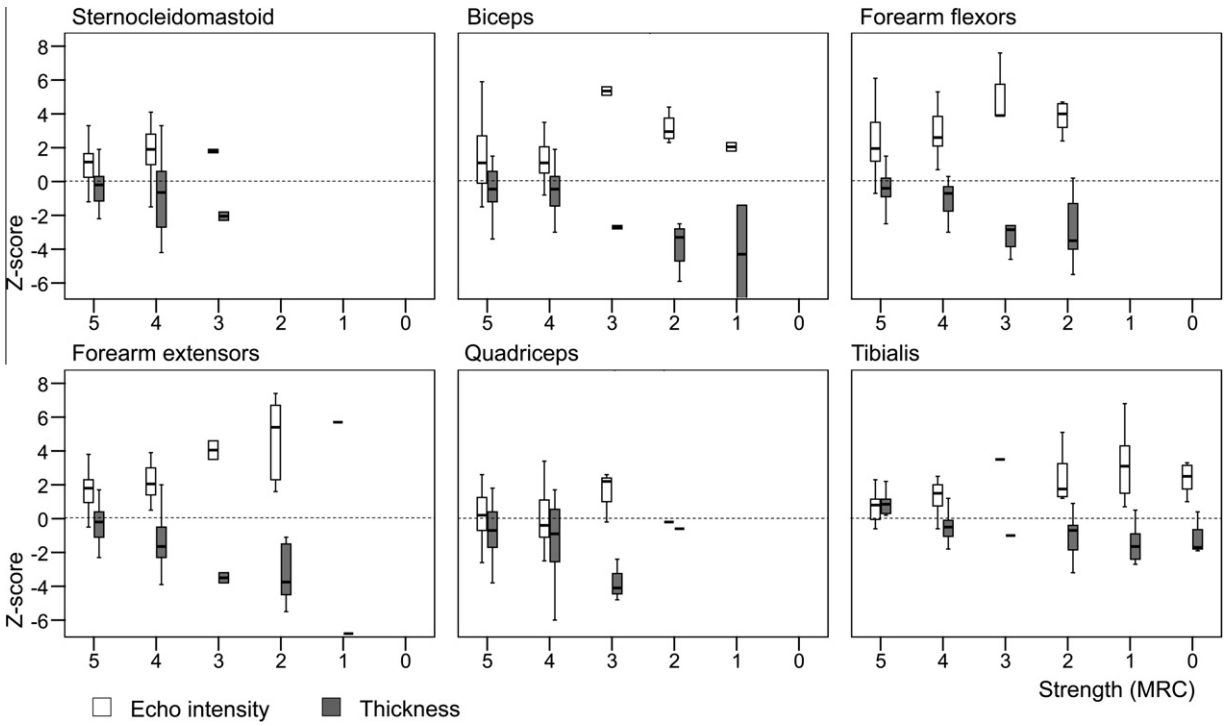

Fig. 1. Baseline standardized muscle thickness and echo intensity as a function of strength, for the individual muscles and muscle groups. In this figure MRC grade 5−, 4+, 4 and 4− were combined into one group: MRC grade 4.