DELTOID STRENGTH RATIO: A NEW PROMISING PROGNOSTIC MARKER FOR THE STRATIFICATION OF FLAIL ARM SYNDROME

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Introduction

Upper limb lower motor neuron syndromes (UL-LMNs) are clinically characterized by muscle wasting, weakness and hyporeflexia, without sensory involvement.[1] **Flail arm syndrome** (FA) is the most common motor neuron disease with onset in the upper limbs.[2,3] Prognosis vary greatly among patients with FA.

Objectives

To **clinically characterize FA** cases and identify potential new **prognostic biomarkers**.

Materials and methods

Clinical and instrumental data from **211 patients** with UL-LMNs, referred to MND Center at the University Hospital of Padova from 2019 to 2024, were collected. A descriptive and survival analysis of the different disease entities was conducted. Particular attention was given to **FA**, which was further categorized into **typical** and **atypical forms**. Patients were classified as having an **atypical flail arm** phenotype if they exhibited a flail arm–like presentation with distal onset, with involvement of proximal upper limb muscles after the first year of disease progression, and did not meet diagnostic criteria for other UL-LMNs.

A regression analysis was performed to identify potential **prognostic biomarkers**, considering **survival**, **time to involvement of the contralateral upper limb**, as well as the **lumbosacral**, **bulbar**, and **respiratory regions**.

Inclusion Criteria	Exclusion Criteria
Onset of symptoms predominantly involving the upper limbs with signs of lower motor neuron impairment.	Weakness confined to distal upper limb muscles without proximal involvement within at least 12 months from symptom onset.
No significant weakness or atrophy in the lower limbs, and no bulbar or respiratory involvement for at least 1 2 months from symptom onset.	Age below 18 years at symptom onset (juvenile onset).

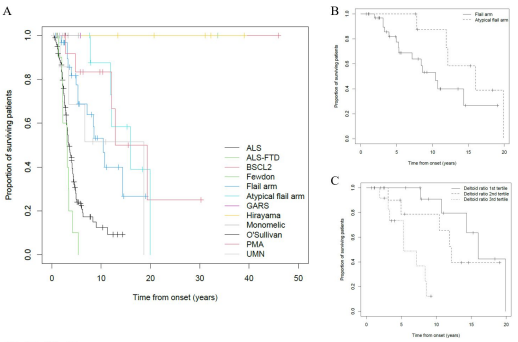
Diagnostic criteria for flail arm syndrome proposed by Gromicho et al. (adapted from Wijesekera et al.)[3,4]

In flail arm syndrome, deltoid weakness often progresses rapidly. Based on clinical observation, a subset of patients showed a slower progression of deltoid weakness despite comparable rates of decline in the biceps and triceps brachii. This pattern appeared to be independent of the site of symptom onset (proximal or distal). A "**deltoid strength ratio**" was developed to quantify this decline, adjusting for time from symptom onset.

$$Deltoid\ strength\ ratio = \frac{10 - deltoid\ sum\ score}{time\ from\ symptom\ onset\ to\ first\ visit}$$

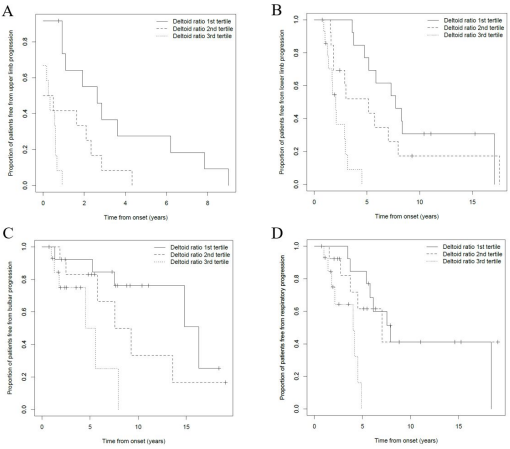
Results

We included 35 patients with typical FA, 9 with atypical FA, 6 with Hirayama disease, 6 with monomelic amyotrophy, 2 with distal hereditary motor neuronopathy type V, 1 with FEWDON-MND, and 1 with O'Sullivan–McLeod syndrome. Survival in these conditions differs significantly from that observed in classic amyotrophic lateral sclerosis, their primary clinical mimic.



Survival curve expressed in years for the **study population** (A). Kaplan–Meier curves representing **overall survival** in patients with **flail arm and atypical flail arm phenotypes**, stratified by **clinical phenotype** (B) and by **deltoid strength ratio** divided into tertiles (C).

In patients with both typical and atypical FA, **rapid progression of deltoid muscle weakness** was associated with **shorter survival** ($p < 0.01$), as well as **earlier involvement of the contralateral upper limb** ($p < 0.01$) **and lower limbs** ($p < 0.01$), regardless of the specific category. The presence of upper motor neuron signs correlated with a faster rostral-to-caudal spread of lower motor neuron degeneration ($p = 0.02$). Patients with a distal-onset showed a longer time to bulbar involvement ($p = 0.02$), and a similar trend was observed for respiratory involvement ($p = 0.06$); however, these latter analyses were limited by the small number of events.



Kaplan–Meier curves illustrating the **time to contralateral upper limb involvement** (A), **lower limb involvement** (B), **bulbar involvement** (C), and **respiratory involvement** (D) in patients with flail arm and atypical flail arm phenotypes, stratified by **deltoid strength ratio** divided into tertiles.

Discussion and conclusions

The significant differences in survival across the various pathologies highlight the importance of a systematic and structured diagnostic approach. The strong association between deltoid strength ratio and survival, regardless of phenotype (flail arm vs atypical flail arm), and the lack of a significant association between phenotype and survival, suggest the need for a revision of the criteria proposed by Gromicho et al.[3] The deltoid strength ratio emerges as a promising new prognostic marker for stratifying patients with flail arm syndrome.

Bibliography

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