THE EPIDEMIOLOGY OF PRIMARY LATERAL SCLEROSIS: A POPULATION-BASED STUDY

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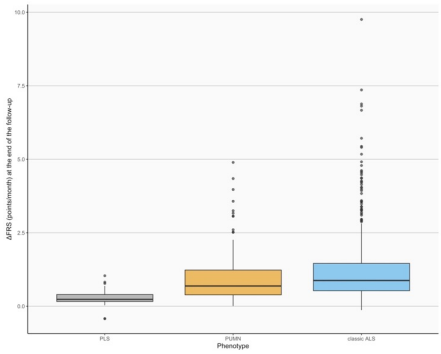
Background

Primary Lateral Sclerosis (PLS) is a rare neurodegenerative disease affecting the upper motor neuron[1]. In this population-based study, we described its epidemiology in northern Italy, comparing PLS patients with those with predominant UMN (PUMN) and classic ALS.

Figure 1. ΔFRS at the end of the follow-up across different motor neuron disease phenotypes.



Methods

Patients from the PARALS registry[2] diagnosed with probable or possible PLS between 2007 and 2011 were included. Crude annual incidence rates were calculated, along with age- and sex-specific rates. A survival analysis was performed to identify prognostic factors at diagnosis. Covariates included sex, age at onset, site of onset, diagnostic delay, FVC at diagnosis, ΔFRS (calculated as (48 – ALSFRS-r score at diagnosis) divided by the diagnostic delay), and ΔBMI (calculated as the difference between premorbid BMI and BMI at diagnosis, divided by the diagnostic delay).

Table 1. Demographical and clinical characteristics of patients across the motor neuron phenotypes.

	Classic ALS (n=730)	PUMN (n=197)	PLS (n=57)	p-value
Sex, M (%)	448 (62.2)	111 (59.4)	21 (36.8)	0.001
Onset age, median (IQR)	66.9 (58.8-73.9)	64.3 (54.4-71.7)	63.5 (54.9-70.4)	<0.001
Onset site, n (%)				
Bulbar	0 (0.0)	0 (0.0)	11 (19.3)	<0.001
Lower limbs	317 (44.0)	156 (83.4)	42 (73.7)	
Upper limbs	403 (56.0)	31 (16.6)	4 (7.0)	
Onset side, n (%)				
Bilateral	181 (25.3)	78 (41.9)	28 (60.9)	<0.001
Unilateral	535 (74.7)	108 (59.1)	18 (39.1)	
Diagnostic delay, median (IQR)	9.6 (6.5-13.7)	11.6 (7.5-21.8)	18.7 (10.6-29.9)	<0.001
Familial history, positive (%)	68 (9.6)	12 (6.7)	0 (0)	0.031
C9orf72, expanded (%)	47 (7.3)	6 (3.6)	0 (0.0)	0.038
missing	78 (10.8)	21 (11.2)	8 (14.0)	
SOD1, mutated (%)	13 (2.0)	5 (3.0)	0 (0.0)	0.423
missing	83 (11.5)	22 (11.7)	9 (14.0)	
TARDBP, mutated (%)	7 (1.1)	3 (1.8)	0 (0.0)	0.552
missing	83 (11.5)	22 (11.7)	9 (14.0)	
FUS, mutated (%)	3 (0.5)	0 (0.0)	0 (0.0)	0.605
missing	83 (11.5)	22 (11.7)	9 (14.0)	
ALSFRSr total score at diagnosis, median (IQR)	41 (36-45)	41 (36-44)	43 (40-45)	0.024
missing	42 (5.8)	15 (8.0)	5 (8.8)	
ΔFRS at diagnosis, median (IQR)	0.71 (0.38-1.39)	0.61 (0.30-1.13)	0.29 (0.19-0.51)	<0.001
missing	42 (5.8)	15 (8.0)	5 (8.8)	
FVC, median (IQR)	90.0 (73.0-100.0)	92.0 (79.5-100.0)	98.0 (73.0-100.0)	0.352
missing	111 (15.4)	32 (17.1)	13 (22.8)	
NIMV, yes (%)	324 (48.1)	70 (40.2)	16 (38.1)	0.099
Gastrostomy, yes (%)	157 (24.0)	48 (28.6)	6 (15.8)	0.206
Tracheostomy, yes (%)	82 (12.6)	18 (10.8)	0 (0.0)	0.059

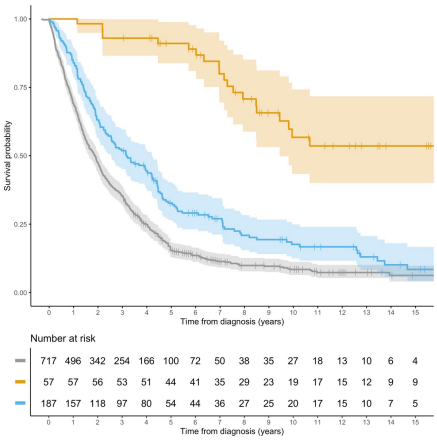
Results

A total of 57 PLS patients (2.7%) were included, with a crude incidence rate of 0.084 per 100,000 person-years. Compared to PUMN and classic ALS, PLS patients were younger (median onset age 63.5 years, IQR 54.9–70.4) and predominantly female (**table 1**). Bulbar onset occurred in 11 cases (19.3%), all of whom later developed spinal symptoms.

PLS was associated with slower disease progression, as indicated by a longer diagnostic delay which was nearly twice as long as in classic ALS (18.7 vs. 9.6 months). Reflecting this longer diagnostic delay, although the total ALSFRS-r score at diagnosis in the PLS group was only slightly higher than in the other groups, their progression rate at that time was significantly lower, decreasing from 0.71 points/month in classic ALS to 0.61 in PUMN and 0.29 in PLS (**figure 1**).

At censoring, 38 patients (66.7%) were still alive with a median survival of 8.3 years, IQR 5.7–12.3), significantly longer with respect to PUMN (2.7, IQR 1.4-5.8) and classic ALS patients (1.6, IQR 0.7-3.4) (**figure 2**). This corresponded to a point prevalence of 0.89 per 100,000. Survival was significantly associated with age at onset (HR 1.17, 95% CI: 1.05–1.33, p = 0.001), male sex (HR 4.41, 95% CI: 1.24–15.6, p = 0.02), and FVC at diagnosis (HR 0.95, 95% CI: 0.93–0.98, p = 0.006).

Figure 2. Kaplan-Meier curves and risk tables stratifies according to motor neuron phenotypes (grey = classic ALS; blue = predominant UMN; orange = Primary Lateral Sclerosis).



Conclusions

PLS was confirmed to be rarer than other ALS phenotypes. Patients had a higher age at onset than previously reported[3] and a female predominance. Sex, age at onset, and respiratory function were key prognostic factors.

References

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