

# PHOSPHATEMIA IS AN INDEPENDENT PROGNOSTIC FACTOR IN AMYOTROPHIC LATERAL SCLEROSIS

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## Background

The search for reliable prognostic factors in ALS remains ongoing<sup>1</sup>. Although the rate of decline on the ALS Functional Rating Scale is considered one of the most reliable predictors of disease progression, the scale has several limitations that prevent it from accurately capturing the extent of motor neuron damage. As a result, considerable efforts have been directed toward identifying biomarkers that can quantify motor neuron injury in a reliable, sensitive, and objective manner. Among these, neurofilaments have emerged as the most prominent example. However, given the complexity of the disease and the diverse clinical needs, it is unlikely that a single biomarker will be sufficient to address all aspects of prognosis. The aim of this study was to evaluate the prognostic value of several biomarkers associated with muscle damage.

## Results

A total of 1,444 and 1,023 patients were included in the PARALS and PROACT cohorts, respectively (table 1). Only creatinine (HR=0.65, 95% CI 0.50–0.85) and phosphorus (HR=1.14, 95% CI 1.05–1.24) showed a significant association with survival in the PARALS cohort (figure 1; table 2). These findings were further validated in the PROACT cohort (creatinine HR=0.21, 95% CI 0.13–0.35, p<0.0001; phosphorus HR=2.35, 95% CI 1.13–4.88, p=0.02). Longitudinal data from the PROACT database showed that an increase of 0.1 mmol/l per month in phosphate levels was also associated with a hazard ratio of 8.26 (95% CI: 1.07–96.6, p=0.044).

**Table 1.** Demographical and clinical characteristic of patients included in the PARALS and PROACT cohorts.

	PARALS cohort (n=1444)	PROACT creatinine cohort (n=1023)	p-value	PROACT phosphorus cohort (n=639)	p-value
Sex, M (%)	812 (56.2)	634 (62.0)	0.005	303 (47.6)	0.025
Onset age, years [median (IQR)]	68.7 (60.8-74.7)	58.0 (51.0-66.0)	<0.001	58.0 (51.0-65.0)	<0.001
Onset site, spinal (%)	958 (66.3)	802 (78.4)	<0.001	495 (77.6)	<0.001
Diagnostic delay, months [median (IQR)]	9.6 (5.6-13.6)	9.1 (5.6-14.1)	0.321	8.8 (5.3-12.9)	0.027

**Table 2.** Cox univariate and multivariable model in the PARALS cohort.

Blood biomarker	Univariate analysis		Multivariable analysis	
	HR (95%CI)	p-value	Adjusted HR (95% CI)	p-value
Creatine kinase	0.96 (0.93-0.99)	0.010	0.98 (0.95-1.00)	0.089
Creatinine	0.65 (0.50-0.85)	0.796	0.65 (0.50-0.85)	0.001
Phosphorus	1.15 (1.06-1.24)	<0.001	1.14 (1.05-1.24)	0.001
Potassium	1.01 (0.99-1.03)	0.241	1.00 (0.99-1.02)	0.611
Aspartate aminotransferase (AST)	1.04 (0.99-1.09)	0.094	1.04 (0.99-1.09)	0.083
Alanine aminotransferase (ALT)	1.00 (0.98-1.03)	0.834	1.01 (0.99-1.04)	0.309

## Conclusions

Creatininemia was confirmed as a prognostic marker in ALS<sup>3</sup>. Additionally, both phosphatemia levels at diagnosis and its rate of change over time were identified as a potential prognostic marker for ALS. As with other blood biomarkers, phosphate levels are cost-effective and minimally invasive to measure, supporting their potential use in clinical trials.

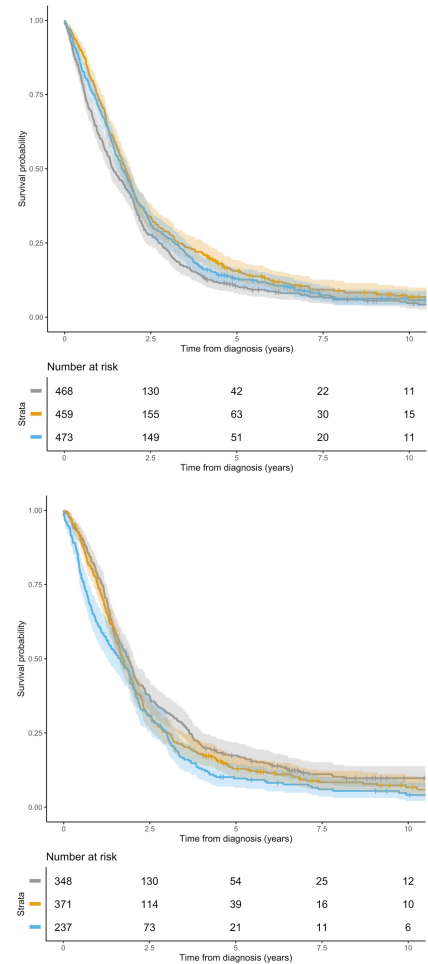
## References

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## Methods

Data from PARALS were considered for this study<sup>2</sup>. Survival was defined as the time from diagnosis to death, tracheostomy or the censoring date. Blood levels of potassium, creatinine, creatine kinase, phosphorus, AST and ALT diagnosis were evaluated as potential prognostic biomarkers. A Cox model was developed for each biomarker and adjusted for sex, onset age, onset site and diagnostic delay. Significant findings from PARALS were evaluated in the PRO-ACT database. Additionally, a joint model was constructed to evaluate the prognostic role of phosphatemia slope over time using longitudinal data from PRO-ACT.

**Figure 1.** Kaplan-Meier curves and risk tables stratified according to creatinine (upper) and phosphorus (lower) tertiles in the PARALS cohort. Grey = lower tertiles; yellow = medium tertiles; blue = higher tertiles.



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