Exploring the pnenotypic heterogeneity of Amyotrophic Lateral Sclerosis through blood biomarkers: a prospective study.

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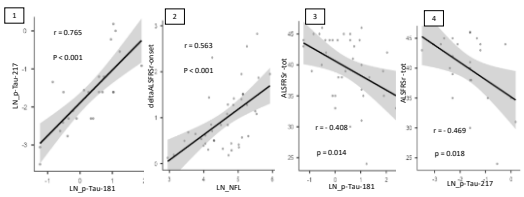
Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative condition exhibiting substantial phenotypic variability, which poses challenges in forecasting both its clinical trajectory and prognosis. In this study, we seek to examine such heterogeneity by analyzing a panel of blood-based biomarkers — serum neurofilament light chain (NfL), phosphorylated tau 181 (p-tau 181), and phosphorylated tau 217 (p-tau 217) — within a prospective cohort of ALS patients evaluated across multiple time points.

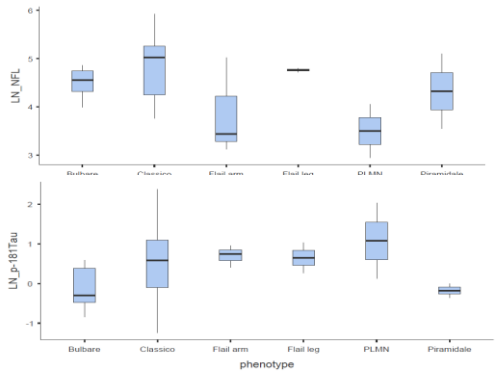
Results

Our preliminary results from 80 ALS patients displayed a good correlation between the two isoforms of p-tau, p-tau 181 and p-tau 217 (Figure 1).



A positive correlation between serum NfL and deltaALSFRSr (Figure 2), as well as a negative correlation between both isoforms of p-tau and total ALSFRSr (Figure 3 and 4), were found.

We observed that p-tau 181 levels were elevated in patients with lower upper motor neuron scores, while creatine kinase (CK) demonstrated a comparable trend and neurofilament light chain (NfL) displayed the opposite pattern. Notably, a significant correlation was identified between p-tau 181 and CK levels (r = 0.653, p < 0.001)



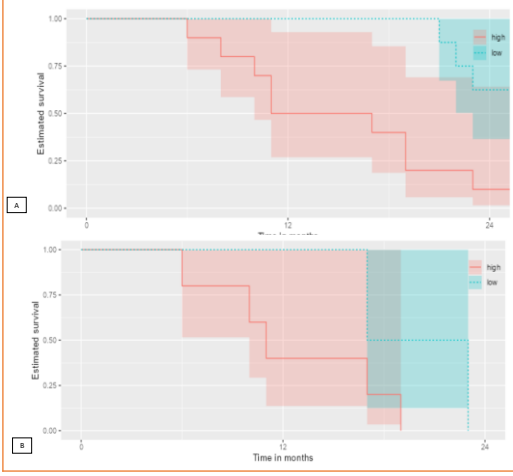
NfL and p-tau 181 across phenotypes. No observations available for respiratory and PUMN phenotype in our cohort.

Methods and sample presentation

- ✓ Phenotypic characterization and biomarker collection are conducted at baseline and at multiple time points throughout the disease course (3, 6, 9, and 12 months).
- ✓ Biomarkers are analyzed using a chemiluminescent enzyme immunoassay (CLEIA) at the 'Città della Salute e della Scienza' laboratory in Turin.
- ✓ Between July 2023 and July 2024, we recruited 80 patients, yielding a cohort with a slight male predominance (52.5% vs 47.5%), a mean age at diagnosis of 67.7 years, and a diagnostic delay of 12.2 months, consistent with data reported in the literature

Results

We investigated the neutrophil-to-lymphocyte ratio (NLR), a marker of inflammatory status and a negative prognostic factor, and confirmed both NLR (Figure A) and NfL (Figure B) correlation to survival and disease progression.



Conclusions

- ✓ The integration of multiple biomarkers may contribute to a more accurate phenotypic and prognostic profiling of patients.
- ✓ Ongoing data collection is expected to yield stronger evidence on the intricate relationship between blood biomarkers and ALS heterogeneity, thereby enhancing our understanding of the biological mechanisms underlying the disease.

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