OBSTRUCTIVE SLEEP APNEA IN AMYOTROPHIC LATERAL SCLEROSIS: DIAGNOSTIC CHALLENGES AND PREDICTIVE MODELING

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INTRODUCTION

- Amyotrophic lateral sclerosis (ALS) includes both motor and **non-motor symptoms**, such as sleep disturbances.
- Although their **high prevalence** and **clinical significance**, sleep-related issues are still **overlooked** during ALS patients' clinical assessments
- Current knowledge revolves around **subjective measures**.

AIMS

Explore sleep disorders' **prevalence**, **characteristics**, and **clinical impact** among ALS patients

METHODS

Observational, monocentric (University Hospital of Parma, Italy), prospective study
Variables collected:

- **Anthropometric data** (e.g., age, weight, height)
- **Disease descriptors** (e.g., symptom onset, system primarily affected, initial need for supportive treatments, etc.)
- **Disease severity** (ALS-FRS-r)
- **Cognitive performances** (ECAS tool)
- **Sleep quality** (PSQI)
- **Sleep perception** (DBAS-16)
- **Daytime sleepiness** (ESS)
- **Risk of OSA** (BQ)
- **Health-related quality of life** (SF-36)

Level 3 polysomnography (home sleep apnea testing) with additional specific electrodes for muscle activity

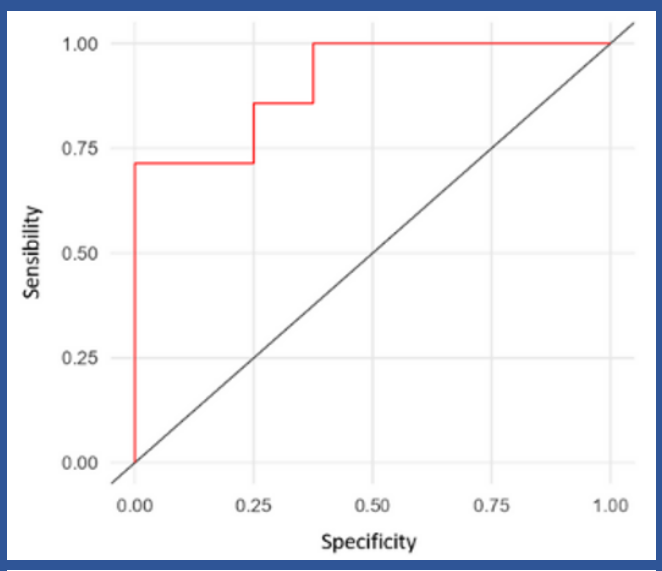

Fig. 1: ROC curve representing the reliability in predicting the presence of OSA with a 4-variable model: BMI, PSQI score, biological sex and pseudobulbar symptoms.

RESULTS

22 ALS patients enrolled: 70.57 ± 10.8 years; 12 males and 10 females; mean disease duration 21.3 ± 21.64 months.
Sleep questionnaires: 86.4% reported sleep disturbances (20% insomnia symptoms, 55% nocturnal leg cramps, 15% RLS symptoms)

- *Comorbid insomnia* ↔ FTD-related **behavioral changes** (p = 0.0006)
- *Female patients* → Worse subjective **sleep quality** (p = 0.04) and higher **daytime fatigue** (p = 0.04).

Polysomnography data: 57.1% of OSA, 23.8% of PLMD → Mild (5-15/h) 33.3%, Moderate (15-30/h) 14.3%, Severe (>30/h) 9.5%

- *Male patients* → Higher odds of OSA (72.7% vs 40%), **higher AHI values** (p = 0.01), **higher ESS scores** (p = 0.05)
- *Berlin Questionnaire* → Only 3 out of 21 patients had a high risk of OSA (vs 12 diagnosed with HSAT, and 5 with moderate-severe forms)

OSA risk predictive score: Body Mass Index, Pittsburgh Sleep Quality Index total score, sex, and bulbar involvement (Fig. 1)

- 87.5% specificity, 80% accuracy, AUC 0.911

No correlation between sleep disorders and ALS severity (ALS-FRS-r score and subscores)
Survival analysis: Detrimental correlation between AHI values (cut-off threshold: 3.8 events/h) and 12-month survival (67% vs. 100%) (Fig. 2)

DISCUSSION

- **High prevalence** of sleep disorders among ALS patients, confirmed with both subjective and objective measures;
- ALS severity scales could be limited for a multidimensional approach to these patients, neglecting specific domains (e.g., bulbar and respiratory systems);
- Traditional screening tools might be inadequate for ALS patients due to poor sensitivity;
- **Predictive model for OSA risk** integrating BMI, sex, PSQI, and bulbar involvement displayed 80% accuracy;
- **ALS patients' peculiar features** (increased sensitivity to muscle atonia, respiratory muscle exhaustion, loss of bulbar motor neurons) could foster upper airways collapsibility and impair loop gain control;
- **Intermittent hypoxia** due to obstructive apnea may promote neuronal death, oxidative stress, and inflammation, supporting a worse prognosis in ALS+OSA patients;
- **Treatment with NIV** can neutralize the negative survival impact of OSA and also improve quality of life.
- **Limitations:** small sample size, due to ALS epidemiology and monocentric design.

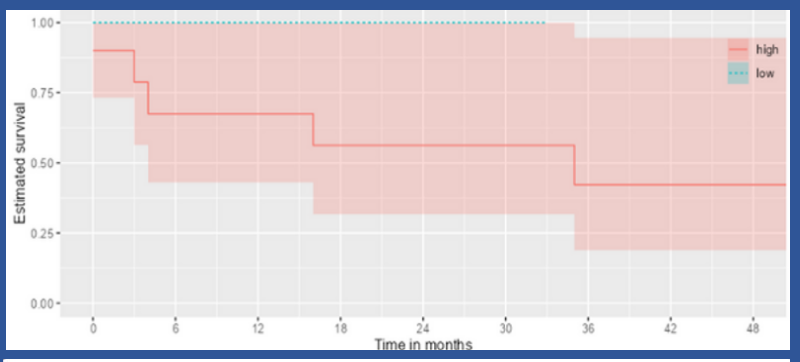

Fig.2: Kaplan-Meier survival curve estimating patients' survival probability over time stratified in two groups according to the AHI value, considering a cut-off of 3.8 events/h.

CONCLUSIONS

- Include **sleep evaluation** in the **routine workup** of ALS patients;
- **Include complementary information** in conventional screening processes;
- Consider also other respiratory patterns suggestive of **excessive respiratory effort**;
- **Prompt treatment** of sleep-breathing disorders mitigates the negative impact on prognosis.