PROGNOSTIC INFLUENCE OF PRE-MORBID SMOKING HABITS, DIABETES, ARTERIAL HYPERTENSION AND VASCULAR RISK PROFILE ON PHENOTYPE AND OUTCOME OF ALS PATIENTS: A POPULATION-BASED STUDY

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Introduction

The phenotype of ALS, such as age at onset, site ad type of onset, and survival, is quite heterogeneous, and the factors influencing this heterogeneity are largely unknown. Several factors have been found to influence ALS phenotype, including the genetic background, age and gender, pre-morbid diseases, life habits and physical activity, but data are sparse and contradictory. Attention has been also devoted to the influence of pre-morbid vascular risk factors, including cigarette smoking, on ALS prognosis, but no comprehensive study of these factor has been performed.

Aim

To evaluate the effect of smoking, diabetes, hypertension and vascular risk profile on ALS phenotype and prognosis in a population-based cohort of patients.

Methods

A total of 650 ALS patients from the Piemonte and Valle d'Aosta Register for ALS (PARALS), incident in the 2007-2011 period, were recruited. Information about premorbid smoke habits, chronic obstructive pulmonary disease (COPD), diabetes mellitus, arterial hypertension (AH) were collected at the time of diagnosis. The vascular risk of patients was estimated according to the Joint British Societies' guidelines on prevention of cardiovascular disease in clinical practice (JBS2).

Results

Current smokers had a significantly shorter median survival (1.9 years, interquartile range [IQR], 1.2-3.4) compared to former (2.3, IQR 1.5-4.2) and never smokers (2.7 years, IQR 1.8-4.6) (p=0.001). Patients who were currently smoking at ALS onset had a younger age at onset (64.9 years, SD 11.6) than both former (67.6, SD 9.7) and never smoker (66,3 years, SD 10.7). The median survival time of patients with COPD was lower than that of patient without COPD (COPD, 1.7 years, IQR 0.9-2.5; non-COPD 2.6, IQR 1.5-4.3) (p=0.01). Diabetes and arterial hypertension did not influence ALS prognosis. Patients with a lower vascular risk profile had a better prognosis than those with intermediate and higher risk profiles. However, only smoking habits and CODP were retained in Cox multivariable model

Conclusion

Smoking status is an independent prognostic factor with an increased odds ratio for current smokers vs. never smokers of 1.53 (95% c.i. 1.22-1.92, p=0.0001). Its influence is independent of the presence of COPD or the respiratory status at time of diagnosis. Diabetes mellitus and AH did not modify either the phenotype or the prognosis of ALS. This study indicates that environmental factors and personal habits may not only represent risk factors for the onset of ALS but can also influence its phenotype and prognosis.

Factor	
Gender (female)	290 (44.6%)
Mean age at onset (years, SD)	66.4 (10.6)
Diagnostic delay (months, SD)	11.3 (10.9)
Site of onset (bulbar)	203 (31.2%)
El Escorial classification at diagnosis	Possible: 209 (32.1%) Probable Laboratory Supported: 69 (10.6%) Probable: 137 (21.1%) Definite: 235 (36.2%)
Mean ALSFRS-r score at diagnosis	40.2 (6.5)
C9orf72 positive §	33 (6.1%)
Mean BMI at diagnosis (SD)	24.3 (4.3)
Mean FVC at diagnosis (SD) *	82.6 (26.8)
Type 2 diabetes	59 (9.1%)
Arterial hypertension	296 (45.5%)
Smoking	Never 347 (53.4%) Former 182 (28.0%) Current 121 (18.6%)
Cardiovascular risk profile	Low: 462 (71.1%) Intermediate: 141 (21.7%) High: 47 (7.2%)

Table 1. Demographic and clinical characteristics of patients

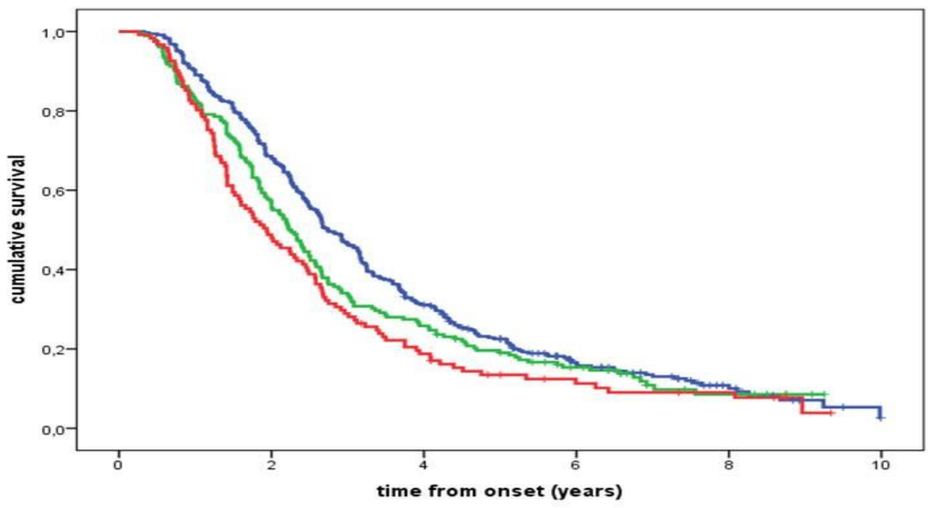

Fig 1. Kaplan-Meier curves by smoking status at time of ALS onset. The blue line represents never smokers, the green line former smokers and the red line current smokers. p=0.001, linear trend.

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