THE PROGNOSTIC VALUE OF THE SPREADING OF SYMPTOMS AT DIAGNOSIS IN ALS: A POPULATION-BASED STUDY

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Introduction

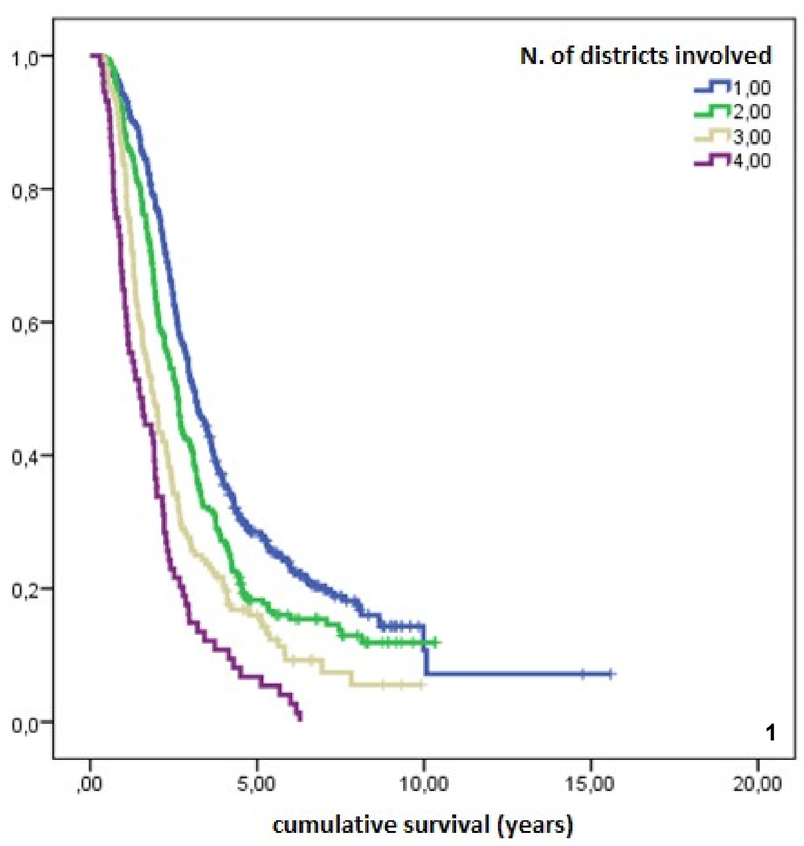
In ALS, the rate of disease spread is likely correlated to the severity of the neuro-axonal degeneration and consequently to the disease progression and survival. The spreading pattern of degeneration of cortical, brainstem and spinal motor neurons is yet to be completely understood. Recent studies has tried to identify a correlation between the disease generalisation trend and the patients outcome, in order to better define the ALS natural history and to provide new primary outcome measures for clinical trials [1,2].

Aim

To assess the pattern of disease involvement in different body regions (upper limbs, lower limbs, bulbar and respiratory) at diagnosis and how it correlates to overall survival in a population-based series of ALS patients.

Methods

Among the 879 ALS patients incident in the period 2007-2012 in Piemonte and Valle d'Aosta, 810 (92.2%) were included in the study (382 women and 428 men; mean age at onset 66.3 years [SD 10.9]). The time of involvement of different regions was obtained from the ALSFRS-R score performed during the follow-up visits. The site has been considered as affected if the sub-score was at least one point lower than the maximum awarded to that region (ALSFRS-R domains 1, 2 and 3 for the bulbar region, 4 and 5 for the upper limbs, 8 and 9 for the lower limbs, and 10, 11 and 12 for the respiratory muscles



The different involvement patterns were then analysed according to sex, age at onset, site of onset, PEG, NIV, tracheostomy and survival.

Results

In 291 (35,9%) patients, the disease onset was at the upper limbs, in 275 (34,0%) was bulbar, in 227 (28,0%) was at lower limbs and in 17 (2,1%) was respiratory. In 367 patients (45.3%) only one region was affected at diagnosis, two regions were involved in 217 patients (26.8%), three in 152 patients (18.8%), and four in 74 patients (9.1%). The number of affected regions at diagnosis progressively increased with the increase of the age at onset (p=0.0001).

This trend was not determined by a delayed diagnosis, since the interval between symptom onset and diagnosis (overall mean 0.97 years, SD 0.96) did not change according to the number of affected regions at diagnosis (p=0.48) and the different age groups (p=0.30). Moreover, the number of affected regions at diagnosis was related to survival (1 region, median survival time 3.1 years, 2.1-5.6; 2 regions 2.6 years, 1.7-4.2; 3 regions, 1,8 years, 1.2-3.1; 4 regions, 1.5 years, 0.8-2.4; p=0.0001) and its correlation to the overall outcome is independent from the length of the onset-diagnosis interval (p=0.0001) and the age at onset (p=0.0001).

Conclusions

The symptoms burden at diagnosis and the different spreading patterns in ALS patients are related to overall survival: those results can provide a substantial contribution in defining the disease outcome.

References

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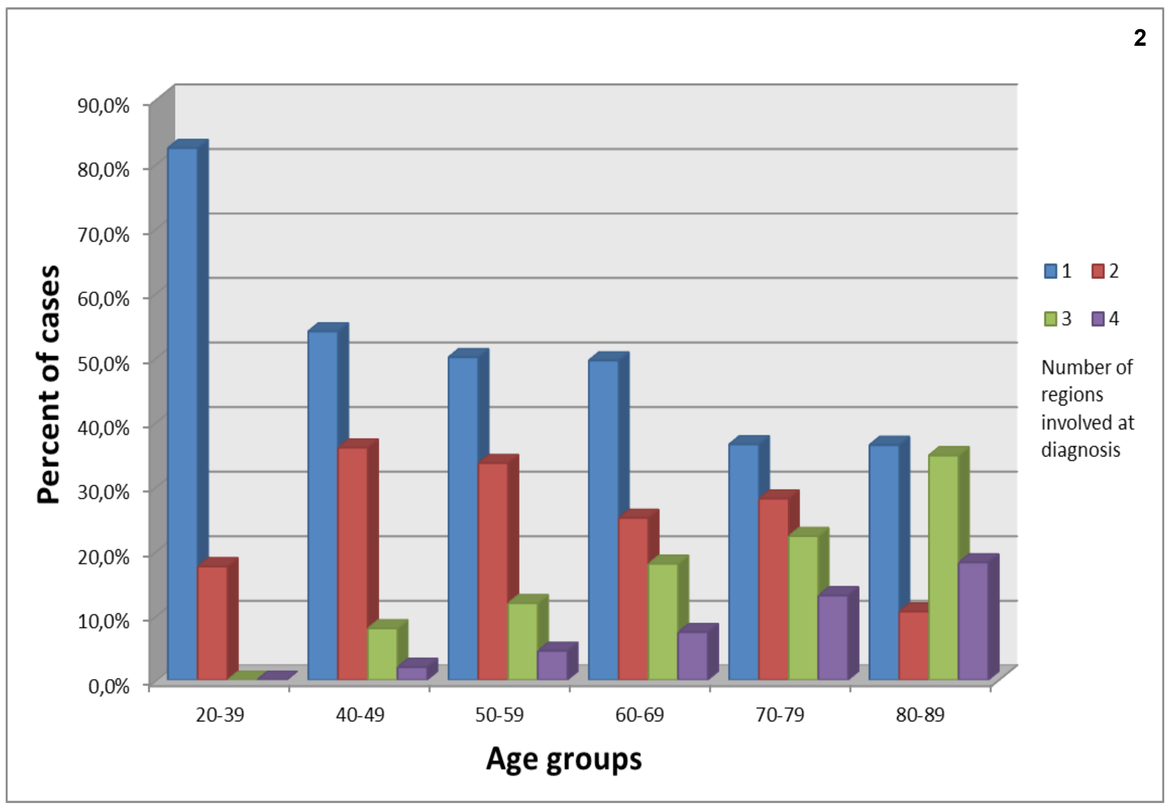

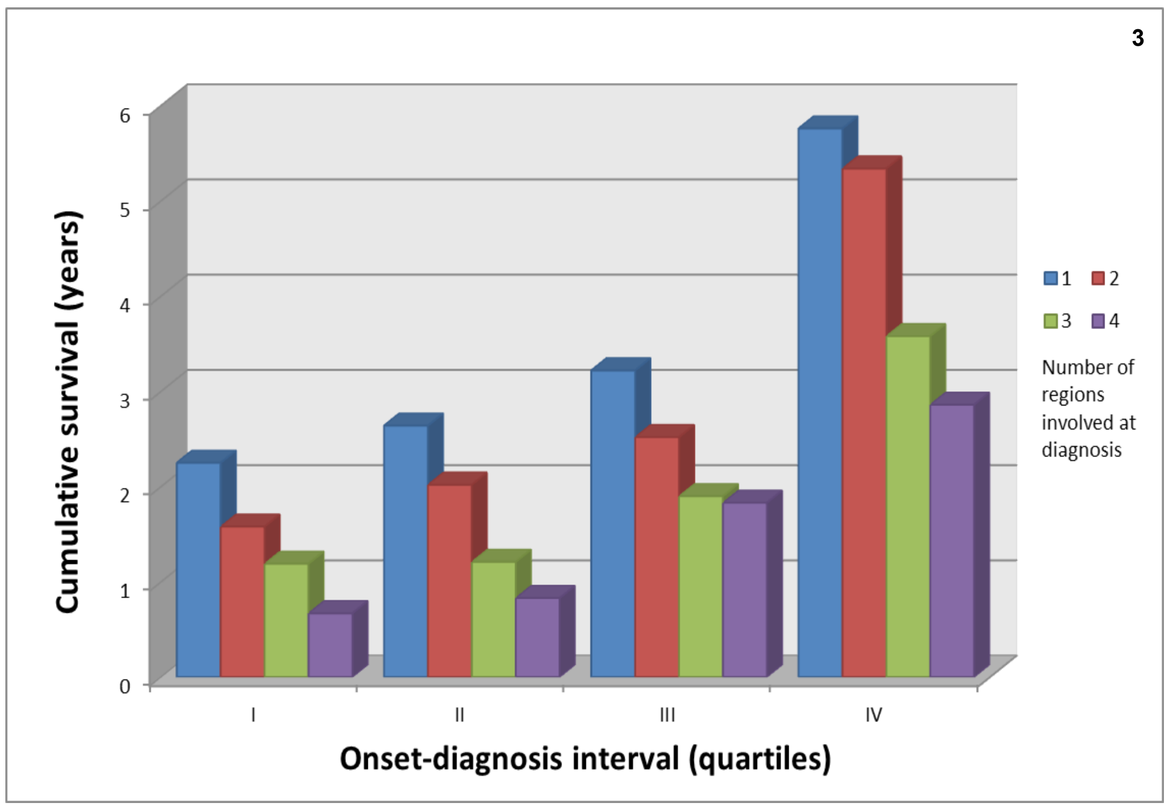

Figure 1. Cumulative survival related the number of affected regions at diagnosis (p=0.0001) **Figure 2.** Number of regions involved at diagnosis according to different age groups. **Figure 3.** Cumulative survival according to number of region involved, subgrouped by onset-diagnosis interval (quartiles); I quartile: 0-5 months, II quartile: 6-8 months, III quartile: 8-14 months, IV quartile: >14 months