

# Prognostic factors of post-tracheostomy survival in ALS: a multicenter study

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## Introduction and aim of the study

Amyotrophic Lateral Sclerosis (ALS) is a relentless neurodegenerative disease leading to death within 3 to 5 years from symptoms onset, primarily due to respiratory failure. A small percentage of patients choose to undergo tracheostomy and invasive ventilation (TIV) to extend their survival. Although considerable differences in the use of TIV and post-tracheostomy survival of ALS patients have been described across countries, the factors driving the variability in survival after tracheostomy remain less understood (Chiò *et al.* 2010, Hayashi *et al.* 2020, Masrori *et al.* 2020). Our study aimed to characterize ALS patients who underwent tracheostomy across three Italian population-based cohorts and to identify prognostic factors associated with post-tracheostomy survival.

## Methods

Data from the Piemonte and Valle d'Aosta Register for ALS (PARALS), the Emilia Romagna Region ALS register (ERRALS) and a South-Sardinia ALS incident cohort were used. Continuous and nominal variables were compared among the three cohorts. Post-tracheostomy survival across centers was compared using the Kaplan-Meier analysis, while the Cox proportional hazard ratio was used to identify prognostic factors. In particular, the sex, onset site, diagnostic delay, age at tracheostomy, gastrostomy placement and discharge modality (home vs nursing homes) were considered as possible predictors.

## Results

A total of **180 (12.4%)**, **205 (16.4%)** and **120 (33.4%)** patients underwent TIV in PARALS, ERRALS and Sardinian cohort, respectively (see Figure 1). PARALS and ERRALS patients did not significantly differ in demographic characteristics, while Sardinians showed higher rates of positive ALS family history (21.7% vs 8.9% in PARALS and 9.4% in ERRALS,  $p=0.003$  and  $0.004$ ), *TARDBP* mutations (18.2% vs 0.0% and 1.9%,  $p<0.001$  both) and a longer median post-tracheostomy survival (23.1 vs 15.7 and 13.2 months,  $p=0.012$  and  $0.003$ ).

Sardinian patients showed longer survival compared to those from other centers ( $p=0.0056$ ), with this advantage being even more evident among patients home-discharged (48.5 vs 25.6 vs 18.7 months,  $p=0.002$  and  $<0.001$ ) (see Figure 2). In the overall cohort, only **age at tracheostomy** (HR=1.02,  $p=0.031$ ) and **being discharged to a nursing home** (HR =2.06,  $p<0.001$ ; home-discharge used as reference) were associated with post-tracheostomy survival; the latter was also confirmed in each cohort (see Figure 1).

## Conclusions

Our study shows that younger age at tracheostomy and home-discharge are associated with longer survival in tracheostomized ALS patients across all the three cohorts. Notably, Sardinian patients showed a longer post-tracheostomy survival. The knowledge of factors driving post-tracheostomy survival may help both clinicians and patients in decision-making and disease management.

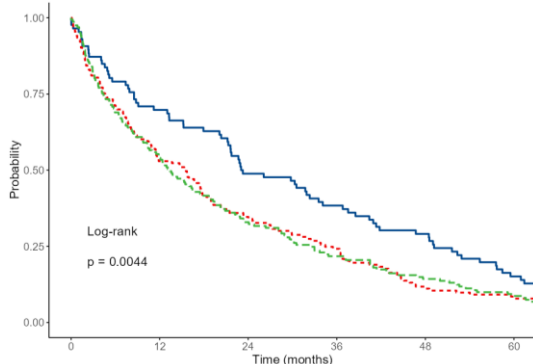


Figure 2. Kaplan-Meier curves in Sardinian (blue line), PARALS (red dashed line) and ERRALS (green dashed line) cohorts. The curves show a clear survival advantage among the Sardinian cohort. Log-rank analysis confirmed a significant difference in post-tracheostomy survival rate among the three cohorts ( $p=0.0044$ )

	Overall		Sardinian		PARALS		ERRALS	
	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value
Cohort(PARALS)	1.93 (1.38-2.69)	<0.001*						
Sex(M)	1.40 (1.06-1.85)	0.018*	1.43 (0.85-2.41)	0.176	1.85 (1.19-2.89)	0.007*	0.97 (0.54-1.72)	0.904
Onset site (spinal)	1.05 (0.78-1.42)	0.744	1.00 (0.57-1.76)	0.995	1.09 (0.69-1.71)	0.722	1.32 (0.70-2.50)	0.389
Diag. delay	1.02 (1.00-1.03)	0.021*	1.01 (0.99-1.03)	0.259	1.04 (1.00-1.08)	0.027*	0.99 (0.94-1.03)	0.579
Age at tracheo	1.02 (1.00-1.04)	0.024*	1.02 (0.99-1.05)	0.240	1.01 (0.99-1.04)	0.311	1.03 (0.99-1.06)	0.114
Peg timing (pre)	1.10 (0.82-1.47)	0.532	0.81 (0.46-1.41)	0.457	1.11 (0.72-1.71)	0.648	1.77 (0.84-3.73)	0.135
Post-tracheo discharge (nurs)	2.05 (1.47-2.88)	<0.001*	2.52 (1.41-4.48)	0.002*	2.06 (1.15-3.71)	0.016*	2.64 (1.25-5.57)	0.011*

Table 1. Model 2: Cox multivariate regression analysis excluding patients dead in hospital and/or within one month from tracheostomy. In this model, "Post-tracheostomy discharge" was added to the other covariates.

## Rate of tracheostomy in ALS patients

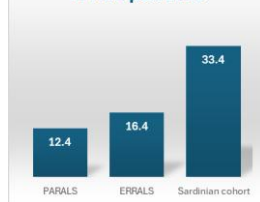


Figure 1. Rate of tracheostomy across the three cohorts.