

Predictors of adaptation to non-invasive ventilation in Amyotrophic Lateral Sclerosis

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INTRODUCTION

Non-invasive ventilation (NIV) is currently the treatment for ALS-related respiratory failure. It is known that NIV increases survival, improves quality of life (QoL) and it is the preferred therapy to alleviate respiratory symptoms. In recent years, several studies have demonstrated that in ALS patients NIV for at least four consecutive hours during sleep relieves symptoms of alveolar hypoventilation and improves both survival and quality of life (Volanti et al.)
 Despite the benefits resulting from NIV administration, about one out of three patients do not tolerate NIV. It has been described that bulbar onset is a negative predictor to NIV tolerance. (Aboussouan LS et al.)

AIM: The aim of this study was to evaluate the impact of functional, cognitive, neurobehavioural and respiratory status on NIV tolerance in patients with ALS.

METHODS

Cross-sectional study performed on patients consecutively hospitalized at the Nemo Sud Clinical Center who underwent a NIV starting training. All of them were diagnosed with a probable/definite ALS, according to the El Escorial World Federation of Neurology revised criteria.

All patients underwent: neurological and functional assessment (MRC, ALSFRS-r), spirometry for expiratory Forced Vital Capacity (FVC), arterial blood gases analysis, overnight pulse oximetry, Borg Dyspnoea Scale and neuropsychological and affective assessment.

ALS Functional Rating Scale revised (ALSFRS-r)¹⁵ has been administered. Its subscores were analyzed as follow: the "bulbar score" was obtained adding the results of items 1 to 3; item 2 was also separately analyzed for the presence of sialorrhea. We considered sialorrhea as present if the item 2 ALS-FRS-r subscore was ≤ 2 ; the "upper limb", "lower limb" and "respiratory" scores were obtained adding the results of items 4 to 6, 7 to 9 and 10 to 12 respectively.

The neuropsychological and affective status was assessed using the Edinburgh Cognitive and Behavioural ALS Screen (ECAS), considering both the ECAS total score and the ALS specific score, the Frontal Assessment Battery, the Progressive Matrices 47 (PM47), the Hospital Anxiety and Depression Scale (HADS) and the Neurobehavioral Rating Scale – Revised (NRS-R).

Time of adaptation is defined as the number of days required by patient to tolerate NIV for at least 4 hours continuously during sleep.

Statistical analysis

Statistical analysis were made using SAS 9.3 (SAS Institute, Inc, Cary, NC) software. Data were reported in text and tables as mean and standard deviation for continuous variables and numbers and percentages for those non-continuous. For each variable we used Shapiro-Wilk test to evaluate the normality of the distribution and Levene test to evaluate the homogeneity of variance. Correlation univariate analysis was made using the Pearson correlation coefficient and the non-parametric Spearman rank correlation coefficient as appropriate, using a p value < 0.20, while for the multivariable analysis, the multiple regression model adjusting for age, sex and respiratory assessments was used, with a significance level alpha < 0.05.

RESULTS

Seventy-two patients started the NIV training in our multidisciplinary setting and were included in the study.

According to the clinical onset patients belonged to these phenotypes: 23 bulbar and 49 non bulbar. The latter were further classified as 31 classic, 4 flail arm, 2 flail leg, 5 pure lower motor neuron, 5 pyramidal and 2 respiratory.
 Patients adapted were 63/72 (87,5%).

Clinical data of the 63 adapted patients are summarized in table 1.

The average time of adaptation was $7,82 \pm 5,27$ SD days.

Correlation between time of adaptation and neurological, functional, cognitive and neurobehavioural and respiratory data at univariate analysis are showed in table 2.

After the multivariable analysis the statistical significance correlation was confirmed for: NRSR- F1 (deficit in intentional behaviour), NRSR- F5 (consisted mainly of problems in speech and expressive and comprehension language skills), ALS-FRS-R respiratory subscore, Borg Dyspnoea Scale scores and presence of sialorrhea (Table 3).

Main clinical data of patients non-tolerant to NIV are detailed in table 4.

CONCLUSIONS

- In our study we obtained a high rate of adaptation (87,5%), in line with previous evidence.
- Interestingly we didn't find a significant correlation between time of adaptation and bulbar symptoms, whereas we found a correlation only with the presence of sialorrhea.
- In keeping with previous evidence, 66,6% of non-tolerant patients had bulbar onset and 77,7% had sialorrhea.
- Our study better specifies which are the cognitive and neurobehavioral dysfunctional pattern that may interfere with NIV adaptation. It included dysexecutive behavioral changes and language dysfunction. Therefore the lack of understanding of disease severity and the presence of deficit in planning, initiative, motivation and conceptual organization might be the factors most affecting NIV training.
- Borg Dyspnoea Scale scores and respiratory symptoms are strong predictor to good adaptation. They are related to a quick adaptation to NIV and are regularly absent or mild in the nine non-tolerant patients.

Our study suggest the importance of a personalized multidisciplinary approach to improve NIV adaptation. Hospitalization may be necessary for patients who have negative adaptation predictors such as neuropsychological impairment, sialorrhea and absence of respiratory symptoms. A quicker ambulatory approach may be firstly tried in patients with good executive functioning, especially if they have dyspnoea and a good management of saliva.

NIV- tolerant patients

Table 1. Clinical characteristics (adapted patients)

	(MEAN \pm SD)
Patients adapted	63/72 (87,5%)
Time of adaptation	(7,8 \pm 5,3)
Age	(63,9 \pm 10,6)
Male sex	29 (46%)
Presence of sialorrhea	40 (63,4%)
Bulbar onset	17 (26,9%)
ECAS total score	(84,7 \pm 27,8)
ECAS ALS specific score	(61,0 \pm 21,9)
ECAS non ALS specific score	(23,6 \pm 7,2)
ECAS language	(18,8 \pm 6,3)
ECAS verbal fluency	(23,6 \pm 7,2)
ECAS executive function	(29,0 \pm 10,2)
ECAS memory	(14,7 \pm 5,1)
ECAS visuo-spatial ability	(9,0 \pm 3,0)
Frontal Assessment Battery	(13,8 \pm 2,8)
PM47	(25,1 \pm 6,5)
NRSR-F1	(1,9 \pm 0,6)
NRSR-F2	(2,7 \pm 0,7)
NRSR-F3	(1,7 \pm 0,5)
NRSR-F4	(2,1 \pm 0,7)
NRSR-F5	(2,1 \pm 0,8)
Total NRSR	(52,3 \pm 11,0)
Anxiety (HADS Scale)	(9,1 \pm 4,5)
Depression (HADS Scale)	(6,3 \pm 4,4)
Blood gas analysis PaO ₂ mmHg	(78,4 \pm 11,6)
Blood gas analysis PaCO ₂ mmHg	(45,6 \pm 11,3)
Forced vital capacity	(1,29 \pm 0,8)
Supine forced vital capacity	(0,44 \pm 0,3)
Nocturnal oximetry T90	(0,1 \pm 0,2)
Borg Dyspnoea Scale	(3,12 \pm 2,04)
ALS-FRS-R total score	(23,35 \pm 9,73)
Bulbar score	(5,20 \pm 3,71)
Upper limbs score	(5,37 \pm 4,28)
Lower limbs score	(5,96 \pm 4,26)
Respiratory score	(6,78 \pm 2,32)

Table 2. Univariate analysis

	p-value
Age	0,22
Male sex	0,05
Presence of sialorrhea	0,01
Bulbar onset	0,38
ECAS total score	0,39
ECAS ALS specific score	0,50
ECAS non ALS specific score	0,05
ECAS language	0,31
ECAS verbal fluency	0,33
ECAS executive function	0,76
ECAS memory	0,16
ECAS visuo-spatial ability	0,05
Frontal Assessment Battery	0,32
PM47	0,45
NRSR-F1	0,15
NRSR-F2	0,23
NRSR-F3	0,27
NRSR-F4	0,13
NRSR-F5	0,07
Total NRSR	0,26
Anxiety (HADS Scale)	0,11
Depression (HADS Scale)	0,10
Blood gas analysis PaO ₂ mmHg	0,06
Blood gas analysis PaCO ₂ mmHg	0,005
Forced vital capacity	0,99
Supine forced vital capacity	0,98
Nocturnal oximetry T90	0,83
Borg Dyspnoea Scale	0,007
ALS-FRS-R total score	0,28
Bulbar score	0,05
Upper limbs score	0,10
Lower limbs score	0,58
Respiratory score	0,01

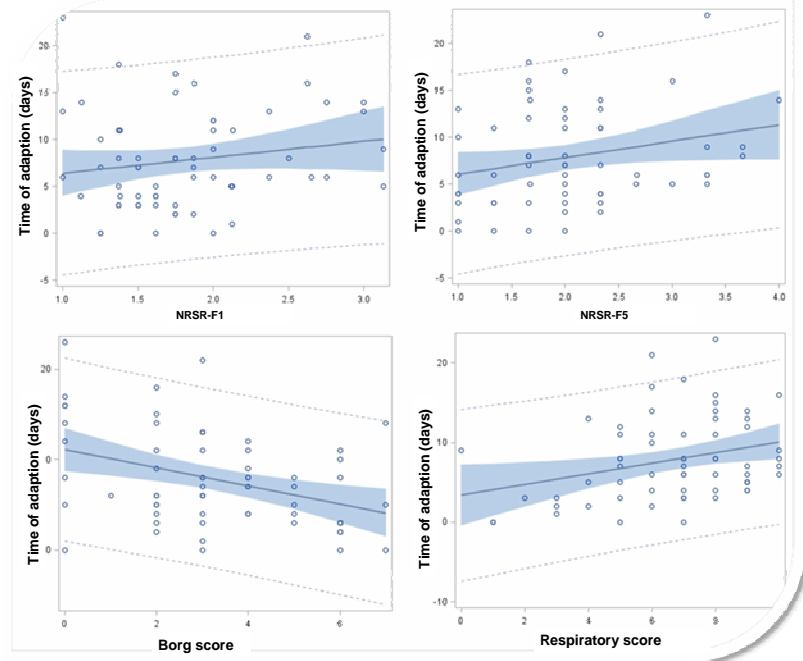
Non-tolerant patients

Table 4. Non-tolerant patients: clinical characteristics

	(MEAN \pm SD)
Patients adapted	9
Time of adaptation	unadapted
Age	67,3
Male sex	3 (33,3%)
Presence of sialorrhea	7 (77,7%)
Bulbar onset	6 (66,6%)
ECAS total score	67,9
ECAS ALS specific score	48,1
ECAS non ALS specific score	19,8
ECAS language	16,1
ECAS verbal fluency	10
ECAS executive function	22
ECAS memory	13
ECAS visuo-spatial ability	7
Frontal Assessment Battery	10,6
PM47	21,9
NRSR-F1	2,3
NRSR-F2	1,4
NRSR-F3	1,7
NRSR-F4	2,3
NRSR-F5	2,5
Total NRSR	56,9
Anxiety (HADS Scale)	7,3
Depression (HADS Scale)	7
Blood gas analysis PaO ₂ mmHg	83,7
Blood gas analysis PaCO ₂ mmHg	42
Forced vital capacity	0,86
Supine forced vital capacity	0,58
Nocturnal oximetry T90	0,02
Borg Dyspnoea Scale	2,1
ALS-FRS-R total score	22,5
Bulbar score	2,8
Upper limbs score	5,8
Lower limbs score	6
Respiratory score	7,8

Table 3. Significant correlation between time of adaptation and other variables after multivariate analysis

	R	p-value
Presence of sialorrhea	0,30	0,02
NRSR-F1	0,19	0,04
NRSR-F5	0,23	0,04
Borg Dyspnoea Scale	-0,33	0,006
Respiratory score	0,30	0,03



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