Understanding the Use of Noninvasive Ventilation in the Treatment of Amyotrophic Lateral Sclerosis: Results of an International Physician Survey

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INTRODUCTION

- Patients with amyotrophic lateral sclerosis (ALS) require respiratory support as their disease progresses,[1] and noninvasive ventilation (NIV) can provide respiratory support as well as improve quality of life and extend survival[2-5]
- While there is evidence to support the use of NIV in ALS, the best indication for NIV and when to initiate NIV are less clear[1,2]
- Therefore, a lack of uniformity exists regarding the clinical decisions of when and why a physician may prescribe NIV
- It is not uncommon for the decision to initiate NIV to be driven in certain regions, at least in part, by insurance carrier or health care service requirements to fulfill specific criteria for the device to be covered[6]

OBJECTIVES

- To identify state-of-the art practices of NIV use among ALS specialists internationally and to better understand the similarities and differences regarding NIV initiation, obstacles to use, preferred equipment, and other areas of unmet need in the use of NIV for ALS

METHODS

Study design

- A 25-item questionnaire on the timing and use of NIV was developed based on knowledge of the literature and clinical experience with NIV
- ALS specialists (physicians [MDs, DOs], nurse practitioners, and physician assistants) practicing at ALS centers in several countries in North America, Europe, and Australia were identified to participate through their membership in the Northeast ALS Consortium (NEALS) (United States), the European Network to Cure ALS (ENCALS) (Europe), and ALS Canada (removing any duplicates)
- The questionnaire was sent via SurveyMonkey® and responses were collected
- Results from SurveyMonkey for the United States (US) and Europe (EUR) (because of the very small number of Canadian and Australian responses) were analyzed

Statistical methods

- Descriptive statistics and Pearson's chi square analysis comparing the US and EUR responses were performed
- Ranked questions were evaluated using weighted averages with the highest rating/most popular given the value 1, the next highest/most popular response the value 2, and so on. These numerical values were multiplied by the fraction of respondents who gave that answer and then all values were added together for a final weighted value. Lowest values signify the most popular/highest-rated answers. Answers given by less than 5% of the sample were excluded from the comparisons

RESULTS

Characteristics of respondents and respiratory management in their clinics

- 62.2% (74/119) of respondents treated ≥76 ALS patients/year (US: 56.3% [40/71]; EUR: 70.8% [34/48])

Table 1. Who manages respiratory symptoms in the clinic (check all that apply)?

	US response, n (%)	EUR response, n (%)
Pulmonologists only	18 (25.4)	13 (27.1)
Pulmonologists and neurologists	18 (25.4)	16 (33.3)
Neurologists only	15 (21.1)	11 (22.9)
Neurologists and other medical specialists	9 (12.7)	0
Neurologists, pulmonologists, and other medical specialists	8 (11.3)	5 (10.4)
Other medical specialists only	3 (4.2)	2 (4.2)
Other medical specialists and pulmonologists	0	1 (2.1)
Total respondents	**71**	**48**

Table 2. Most commonly used tests to evaluate respiratory status in the United States versus Europe

	1st	2nd	3rd	4th	5th
United States					
Initial	Upright FVC	Upright MIP	Pulse oximetry[a]	Supine FVC	MEP
Follow-up	Upright FVC	Upright MIP	Pulse oximetry[a]	Supine FVC	MEP
Considering NIV	Upright FVC	Upright MIP	Supine FVC	Pulse oximetry	MEP
Europe					
Initial	Upright FVC	ABGs	MEP	Overnight pulse oximetry	Pulse oximetry[a]
Follow-up	Upright FVC	ABGs	Pulse oximetry[a]	MEP[b] Overnight pulse oximetry[b] Upright MIP[b]	N/A
Considering NIV	Upright FVC	Overnight pulse oximetry	ABGs	Pulse oximetry[a]	SNIP[b] Supine FVC[b] Upright MIP[b] Upright SVC[b]

[a] Single value in clinic; [b] Equally ranked.
ABGs, arterial blood gases; FVC, forced vital capacity; MEP, maximal expiratory pressure; MIP, maximal inspiratory pressure; N/A, not applicable; NIV, noninvasive ventilation; SNIP, sniff nasal inspiratory pressure; SVC, slow vital capacity

Table 3. Most important parameters used for decision-making regarding prescribing NIV

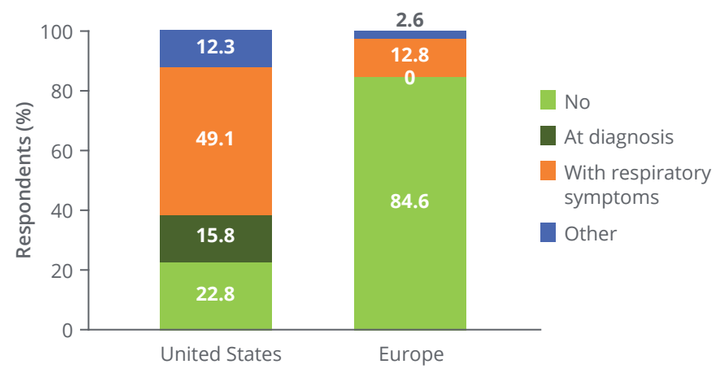
United States (n = 60)	Response total (n)	Weighted average
Upright FVC	58	2.08
Supine FVC	47	2.35
Symptoms of orthopnea and/or dyspnea	54	3.21
Upright MIP	43	3.70
Upright SVC	18	4.39
Supine SVC	14	4.56
Supine MIP	25	4.64
Sleep-related symptoms (eg, morning headache, snoring, restless sleep)	46	4.66
Overnight pulse oximetry	38	5.11
SNIP	13	5.24
ABGs in the clinic	15	5.40
End tidal CO_2	7	5.58
Formal sleep study	34	5.68
Overnight transcutaneous CO_2	5	6.60

Europe (n = 40)	Response total (n)	Weighted average
Symptoms of orthopnea and/or dyspnea	39	2.46
Sleep-related symptoms (eg, morning headache, snoring, restless sleep)	38	3.14
Supine SVC	7	3.58
Supine MIP	5	3.60
Overnight transcutaneous CO_2	10	3.60
ABGs in the clinic	25	3.72
Supine FVC	19	3.79
Overnight ABGs	14	4.28
Overnight pulse oximetry	33	4.43
SNIP	14	4.78
Formal sleep study	20	4.85
Upright FVC	30	4.97
Upright SVC	8	5.00
Upright MIP	13	5.01

ABGs, arterial blood gases; FVC, forced vital capacity; MIP, maximal inspiratory pressure; NIV, noninvasive ventilation; SNIP, sniff nasal inspiratory pressure; SVC, slow vital capacity

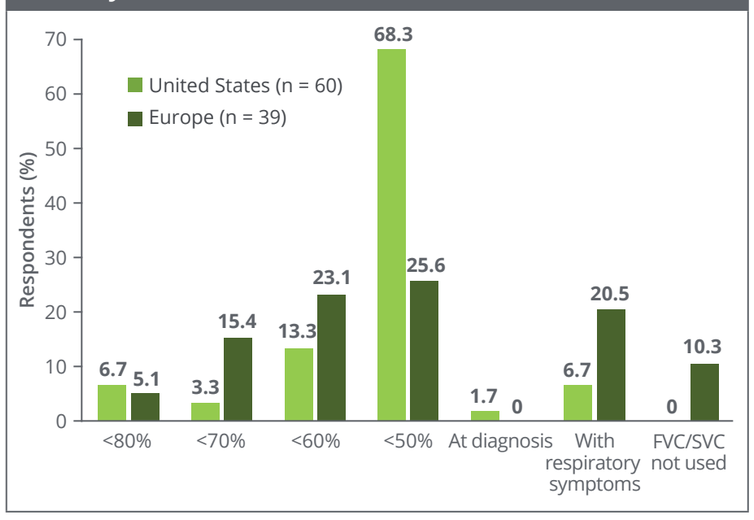
- Insurance was an important factor in decisions regarding NIV prescription
  - This was especially true in the United States, where 70.0% (42/60) of respondents answered that insurance regulations/national health care coverage impact when they initiate NIV compared with only 47.5% (19/40) of respondents in Europe

Figure 1. "If insurance, or other financial constraints were not present, would you alter the timing of when you prescribe NIV?"



At diagnosis = I would initiate it at the time of diagnosis, independent of symptoms or respiratory testing results; With respiratory symptoms = I would initiate it at the time respiratory symptoms develop, independent of respiratory testing results
NIV, noninvasive ventilation

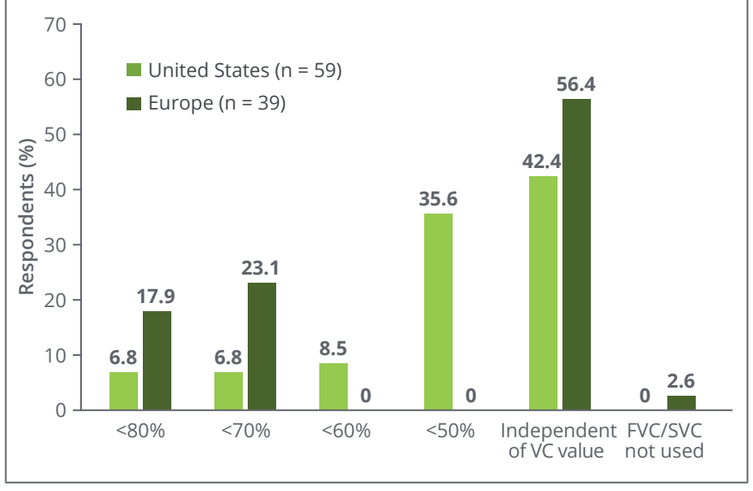
Figure 2. "For a patient WITHOUT respiratory symptoms, at what upright vital capacity (FVC or SVC) would you initiate non-invasive ventilation?"



FVC, forced vital capacity; SVC, slow vital capacity

- Overall, although they used supine forced vital capacity/slow vital capacity (FVC/SVC) less frequently in their decision to initiate NIV, US respondents reported using them similarly as they did upright FVC/SVC in patients with and without respiratory symptoms; compared with ALS specialists in the United States, specialists in Europe used neither as often in the decision to initiate NIV
- Upright maximal inspiratory pressure (MIP), supine MIP, and sniff nasal inspiratory pressure (SNIP) were not used as often as upright and supine FVC/SVC in the decision to initiate NIV either in the United States or, to an even greater extent, in Europe

Figure 3. "For a patient WITH respiratory symptoms, at what upright vital capacity (FVC or SVC) would you initiate non-invasive ventilation?"



Independent of VC value = In the presence of respiratory symptoms, would initiate NIV independent of VC value; FVC/SVC not used = I do not use upright FVC or SVC to decide when to initiate NIV. FVC, forced vital capacity; NIV, noninvasive ventilation; SVC, slow vital capacity

NIV initiation and goals for use

- When recommending NIV, US respondents more often referred patients to home agencies with trials/instructions occurring at home (US: 68.4% [39/57]; EUR: 12.8% [5/39]; $P < .001$); specialists in Europe more often admitted patients to hospital (US: 0% [0/57]; EUR: 41.0% [16/39]; $P < .001$)
- US specialists expressed a preference to use certain ventilators noninvasively (US: 43.9% [25/57]; EUR: 12.8% [5/39]; $P = .002$); most specialists in Europe allowed pulmonologists to decide (US: 19.3% [11/57]; EUR: 64.1% [25/39]; $P < .001$)

Table 4. What do you consider the minimum goal in hours used per 24 hours in order for the patient to benefit from NIV?

	US response, n (%)	EUR response, n (%)
1 h/24 h	3 (5.3)	2 (5.1)
2 h/24 h	1 (1.7)	1 (2.6)
3 h/24 h	1 (1.7)	3 (7.7)
4 h/24 h	28 (49.1)	14 (35.9)
>50% night period	18 (31.6)	13 (33.3)
>90% night period	6 (10.5)	6 (15.4)
Total respondents	**57**	**39**

CONCLUSIONS

- **In the United States, results of VC testing were the most common driver for initiating NIV, while symptoms of dyspnea, orthopnea, or disturbed sleep were the most common reasons for initiation of NIV in Europe**
- **NIV prescribing differs in the United States versus Europe and may be influenced by insurance/financial constraints more so in the United States than in Europe**
  - **These differences not only exist between practices in Europe and United States but have also been found to differ across the United States[7]**
  - **These differences may confound results in ALS treatment studies**
- **The optimal use of NIV can influence patient survival[2-5] underscoring the importance of understanding, communicating, and applying best practices in the use of NIV**
- **The information from this study may inform design of future studies, identify areas warranting additional research in regards to optimizing NIV, and suggest that revisions to evidence-based guidelines on NIV use in ALS may be needed**

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