Avvio al supporto ventilatorio nei Pazienti con patologia neuromuscolare

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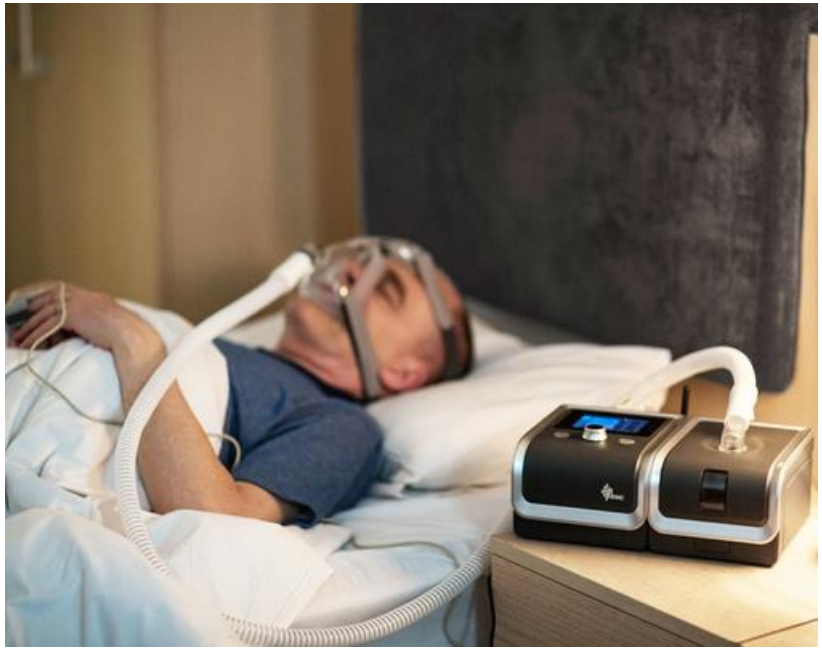
Farò riferimento soprattutto alla VENTILAZIONE NON INVASIVA



Ma in ambito non invasivo vanno considerate strumentazioni di supporto o non propriamente ventilatori quali:

- CPAP
- Strumenti per TOSSE ASSISTITA
- Aspiratori

Col progredire della patologia sarà necessario considerare anche la ventilazione INVASIVA

E’ comunque un trattamento di un certo impegno: il Paziente va correttamente e preventivamente informato e preparato.

Richiede una personalizzazione dello strumento.

Non-invasive ventilation in amyotrophic lateral sclerosis

Ther Adv Neurol Disord

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DOI: 10.1177/1756286419857040

Johannes Dorst and Albert C. Ludolph

Abstract: Non-invasive ventilation (NIV) has become an important cornerstone of symptomatic treatment in amyotrophic lateral sclerosis (ALS), improving survival and quality of life. In this review, we summarize the most important recent developments and insights, including evidence of efficacy, indication criteria and time of initiation, ventilation parameters and adaptation strategies, treatment of complicating factors, transition from NIV to invasive ventilation, termination of NIV and end-of-life management. Recent publications have questioned former conventions and guideline recommendations, especially with regard to timing and prognostic factors; therefore, a fresh look and re-evaluation of current evidence is needed.

Keywords: amyotrophic lateral sclerosis, motor neuron diseases, non-invasive ventilation

Pathophysiology of neuromuscular respiratory failure

	Inadequate ventilation	Hypoxemia	Ineffective cough	Risk for aspiration
Inspiratory muscle weakness*	X	X	X	
Expiratory muscle weakness¶			X	
Upper airway muscle weakness△			X	X

* Inspiratory muscles: diaphgragm, external intercostals, scalenes, sternocleidomastoids, trapezii.
¶ Expiratory muscles: abdominals (internal and external oblique, rectus abdominus, transverse abdominus), internal intercostals.
△ Upper airway muscles: abductors and adductors (pharyngeal, laryngeal).

Progressiva compromissione funzionale

Inefficienza neuromuscolare

Incapacità funzionale

Insufficienza d’organo (respiratoria)

Stratificazione di indagine

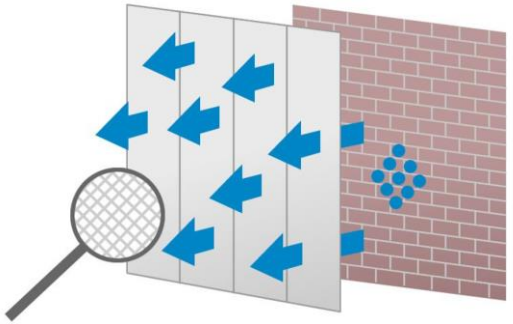
Indagini di **insufficienza d’organo** (tardive): EGA, SpO2

Indagini di **funzionalità**: PFR, MIP, MEP, SNIP, ossimetria

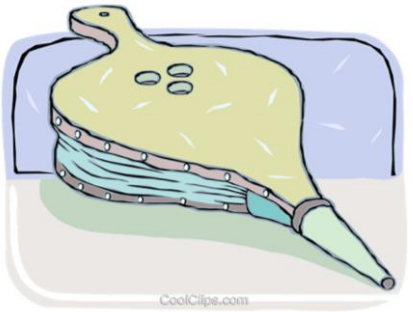
Indagini ancillari: PSG, capnografia

Insufficienza respiratoria

Ipossiemica: basso O2, c'è un problema di scambio gassoso



Ipercapnica: alta CO2, c'è un problema di ventilazione

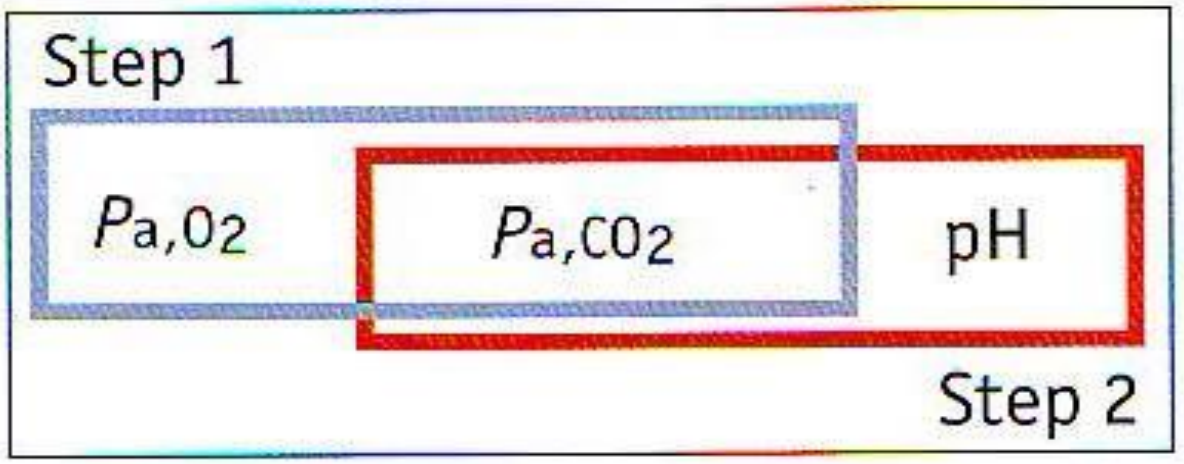


EGA (Emogasanalisi arteriosa)

Lettura in 2 fasi:

1 – Valutazione dello scambio gassoso (ossiemia)

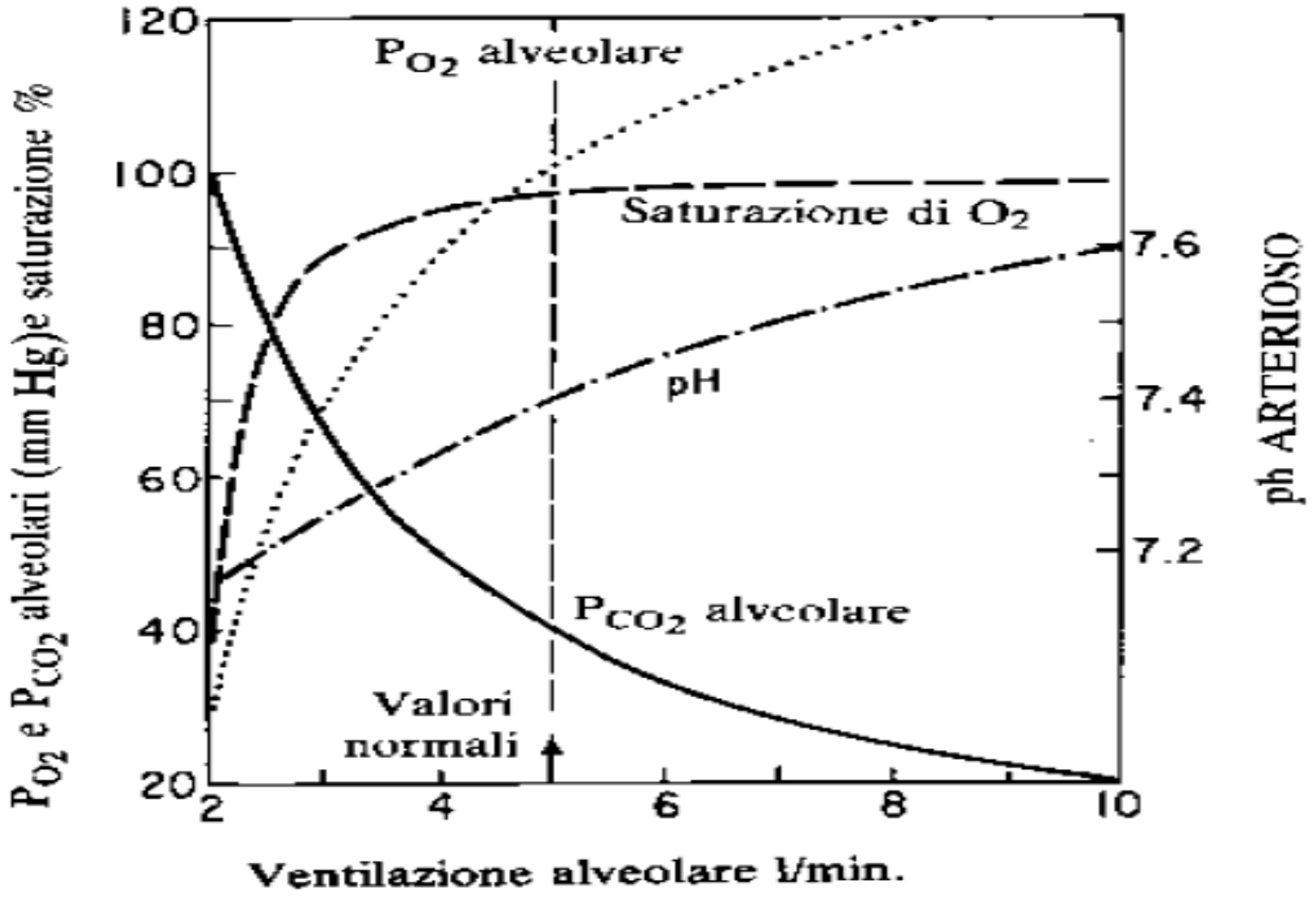
2 – Valutazione dei disturbi acido-base



Step 1 – Valutazione dello scambio gassoso

Step 2 – Valutazione dei disturbi acido-base

$$\underset{\text{Fase gassosa}}{CO_2} \rightleftarrows \underset{\substack{\text{Disciolta}\\ \text{nella fase}\\ \text{acquosa}}}{CO_2} + H_2O \xrightleftharpoons[\text{carbonica}]{\text{Anidrasi}} H_2CO_3 \rightleftarrows H^+ + HCO_3^-$$


120
100
80
60
40
20
P_{O_2} alveolare
Saturazione di O_2
pH
P_{CO_2} alveolare
Valori
normali
2
4
6
8
10
7.6
7.4
7.2
P_{O_2} e P_{CO_2} alveolari (mm Hg)e saturazione %
ph ARTERIOSO
Ventilazione alveolare l/min.

Cause di insufficienza respiratoria

Tabella II. Meccanismi dell'insufficienza respiratoria.

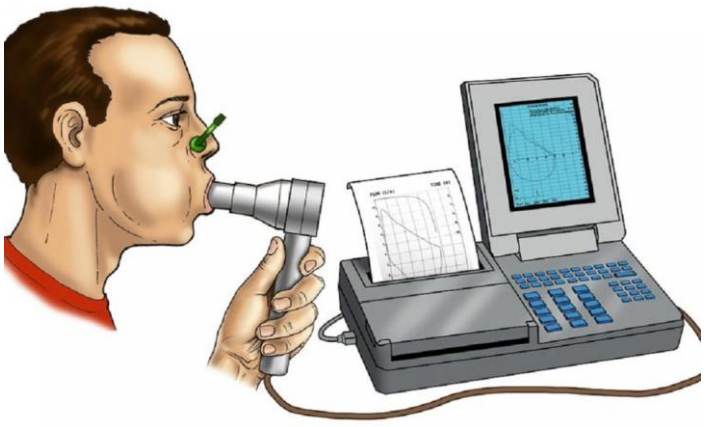
Cause di ipossiemia
Intrapolmonari
• Alterata distribuzione rapporto ventilazione/perfusione
• Shunt anatomico
• Difetto di diffusione alveolo-capillare
Extrapolmonari
• Concentrazione in O_2 dell'aria inspirata
• Ipoventilazione alveolare
• Riduzione della gittata cardiaca
• Riduzione della pressione parziale di O_2 nel sangue venoso misto
• Aumentato consumo di O_2 negli organi periferici
Cause di ipercapnia
Ipoventilazione alveolare
• Ridotto stimolo centrale
• Alterazioni della meccanica della parete toracica
• Debolezza o fatica dei muscoli respiratori
• Respirazione rapida e superficiale

Italian review of respiratory disease – AIPO: n°3 -2009; 116.

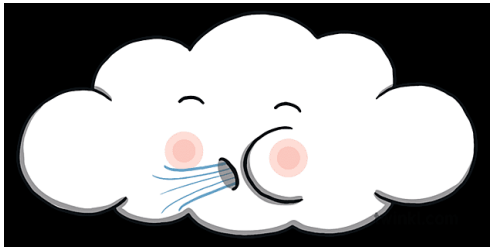
Emogasanalisi arteriosa valori di normalità

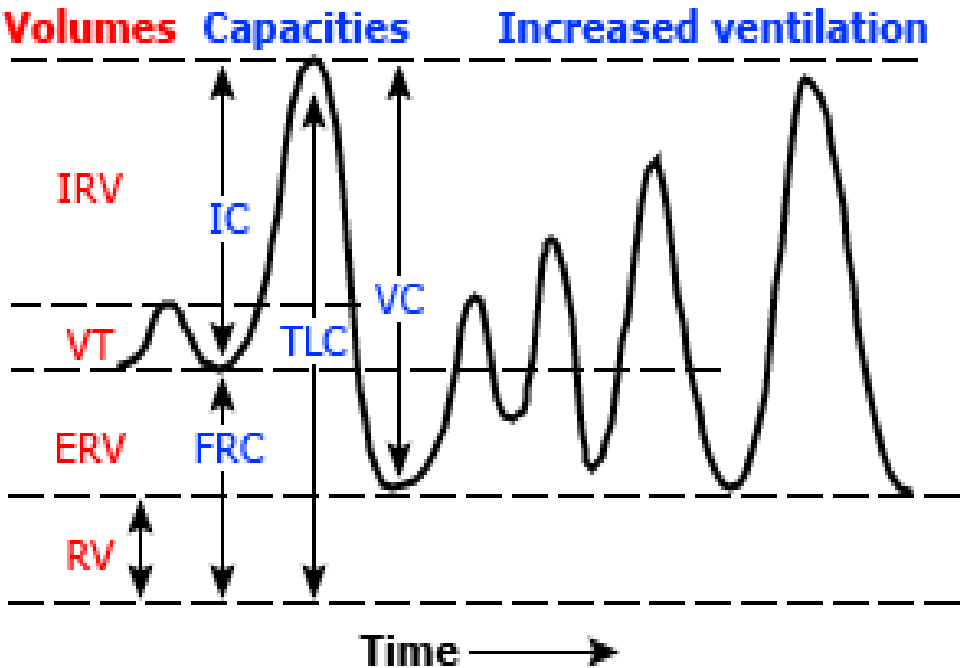
- **pH 7,40 (7,36-7,46)**
- **Pa02 80 - 100 mmHg**
- **PaC02 35 - 45 mmHg**
- **HC03- 22 - 26 mEq/L**
- **BE -1 / +1**

Spirometria e PFR



Pulmonary function tests: Lung volumes and capacities

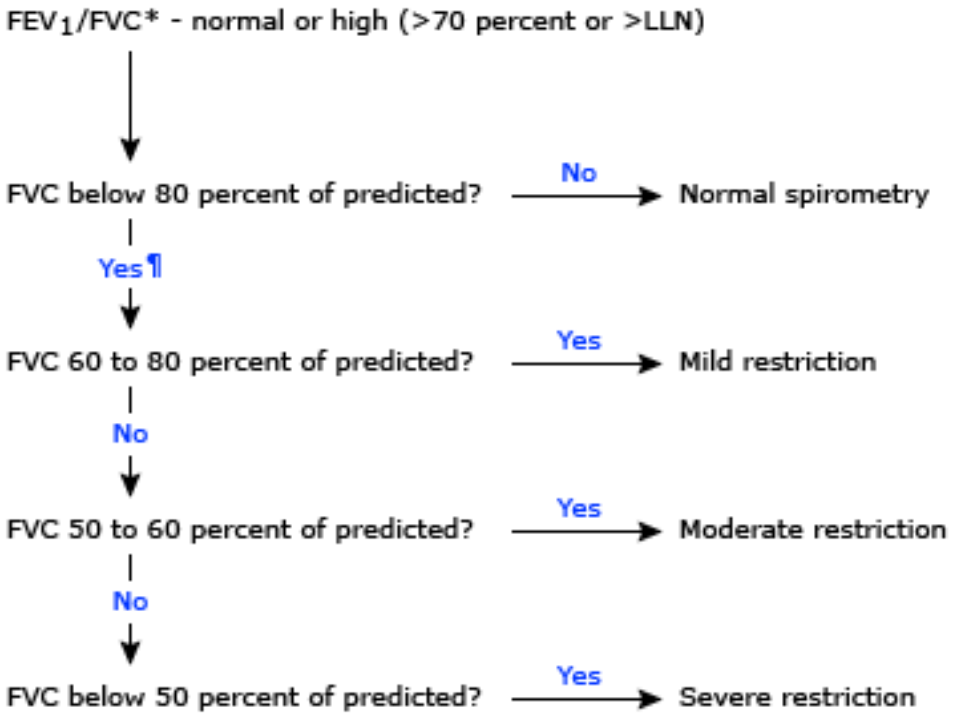




These are boundaries of lung volume within which tidal volume can vary. A lung capacity is a combination of more than one lung volume. TLC, for example, is the combination of FRC plus IC (or the combination of RV, ERV, VT, and IRV). TLC, RV, and their ratio provide the most information about restrictive lung disease and help differentiate between restrictive and obstructive disorders. However, TLC and RV are effort-dependent, so an evaluation of strength and/or effort is needed. In contrast, the FRC is effort-independent.

IRV: inspiratory reserve volume; VT: tidal volume; ERV: expiratory reserve volume; RV: residual volume; IC: inspiratory capacity; FRC: functional residual capacity; TLC: total lung capacity; VC: vital capacity.

Interpretation of office spirometry: Restrictive pattern



Spirometry interpretation flow chart for the detection of a restrictive ventilatory defect.

FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; LLN: lower limit of normal.

* The fifth percentile LLN, as calculated by most spirometers, should be used to detect airway obstruction, rather than the absolute value of the FEV_1/FVC ratio.

¶ Measurement of lung volumes is needed to confirm restriction (ie, total lung capacity below fifth percentile of predicted). A reduced FVC by itself does not prove restriction.

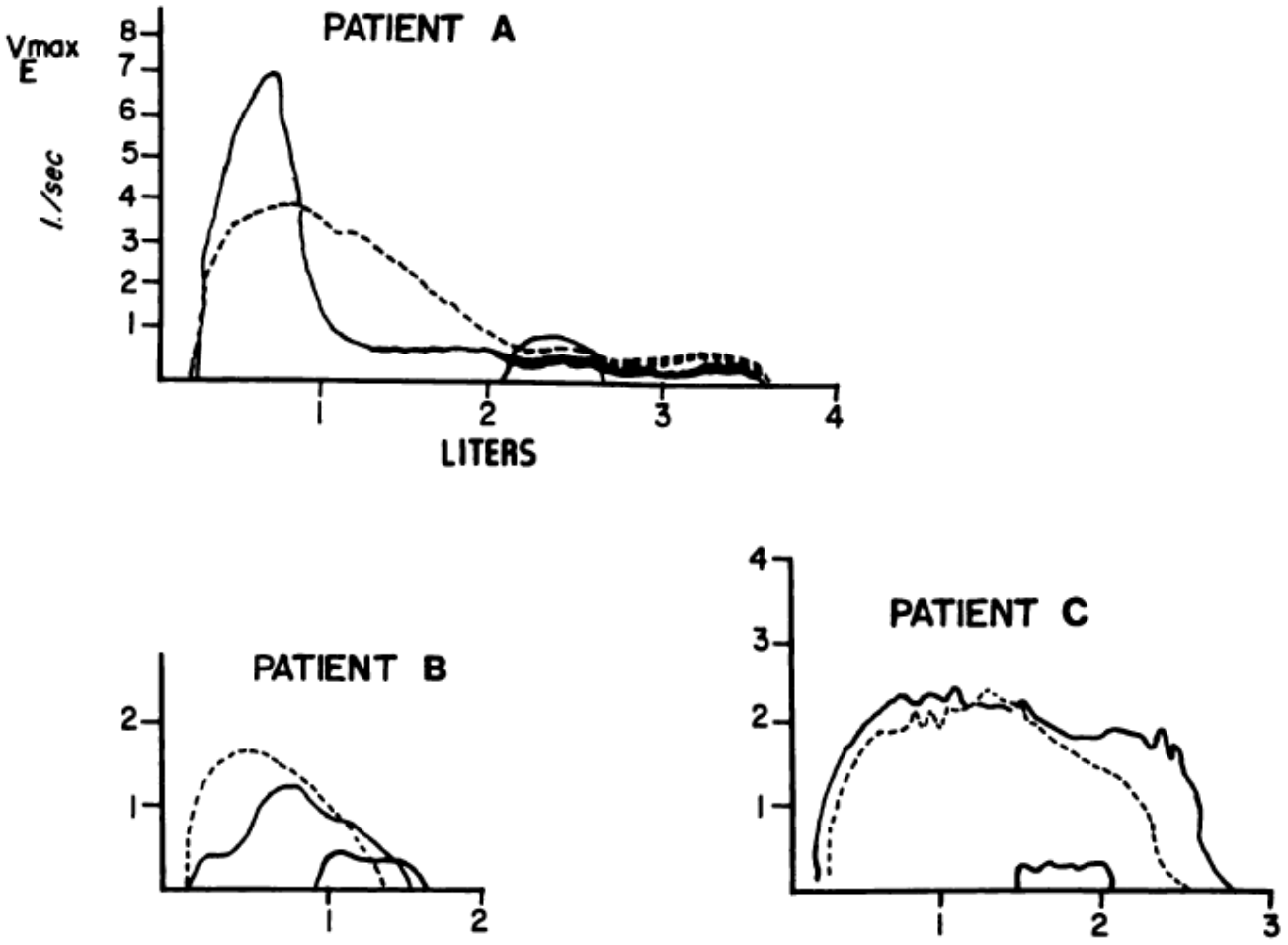


FIGURE 1. Expiratory flow curves with mouthpiece (*solid lines*) and with oral airway (*dotted lines*).

Three patterns of expiratory flow were present, as shown in Figure 1. In all curves, a rapid oscillation representing turbulence of flow was present, so the curves were smoothed for illustration. Two patients (patients A and B) had an improvement in expiratory flow by using an oral airway apparatus (Fig 1). Patient A had a nearly normal peak expiratory flow which abruptly decreased to a low flow rate slightly less than the peak tidal flow rate. Maximal expiratory flow improved after 25 percent and 50 percent of the vital capacity was exhaled but not after 75 percent of the vital capacity was expired with an oral airway. This patient had a predominant bulbar discoordination, which was made worse by effort.

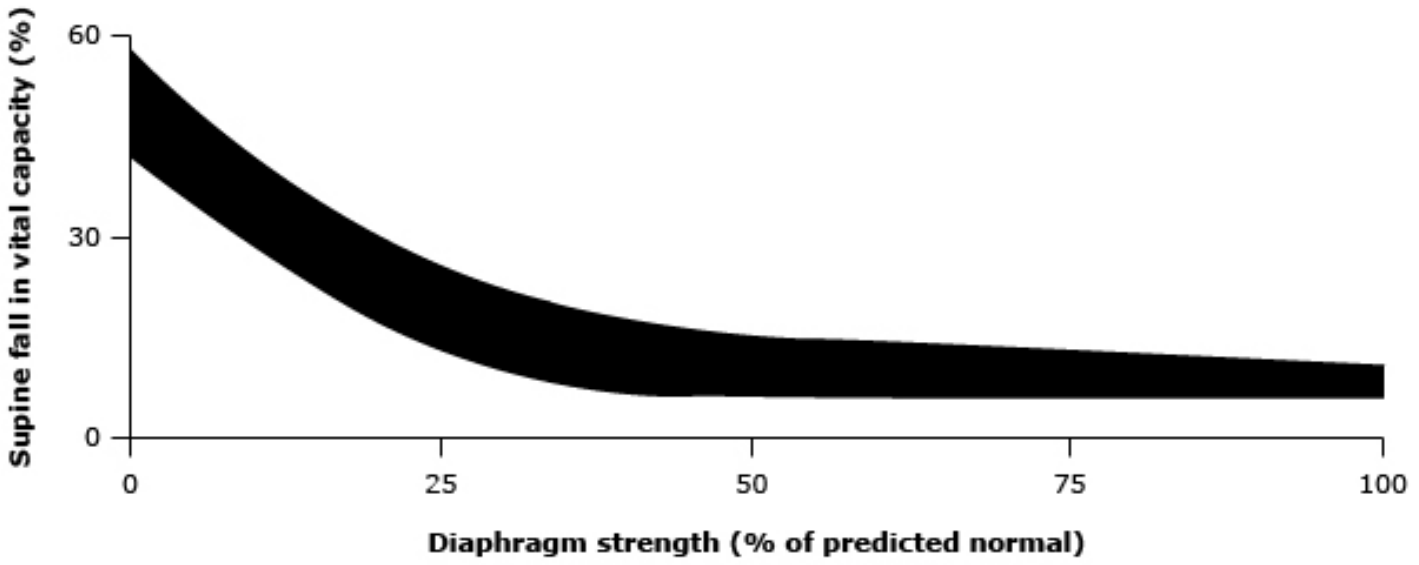
A similar pattern (but less dramatic) was seen in patient B (Fig 1). Maximal expiratory flow was reduced and expiration ceased near the end-expiratory tidal point. The flow with an oral airway minimally improved the maximal expiratory flow rate in early expiration, although the FVC was reduced. Patient B had combined bulbar and spinal muscular paresis. The low maximal flow rate and the loss in expiratory reserve volume are similar to the severe respiratory muscular weakness seen with injury to the cervical cord and poliomyelitis,[1] in that expiratory flow is greatly dependent on recoil forces when a severe expiratory muscular weakness exists.

The remaining patients exhibited a pattern similar to patient C (Fig 1), *ie*, a low maximal expiratory flow curve with a "humped" configuration which was not improved by the oral airway. All had predominantly respiratory muscular weakness and no bulbar symptoms.[2]

Patients with amyotrophic lateral sclerosis usually die in respiratory failure, with both the bulbar and the respiratory muscular disorders contributing.[3] The bulbar discoordination leads to repetitive aspiration and obstruction of the upper airway, and the spinal disease results in poor control of the diaphragm and intercostal and accessory muscles of respiration. Patients with flow limits secondary to bulbar disease (pattern A) may benefit by the timely use of a tracheostomy; however, patients with spinal disease (pattern C) would not be expected to be helped.

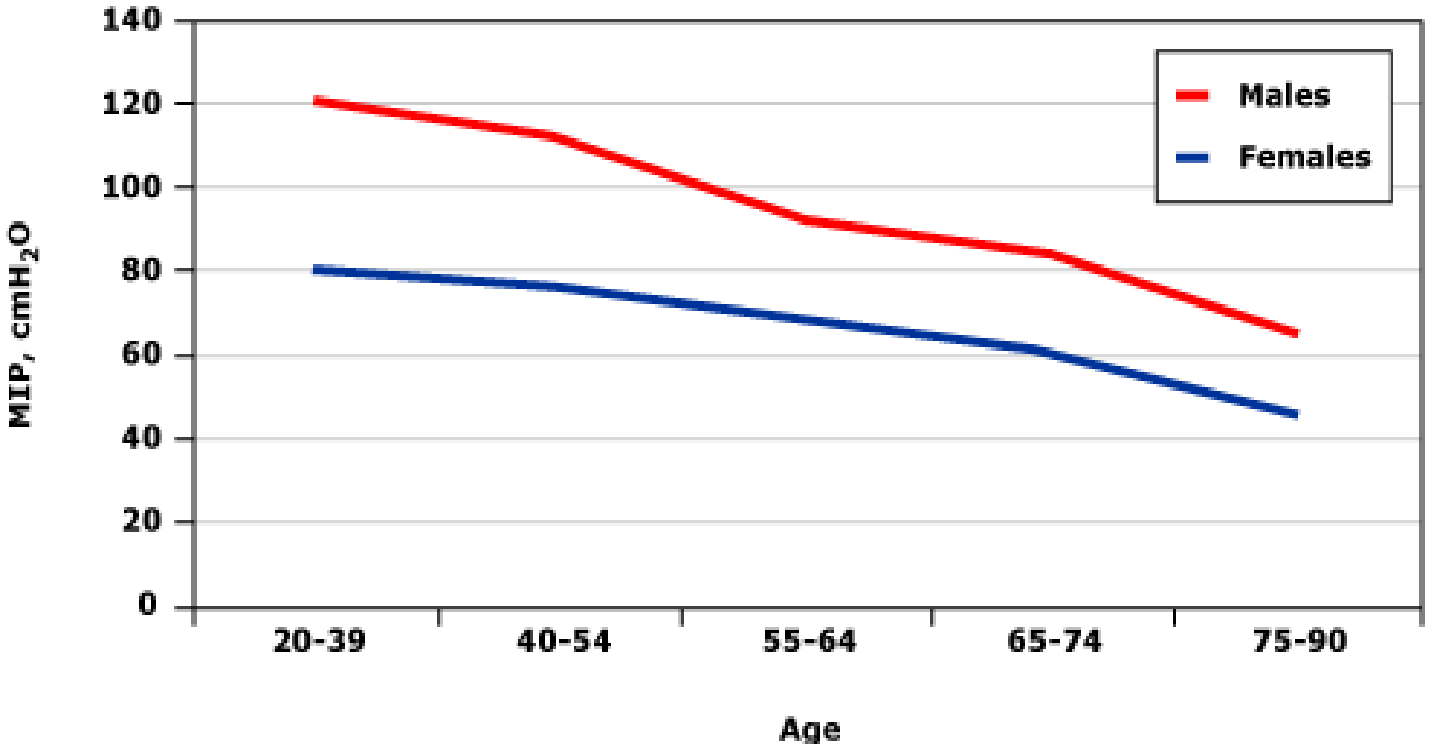
In patients with mixed bulbar and spinal involvement (pattern B), who have a large decrease in vital capacity and show little improvement in expiratory flow rates with an oral airway because of the severe muscular weakness, the efficiency of a tracheostomy to improve flow is questionable. In any case of amyotrophic lateral sclerosis where it is difficult to decide whether to perform a tracheostomy, flow-volume curves with an oral airway may be helpful in making the decision.

Relationship between diaphragm strength and supine position



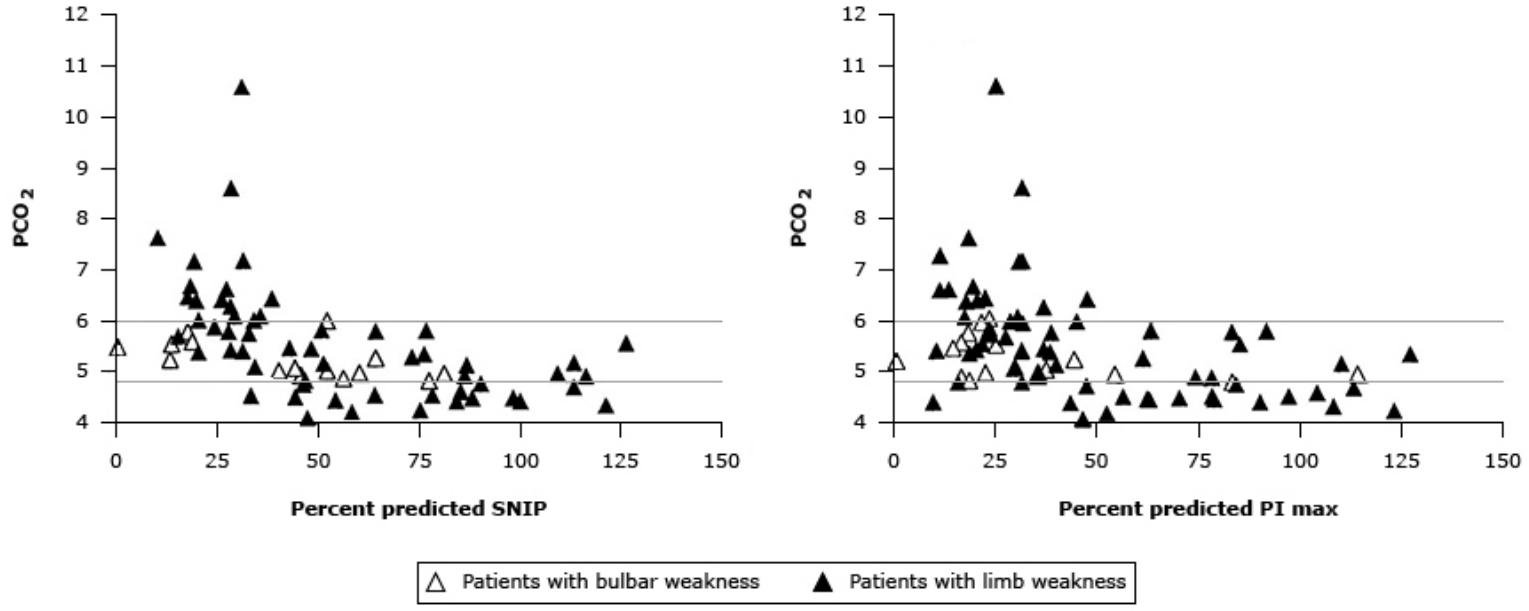
Relationship between percentage fall in vital capacity on adopting the supine posture and diaphragm strength (assessed by measuring transdiaphragmatic pressure during maximum sniffs). Fall in vital capacity is seldom substantial until strength is reduced to 30% of normal.

Normale declino di MIP con l'età

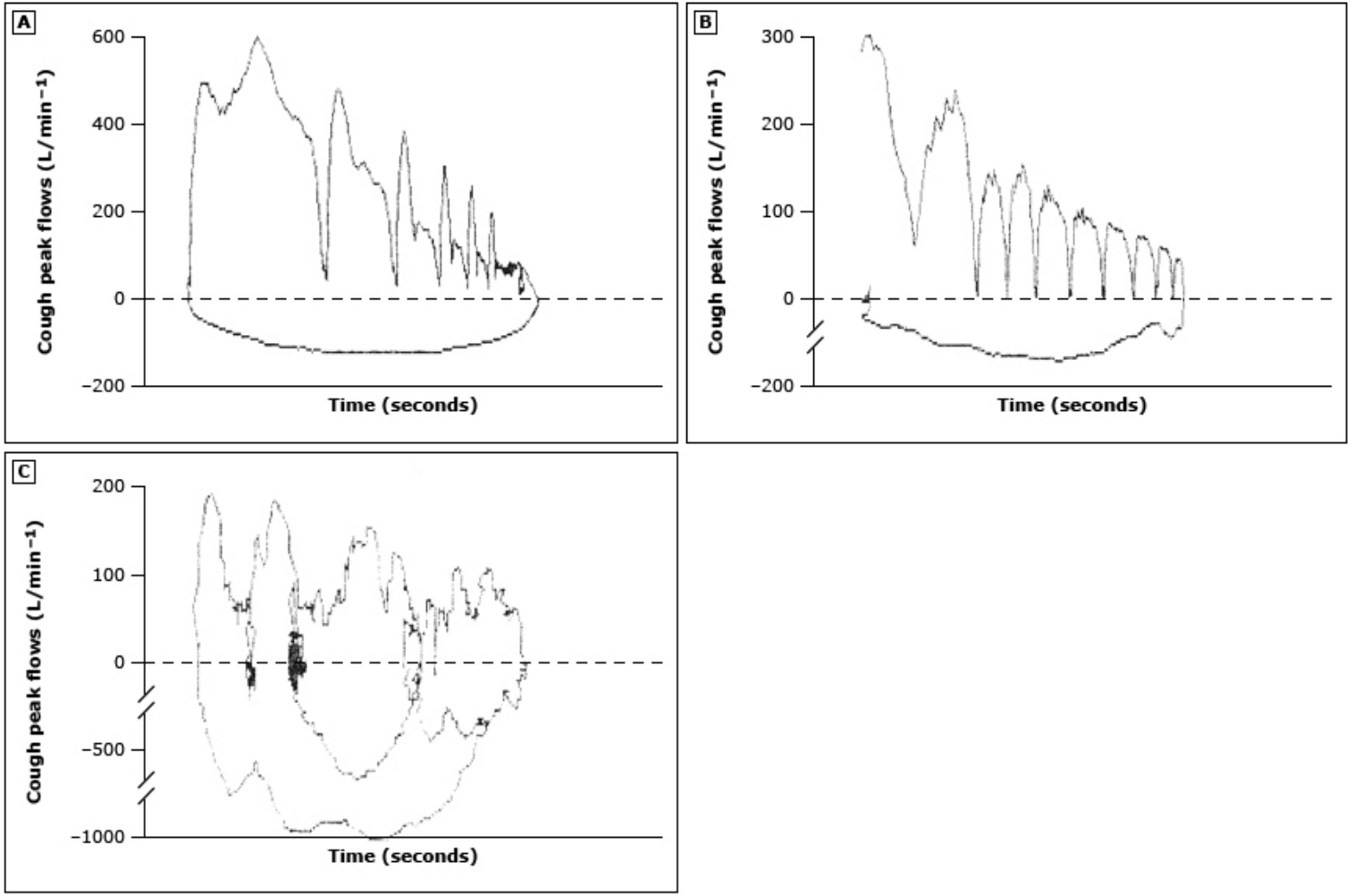


Data from: Harik-Khan, RI, Wise, RA, Fozard, JL. Determinants of maximal inspiratory pressure: the Baltimore Longitudinal Study of Aging. Am J Respir Crit Care Med 1998; 158:1459.

Relationship between maximal sniff nasal inspiratory or maximal inspiratory pressure and arterial pressure of carbon dioxide

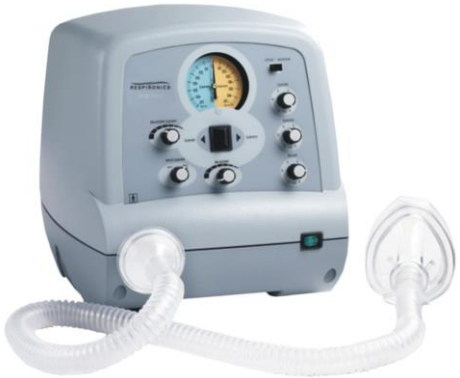


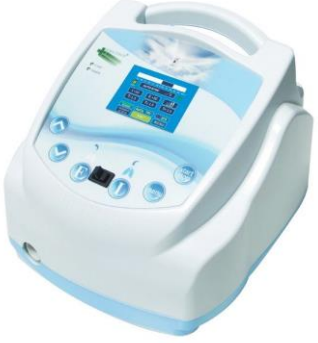
Relationship between sniff nasal inspiratory pressure (SNIP) and maximal inspiratory pressure (PI max; percent predicted) and ear lobe partial pressure of carbon dioxide (PCO_2 in kilopascals [kPa]) in amyotrophic lateral sclerosis patients. Open symbols represent patients with bulbar weakness and closed symbols represent patients with limb weakness. The lines represent the lower and upper limits of normal for ear lobe PCO_2 (4.8 to 6 kPa).



(A) A series of cough spikes superimposed on the maximal expiratory flow volume curve. (B) An example of a patient who was unable to produce cough spikes. (C) A grossly distorted cough flow/volume curve in a bulbar patient.
This test is performed in a pulmonary function laboratory. The patient starts at total lung capacity by taking a large and deep breath and is then asked to cough sequentially without taking additional inspirations. The measured curve is superimposed on an expiratory limb of the flow volume loop (not shown in this figure).

ERS 2020: European Respiratory Journal 2002 19: 434-438;





RESEARCH PAPER

Prevalence of sleep apnoea and capnographic detection of nocturnal hypoventilation in amyotrophic lateral sclerosis

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ABSTRACT

Objective This retrospective study aimed to investigate whether overnight oxymetry and early morning blood gas analysis predict nocturnal hypoventilation (NH) as reflected by night-time hypercapnia in patients with amyotrophic lateral sclerosis (ALS). In addition, prevalence and clinical determinants of sleep apnoea in ALS were evaluated.

Methods In 250 patients with non-ventilated ALS, transcutaneous capnometry was performed along with polysomnography or polygraphy and early morning blood gases.

Results 123 patients were female, and 84 patients had bulbar-onset ALS. 40.0% showed NH, and an apnoea–hypopnoea index (AHI) >5/hour was found in 45.6%. In 22.3%, sleep apnoea and NH coincided. The obstructive apnoea index was significantly higher than the central apnoea index (p<0.0001). Both NH and sleep apnoea were significantly more common in male than in female patients. Sleep apnoea and AHI were associated with better bulbar function . Desaturation time ($t_{<90\%}$) and transcutaneous CO_2 were negatively correlated with

hypoventilation (NH), obstructive sleep apnoea (OSA) and central sleep apnoea (CSA), whereas daytime hypoventilation is defined as partial arterial carbon dioxide pressure (p_aCO_2) >45 mm Hg (>6.0 kPa) or arterial base excess >4 mmol/L[13 14] definition of NH is based on oxymetric and capnometric measures but criteria are heterogenous.[15] These include a p_aCO_2 >55 mm Hg (7.3 kPa) for ≥10 min or an overnight increase of the p_aCO_2 by ≥10 mm Hg (1.3 kPa) from the awake supine value to ≥50 mm Hg (6.7 kPa) for ≥10 min.[16] Alternative definitions comprise peak p_aCO_2 >47 mm Hg (6.3 kPa),[17] >49 mm Hg (6.5 kPa) or >55 mm Hg (7.3 kPa),[13 18 19] mean p_aCO_2 >50 mm Hg (6.7 kPa)[20] or p_aCO_2 of 50–54 mm Hg (6.7–7.2 kPa) with prolonged hypoxaemia.[13] In addition, mean peripheral oxygen saturation (S_pO_2) <90%,[19 21] S_pO_2 <88% for five consecutive minutes[13] and S_pO_2 <90% for ≥10% of recording time have been proposed.[21]

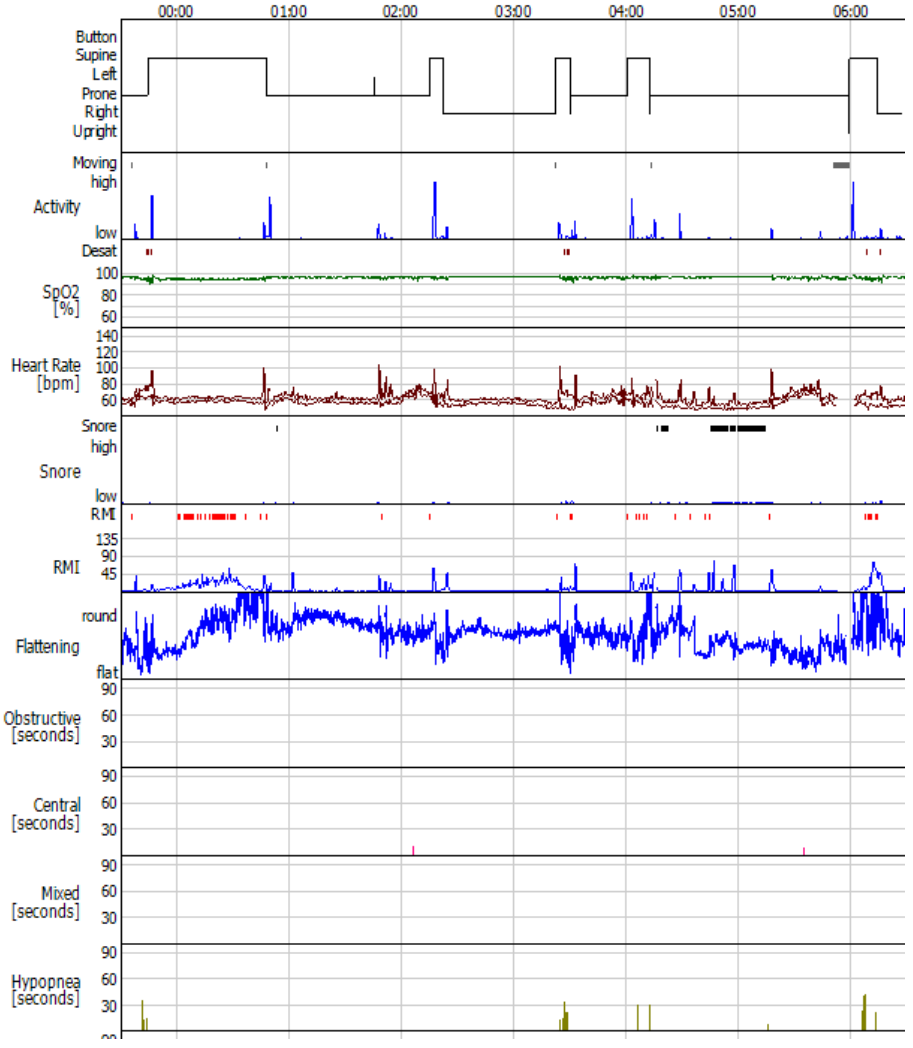
Modern transcutaneous capnometry has been shown to reliably substitute for p_aCO_2,[22] and a

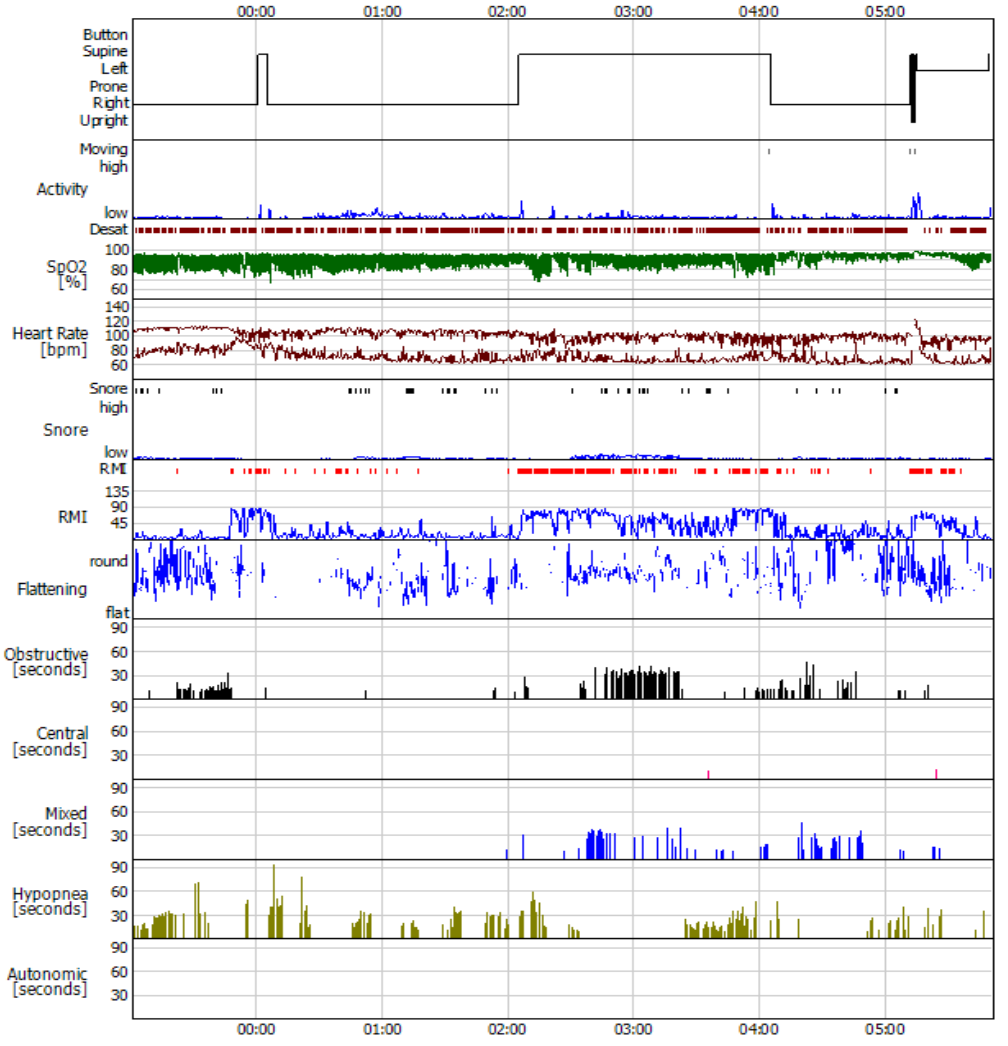
Table 4 Sleep-disordered breathing according to gender and severity of bulbar dysfunction, respectively

	No or mild bulbar dysfunction, female	No or mild bulbar dysfunction, male	Severe bulbar dysfunction, female	Severe bulbar dysfunction, male	p
n	63	94	60	33	–
AHI (/h)	2.4 (7.1)	6.0 (12.1)	3.3 (8.3)	4.4 (8.6)	<0.01*
Maximum $tcCO_2$ (mm Hg)	43.6 (5.4)	47.4 (8.9)	44.4 (6.2)	48.5 (8.0)	<0.01*
AHI >5/h (n/%)	23/36.5	55/58.5	23/38.3	13/39.4	<0.01†
Nocturnal hypercapnia (n/%)	27/42.9	34/36.2	21/35.0	18/54.5	n. s.†

Numbers are depicted as median and IQR.
AHI, apnoea–hypopnoea index; $tcCO_2$, transcutaneous carbon dioxide tension.
*Kruskal-Wallis test.
†χ^2.

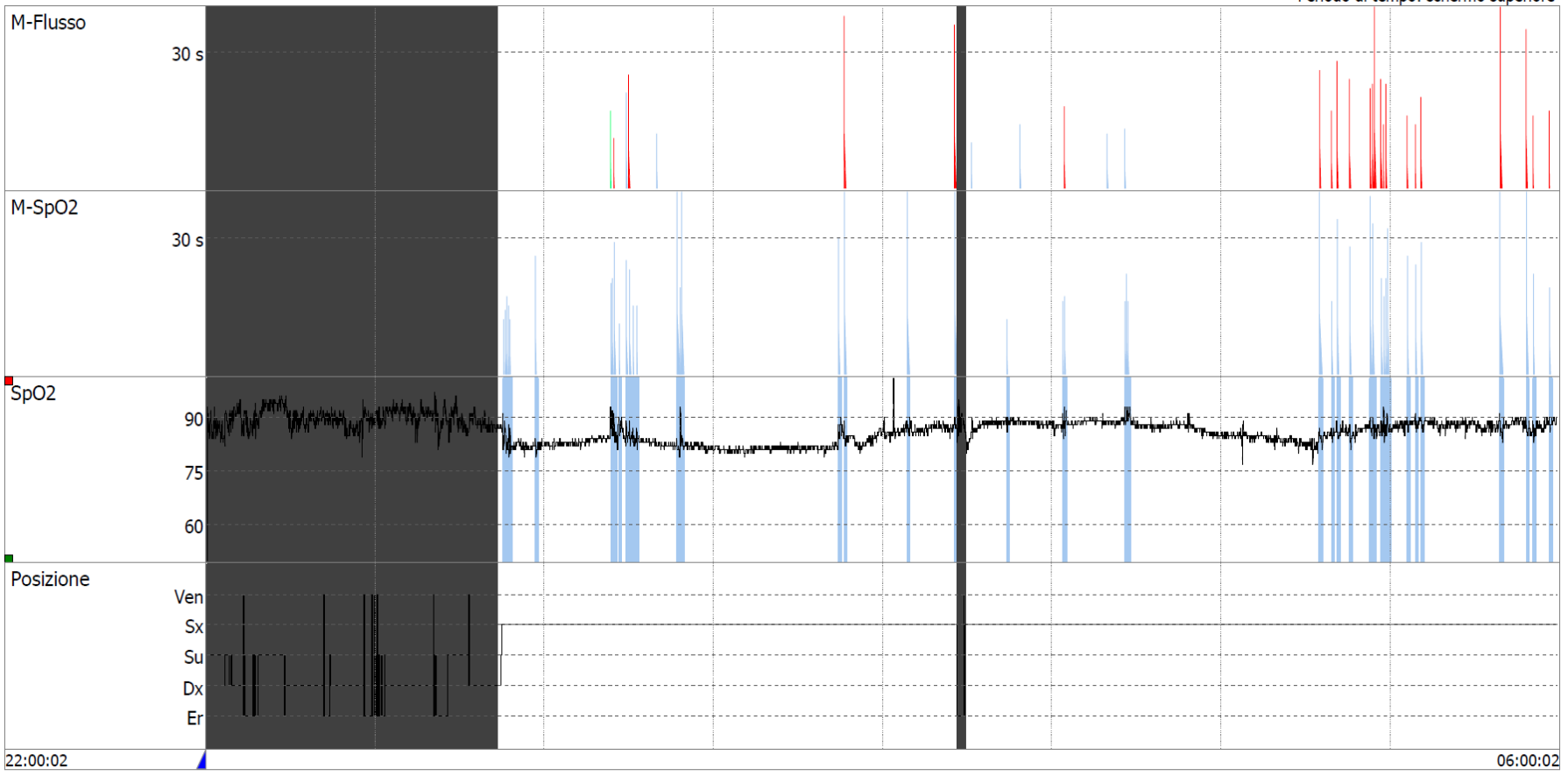
Summary Graph



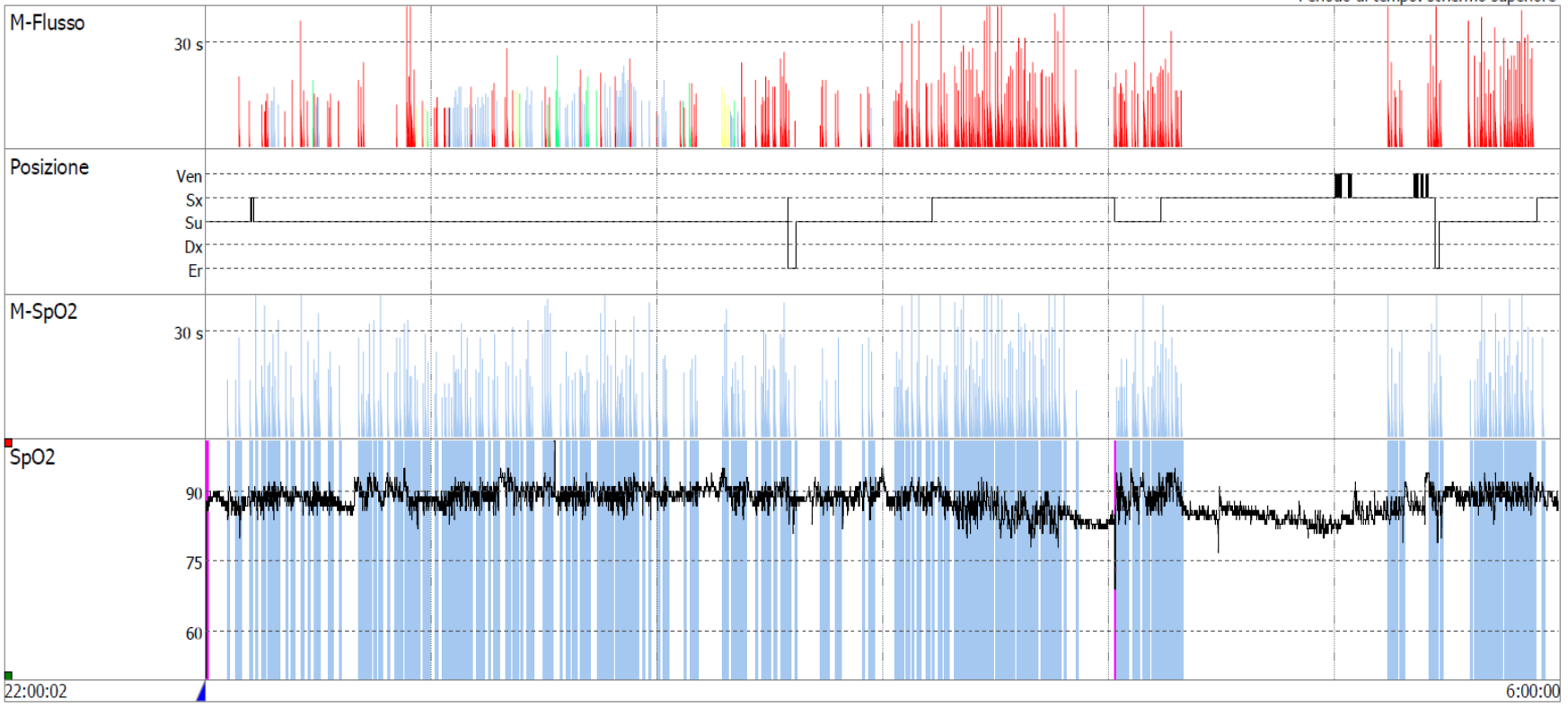


Data di nascita: Fine registrazione: 17.06.2015 - 06:00:02 Valutato con Version 5.12a

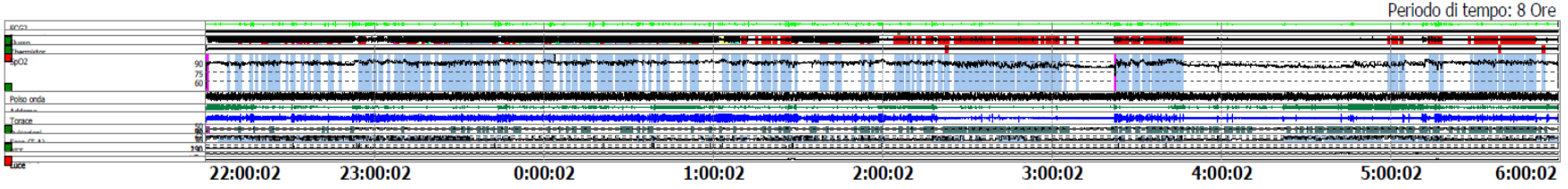
Periodo di tempo: schermo superiore



Periodo di tempo: schermo superiore



Periodo di tempo: 8 Ore



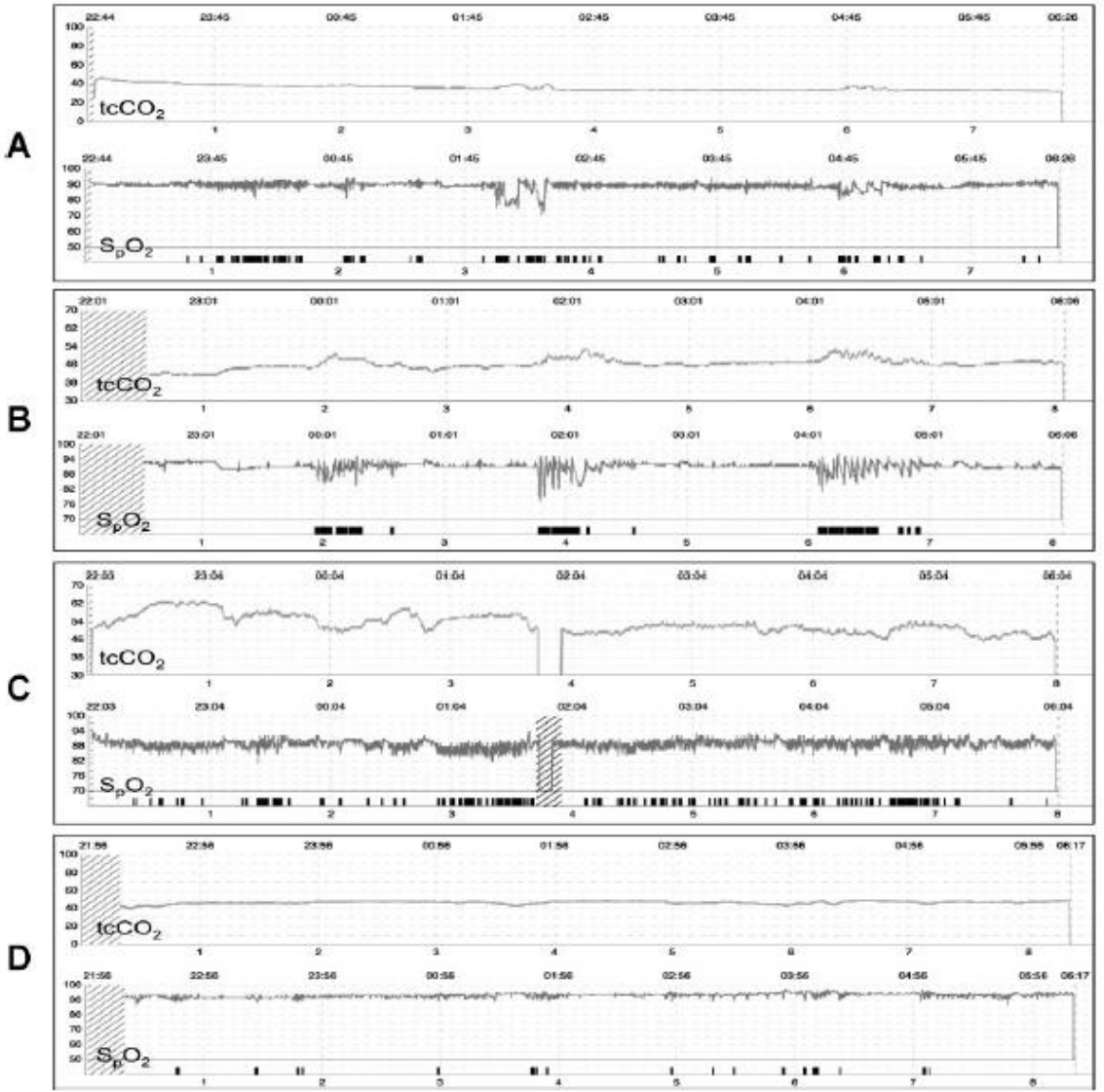


Figure 1 Patterns of sleep-disordered breathing in patients with ALS. Each of the parts (A-D) depicts the $tcCO_2$ curve (upper graph) and the S_pO_2 curve (lower graph), respectively. (A) Intermittent desaturation without hypercapnia in pure obstructive sleep apnoea; (B) REM sleep-associated desaturation and hypercapnia; (C) hypoxaemia and hypercapnia independent of sleep stages; and (D) isolated hypercapnia without significant desaturation or hypoxaemia. S_pO_2, peripheral oxygen saturation; $tcCO_2$, transcutaneous carbon dioxide tension.

Physiologic evidence of respiratory muscle weakness (one or more of the parameters below)
Forced vital capacity <50% predicted
Maximum inspiratory pressure below −60 cm H_2O (ie, less negative than −60 cm H_2O; eg, −50 cm H_2O)
Maximum expiratory pressure <40 cm H_2O
Vital capacity <15 to 20 mL/kg, <60% predicted, <1 liter, or decrease >30 to 50% compared with baseline
Mechanical insufflation-exsufflation flow >150 L per minute
Sniff-nasal inspiratory force <40 cm H_2O
Chronic hypoventilation ¶
Daytime $PaCO_2$ ≥45 mmHg **OR**
Nocturnal hypoventilation with sustained O_2 desaturation (eg, O_2 saturation ≤88 mmHg for >5 consecutive minutes) **AND** symptoms (eg, morning headache, hypersomnolence, etc)
Appropriate diagnosis^
Neuromuscular disease (eg, amyotrophic lateral sclerosis, muscular dystrophy, spinal cord injury)
Chest wall deformity (eg, kyphoscoliosis)
Reversible contributing factors treated (eg, heart failure)
Adequate upper airway function (eg, no bulbar dysfunction)
Patient is awake, alert, appropriate cognition, and does not have uncontrollable seizures

Indicazioni generalmente riconosciute per l'avvio a ventilazione non invasiva/notturna

* There are no data-driven standards for deciding when to initiate noninvasive ventilation, but these are commonly employed and can be used as a general guideline.
¶ In patients with progressive neuromuscular disorders, clinicians should not wait for frank hypoventilation to occur and in most instances noninvasive ventilation should be started when respiratory muscle weakness is evident (refer to the physiologic parameters in this table).

Controindicazioni alla ventilazione non invasiva

Absolute
The need for emergent intubation (eg, cardiac or respiratory arrest, severe respiratory distress, unstable cardiac arrhythmia)
Relative
Nonrespiratory organ failure that is acutely life-threatening
Severe encephalopathy (eg, GCS <10)
Severe upper gastrointestinal bleeding
Hemodynamic instability
Facial or neurological surgery, trauma, or deformity
Significant airway obstruction (eg, laryngeal mass or tracheal tumor)
Inability to cooperate, protect airway, or clear secretions (eg, patients at high risk or aspiration)
Anticipated prolonged duration of mechanical ventilation (eg, ≥4 to 7 days)
Recent esophageal or gastric anastomosis
Multiple contraindications
Insufficient staffing support

Esophageal or gastric distension from air may increase the risk of anastomotic dehiscence.

GCS: Glasgow Coma Score

Adapted with permission from: International Consensus Conferences in Intensive Care Medicine: Noninvasive positive pressure ventilation in acute respiratory failure. Am J Respir Crit Care Med 2001; 163:283.

Table 1. Type and demographics of analyzed primary studies.

Study	Study type	Study size and demographics	Inclusion/exclusion criteria
Bach et al. (1993)	Retrospective	5 unweanable ALS patients with acute or chronic ventilatory insufficiency Diagnosis criteria unknown	Included if: History of acute/chronic ventilator insufficiency History of use of ventilation during ventilator weaning
Pinto et al. (1995)	Prospective controlled trial	18 bulbar ALS patients per El Escorial criteria 11 male, 9 female, ages 51–69	
Cazzolli and Oppenheimer (1996)	Prospective study	75 patients (criteria unknown)	
Aboussouan et al. (1997)	Observational cohort study	39 patients defined by El Escorial criteria 28 males, 11 females	Included if: New orthopnea and/or hypercapnia ($PCO_2 \geq 45$ mmHg)
Kleopa et al. (1999)	Retrospective chart review	122 patients defined by El Escorial criteria 52 males, 70 females, age 62.2 ± 11.8	Excluded if: History of OSA or severe pulmonary diseases History of long term invasive ventilation history
Lyall et al. (2001)	Prospective cohort study	27 patients (criteria unknown)	Included if: Symptoms of sleep-disordered breathing Presence of respiratory muscle weakness and hypoventilation
Jackson et al. (2001)	Prospective randomized single blind study	13 patients by WFN criteria	Included if: ALS presentation < 3 years FVC 70–100% of predicted Excluded if: History of significant OSA History of bullous lung disease History of untreated congested heart disease History of severe pulmonary disease History of NIPPV or IMV use
Newsom-Davis et al. (2001)	Controlled study	19 patients defined by El Escorial criteria	
Butz et al. (2003)	Prospective cohort study	36 patients defined by El Escorial criteria	
Bourke et al. (2003)	Prospective study	22 patients defined by El Escorial criteria Ultimately 10 patients	
Farrero et al. (2004)	Retrospective study	86 patients defined by El Escorial criteria 54 with bulbar involvement	Included if: Bulbar impairment confirmed by deglution or phonation alterations
Bourke et al. (2006)	Randomized controlled trial	41 patients	Excluded if: Current or past NIV use Life-threatening comorbidity Age > 75 years Cannot complete QoL assessment Cannot communicate
Carratù et al. (2009)	Retrospective study	72 patients (criteria unknown)	Excluded if: History of other neurological disease History of lung disease unrelated to ALS
Katzberg et al. (2013)	Pilot, self-controlled study	12 patients defined by El Escorial criteria No bulbar onset ALS patients	Excluded if: Patient on mechanical or artificial respiration History of underlying sleep or respiratory disorders present prior to ALS Current pregnancy or breastfeeding Significant decision-making incapacity
Sancho et al. (2014)	Retrospective observational study	144 patients (unknown criteria)	Excluded if: Presence of previous pulmonary or airway disease Another rapidly progressive disease with survival expectancy < 1 month Severe frontotemporal dementia Refusal of NIV or NIV tolerance < 4 consecutive hours per night
Georges et al. (2014)	Exploratory "proof of concept" study	16 patients defined by El Escorial criteria 5 with initially bulbar ALS	Included if: On NIV for at least 24 h and up to 3 months Signs of diaphragmatic dysfunction Excluded if: Started NIV on emergency context Presence of non-ALS disease likely to alter nutritional and metabolic status
Sanjuán-López et al. (2014)	Retrospective analysis	114 patients defined by El Escorial criteria 64 bulbar onset	Excluded if: History of neuromuscular processes other than ALS Cases only seen in outpatient setting Treated in palliative care centers not associated with study hospital
Terzano and Romani (2015)	Prospective study	36 patients defined by El Escorial criteria	Excluded if: History of previous cerebrovascular events, arterial disease, ischemic heart disease, COPD, or cancer History of acute respiratory failure requiring mechanical ventilation Tracheotomy Inability to perform respiratory measurements
Vrijsen et al. (2015)	Prospective observational study	24 patients defined by El Escorial criteria 10 bulbar impairment	
Martínez et al. (2015)	Prospective study	87 patients defined by El Escorial criteria	Excluded if: History of chronic pulmonary or airway disease History of substance abuse Presence of another rapidly progressive disease with survival expectancy < 1 month Severe frontotemporal dementia
Jacobs et al. (2016)	Single center, prospective, double-blind, randomized, placebo-controlled pilot trial	54 patients defined by El Escorial criteria	Excluded if: FVC < 50% predicted Current involvement in clinical treatment trial Previous or current use of positive pressure ventilation, oxygen therapy History of pneumothorax History of bullous emphysema
Magalhães et al. (2016)	Cross-sectional study	9 patients defined by El Escorial criteria	Excluded if: History of smoking Scoliosis or chest abnormalities Clinical signs of bulbar muscular dysfunction History of tracheostomy
Bédard et al. (2016)	Retrospective study	31 patients defined by El Escorial criteria	
Bertella et al. (2017)	Prospective randomized multicenter study	50 patients defined by El Escorial criteria	Excluded if: Cognitive impairment MIP < 70% predicted Subjective respiratory discomfort Sitting FVC < 70% predicted Rapid loss of MIP and/or FVC > 20% predicted $PaCO_2$ > 45mmHg
Burkhardt et al. (2017)	Retrospective autopsy study	74 deceased patients defined by El Escorial criteria	Excluded if: Assisted suicide causing drug-induced hypoxia
Sancho et al. (2018)	Prospective study	140 patients defined by El Escorial criteria	Excluded if: Presence of bronchial disease Presence of concomitant progressive disease with life expectancy < 1 year NIV use < 4 consecutive hours at night ALS with slow progression (>3 years) Presence of severe frontotemporal dementia associated with ALS

ALS: amyotrophic lateral sclerosis; PCO_2: partial pressure of carbon dioxide; OSA: obstructive sleep apnea; ALSFRS: amyotrophic lateral sclerosis functional rating scale; WFN: World Federation of Neurology; FVC: forced vital capacity; NIPPV: noninvasive positive pressure ventilation; IMV: invasive mechanical ventilation; NIV: noninvasive ventilation; QoL: quality of life; MIP: maximum inspiratory pressure; $PaCO_2$: arterial CO_2 pressure.

Table 1. Guideline recommendations and recent developments.

EFNS	AAN	NICE	Recent developments (level of evidence)
Initiation of NIV			
Clinical signs or FVC < 80% or SNIP < 40 cm H_2O or MIP max < 60 mm H_2O or nocturnal desaturation or pCO_2 > 45 mmHg	Orthopnea or FVC < 50% or SNIP < 40 cm H_2O or MIP < −60 cm or nocturnal desaturation	FVC < 50% or FVC < 80% + orthopnea or SNIP/MIP < 40 cm H_2O or SNIP/MIP < 65 cm H_2O (men), <40 cm H_2O (women) + orthopnea or SNIP/MIP −10 cm H_2O over 3 months	Consider NIV in patients with FVC > 80% and in asymptomatic patients (Ib) Use of capnometry/polygraphy to detect early sleep disturbance (III): (1) nocturnal hypercapnia (2) nocturnal desaturation (3) sleep apnea
NIV in patients with severe bulbar involvement and frontotemporal symptoms			
Patients with bulbar palsy are less compliant with NIV, due in part to increased secretions NIV improves quality of life and prolongs survival in patients presenting with respiratory insufficiency, although this has not been confirmed in patients with bulbar-onset disease.	Bulbar involvement and executive dysfunction: possibly lower compliance with NIV Noncompliance was seen in 75% of patients with ALS and frontotemporal dysfunction No survival benefit was seen in patients with poor bulbar function	Before a decision is made on the use of NIV for a person with a diagnosis of FTD, the multidisciplinary team, together with the respiratory ventilation service, should carry out an assessment that includes the person's capacity to make decisions and to give consent, the severity of dementia and cognitive problems, whether the person is likely to accept treatment, whether the person is likely to achieve improvements in sleep-related symptoms or behavioral improvements, a discussion with the person's family or carers (with the person's consent if they have the capacity to give it)	Bulbar involvement possibly lowers compliance, but consequent symptomatic treatment of secretions can improve NIV acceptance (IV) Several retrospective studies with large numbers of subjects showed a survival benefit for bulbar patients (although less pronounced than in patients without bulbar involvement) (III) Neurobehavioral deficits in patients who do not fulfill the criteria for FTD do not significantly influence the patients' decisions regarding life-prolonging measures (III)
Management of hypersalivation			
Amitriptyline 10 mg 3 times a day Atropine drops 0.5–1% 3–4 ×/d Glycopyrrolate Transdermal scopolamine 1.5 mg every third day Botulinum toxin A/B injected into salivary glands Irradiation of salivary glands	–	Advice on swallowing, diet, posture, positioning, oral care and suctioning Antimuscarinic medicine Glycopyrrolate Botulinum toxin A (second line)	–
Management of tenacious bronchial secretions			
N-acetylcysteine 200–400 mg/d* Beta-receptor antagonists + nebulizer (saline, anticholinergic bronchodilators, mucolytic, furosemide)* Manual-assisted cough MI-E Portable home suction device Room humidifier	MI-E possibly effective HFCWO unproven	Humidification, nebulizers, carbocisteine* Manual-assisted cough Breath stacking Volume recruitment bag MI-E device	Growing evidence for MI-E, but still no high-class evidence studies (IV) HFCWO probably ineffective (IV)

(Continued

Table 1. (Continued)

EFNS	AAN	NICE	Recent developments (level of evidence)
PEG and respiratory function/NIV			
To minimize risks, PEG should be performed before vital capacity falls below 50% of predicted NIV during PEG procedure may be feasible in patients with respiratory impairment	FVC > 50%: low risk FVC 30–50%: moderate risk FVC < 30%: high risk The risk of PEG placement increased when the FVC declined below 50% of predicted	–	PEG insertion under NIV is safe, even in patients with FVC < 50% (III) Establish NIV prior to PEG, use NIV during PEG placement, use minimal sedation (IV)
Diaphragm pacing			
The use of diaphragmatic pacing or respiratory exercises in ALS is not established	–	–	Diaphragm pacing is contraindicated in ALS (Ib)
Indication criteria of IV/transition from NIV to IV			
Severe bulbar weakness or NIV intolerance or declines NIV: propose invasive mechanical ventilation IV has a major impact upon caregivers and should be initiated only after informed discussion Unplanned (emergency) IV should be avoided through an early discussion of end-of-life issues, coordination with palliative care teams and appropriate advance directives	NIV not tolerated: further education regarding documented benefits; evaluate reasons for noncompliance; reintroduce NIV; if not successful: hospice referral for palliative care or IV Unable to maintain pO_2 > 90%, pCO_2 < 50 mmHg or unable to manage secretions: IV IV may be considered to preserve quality of life in patients with ALS who want long-term ventilatory support	–	–
Termination of NIV/IV, end-of-life management			
Discuss the options for respiratory support and end-of-life issues if the patient has dyspnea, other symptoms of hypoventilation or an FVC < 50% Rediscuss the patient's preferences for life-sustaining treatment every 6 months Treatment of dyspnea: opioids alone or in combination with benzodiazepines if anxiety is present Use oxygen only if hypoxia is present	–	If a person on continuous NIV wishes to stop treatment, seek advice from healthcare professionals who have knowledge and experience of stopping NIV	If termination of IV is legal in the patient's country, the advance directive should include whether ventilation should be terminated under certain circumstances, since the patient will eventually lose the ability to communicate (IV)

*In our experience, mucolytic drugs are usually ineffective and may even be harmful if not combined with MI-E.
AAN, American Academy of Neurology; ALS, amyotrophic lateral sclerosis; EFNS, European Federation of Neurological Societies; FTD, frontotemporal dementia; FVC, forced vital capacity; HFCWO, high-frequency chest-wall oscillation; IV, invasive ventilation; (IV), class IV evidence; MI-E, mechanical insufflation–exsufflation; MIP, maximal inspiratory pressure; NICE, National Institute for Health and Care Excellence; NIV, non-invasive ventilation, pCO_2, carbon dioxide partial pressure; pO_2, oxygen partial pressure; PEG, percutaneous endoscopic gastrostomy; SNIP, sniff nasal inspiratory pressure.

Reviews/Mini-Reviews

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Effects of noninvasive ventilation in amyotrophic lateral sclerosis: The complication of bulbar impairment

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Abstract

Amyotrophic lateral sclerosis is a neurodegenerative illness that causes gradual loss of muscle function. Patients eventually develop bulbar impairment, requiring extensive respiratory support. Noninvasive ventilation (NIV) has gained attention as an easily accessible method with promising benefits. We conducted this systematic review to outline the therapeutic effects of NIV, add to previous publications discussing this topic by providing updates on newly completed and ongoing studies, and identify limitations that must be addressed in future trials. A search of PubMed and Cochran for relevant primary studies yielded 26 publications. Studies indicate NIV use is associated with improvements in quality of life, regardless of the severity of bulbar impairment. However, NIV's benefits on survival were limited to patients with less bulbar impairment. In addition, our review found several limitations that undermine the efforts to establish a definitive treatment regimen. Future studies will need to address these problems in order to provide patients with better respiratory care.

Keywords

Amyotrophic lateral sclerosis, ventilation, respiratory, noninvasive

Patient-ventilator asynchrony with nocturnal noninvasive ventilation in ALS

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ABSTRACT

Background: American Academy of Neurology (AAN) practice parameters for amyotrophic lateral sclerosis (ALS) include noninvasive positive pressure ventilation (NIV) for a forced vital capacity (FVC) ≤50% predicted. Despite the limited ability of NIV systems to deliver adequate ventilation synchronous with patient demand, nocturnal patient-ventilator asynchrony has not been systematically studied in patients with ALS prescribed such NIV.

Methods: Twenty-three consecutively recruited patients with ALS reporting consistent use of nocturnal NIV (nNIV) prescribed for FVC ≤50% or orthopnea underwent home nocturnal polysomnography (PSG) on their current nNIV regimen (all used bilevel positive airway pressure). PSG recorded airflow, NIV pressures, thoracic and abdominal respiratory effort, and O_2 saturation by pulse oximetry (SpO_2). Patient-ventilator asynchrony was calculated as an asynchrony index (AI), the number of episodes of asynchrony per hour of nocturnal recording time (RT).

Results: Nineteen patients had an adequate PSG. Their mean AI was 69 ± 46 SD (range 15–146/hour). Mean asynchrony time as a percent of RT was 17% ± 19%. Mean nadir SpO_2 was 85% ± 7%. In multiple regression analysis, no demographic, functional severity (including FVC and ALS Revised Functional Rating Scale), or NIV (including pressure levels and duration of NIV prescription) variables were significantly predictive of degree of patient-ventilator asynchrony.

Conclusions: These findings document frequent nocturnal patient-ventilator asynchrony in patients with ALS consistently using nNIV prescribed as per current AAN practice parameters, and suggest that use of nNIV per these parameters is unlikely to provide patients with ALS optimal nocturnal ventilatory support. *Neurology*® 2011;77:549–555

Initiation

- Appropriately monitored location, oximetry, respiratory impedance, vital signs as clinically indicated
- Patient in bed or chair at >30-degree angle
- Select and fit interface
- Select ventilator
- Apply headgear; avoid excessive strap tension (one or two fingers under strap)
- Connect interface to ventilator tubing and turn on ventilator

Initial settings

Bilevel NIV	CPAP	PSV
▪ Start with low pressure in spontaneously triggered mode with backup rate: Inspiratory pressure at 8 to 12 cm H_2O; Expiratory pressure at 3 to 5 cm H_2O ▪ Gradually increase inspiratory pressure (10 to 20 cm H_2O) as tolerated to achieve alleviation of dyspnea, decreased respiratory rate, increased tidal volume (if being monitored), and good patient-ventilator synchrony ▪ Provide O_2 supplementation as needed to keep O_2 saturation >90%	▪ CPAP level at 5 to 8 cm H_2O ▪ Gradually increase CPAP level as tolerated (up to 20 cm H_2O) to achieve improvement in dyspnea and reduction in respiratory rate ▪ Provide O_2 supplementation as needed to keep O_2 saturation >90%	▪ Inspiratory pressure at 8 to 12 cm H_2O ▪ Positive end-expiratory pressure at 3 to 5 cm H_2O ▪ Gradually increase inspiratory pressure to maximum of 20 cm H_2O to achieve improvement in dyspnea and reduction in respiratory rate

Follow-up

- Check for air leaks, readjust straps as needed
- Add humidifier as indicated
- Consider mild sedation (eg, intravenously administered lorazepam 0.5 mg) in agitated patients*
- Encouragement, reassurance, and frequent checks and adjustments as needed
- Monitor occasional blood gases (within 1 to 2 hours) and then as needed

NIV: noninvasive ventilation; CPAP: continuous positive airway pressure; PSV: pressure support ventilation.
* Care should be taken when using sedatives in patients with underlying lung disorders, especially those with respiratory muscle weakness or neuromuscular disorders.

Adapted with permission from: Mehta S, Hill NS. Noninvasive ventilation. Am J Respir Crit Care Med 2001; 163:540. Copyright © 2001 American Thoracic Society.

Nasal vs. oronasal (full-face) masks: advantages and disadvantages

Variables	Nasal	Oronasal
Comfort	+++	++
Claustrophobia	+	++
Rebreathing	+	++
Lowers CO2	+	++
Permits expectoration*	++	+
Permits speech•	++	+
Permits eating∆	+	-
Function if nose obstructed	-	+

+: possible; ++: most likely; -: not possible.
* Expectoration is possible but requires the assistance of a respiratory therapist with oronasal mask.
• Speech is possible but may vary depending on the degree of respiratory failure.
∆ Eating necessitates oronasal mask removal and may be contraindicated in patients with severe respiratory failure.

Indication criteria of IV/transition from NIV to IV

Severe bulbar weakness or NIV intolerance or declines NIV: propose invasive mechanical ventilation IV has a major impact upon caregivers and should be initiated only after informed discussion Unplanned (emergency) IV should be avoided through an early discussion of end-of-life issues, coordination with palliative care teams and appropriate advance directives	NIV not tolerated: further education regarding documented benefits; evaluate reasons for noncompliance; reintroduce NIV; if not successful: hospice referral for palliative care or IV Unable to maintain $pO_2 > 90\%$, $pCO_2 < 50$ mmHg or unable to manage secretions: IV IV may be considered to preserve quality of life in patients with ALS who want long-term ventilatory support

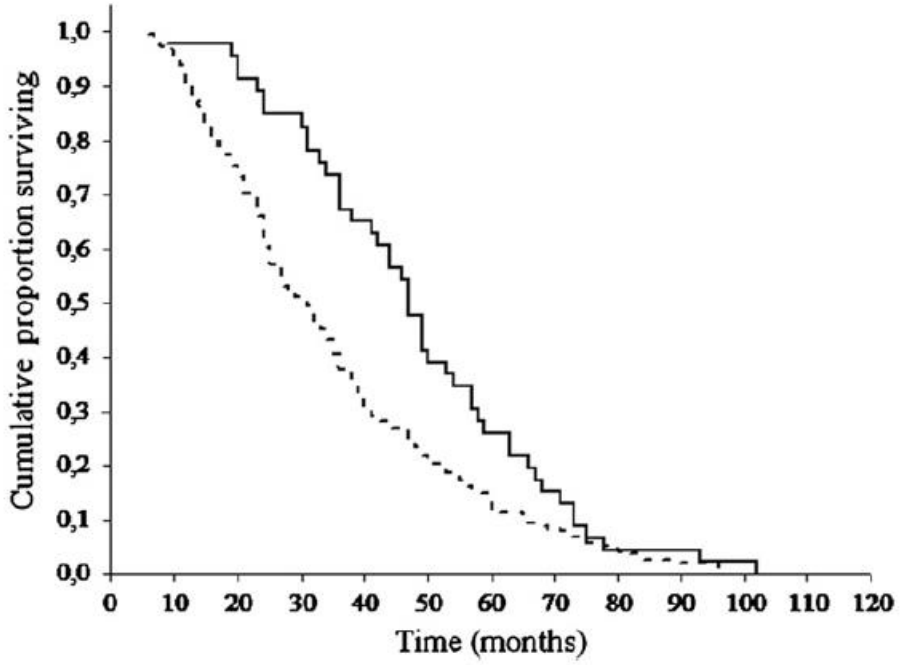
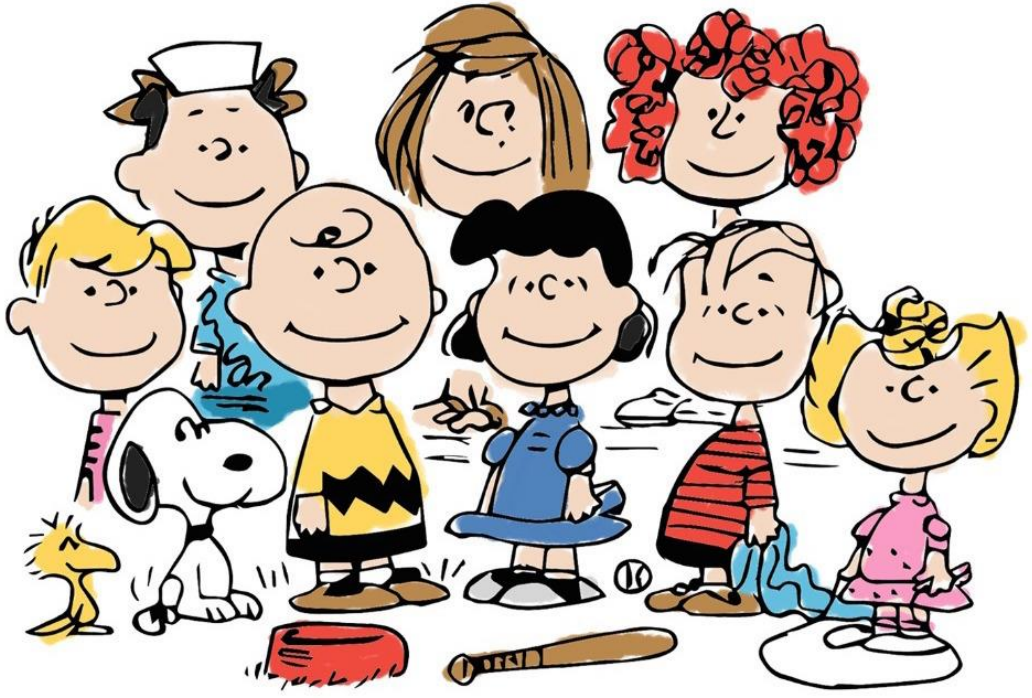


Fig. 1. Kaplan–Meyer survival curve of the ALS patients who underwent tracheostomy (continuous line; median survival [months] 47 [IQR = 33–61]) and ALS patients that died without being submitted to tracheostomy (broken line; median survival [months] 31 [IQR = 20–47]). p = 0.008, log-rank test.

Termination of NIV/IV, end-of-life management			
Discuss the options for respiratory support and end-of-life issues if the patient has dyspnea, other symptoms of hypoventilation or an FVC < 50% Rediscuss the patient's preferences for life-sustaining treatment every 6 months Treatment of dyspnea: opioids alone or in combination with benzodiazepines if anxiety is present Use oxygen only if hypoxia is present	–	If a person on continuous NIV wishes to stop treatment, seek advice from healthcare professionals who have knowledge and experience of stopping NIV	If termination of IV is legal in the patient's country, the advance directive should include whether ventilation should be terminated under certain circumstances, since the patient will eventually lose the ability to communicate (IV)



Grazie :)