UNIVERSITÀ DEGLI STUDI DI FERRARA
- EX LABORE FRUCTUS -

Sclerosi Laterale Amiotrofica

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2° anno – Malattie dell'Apparato Respiratorio
Tronco comune Neurologia

Definizione

La sclerosi laterale amiotrofica (SLA) è una malattia degenerativa del sistema nervoso che colpisce selettivamente i motoneuroni:

- **centrali**: I motoneurone, a livello della corteccia cerebrale
- **periferici**: II motoneurone, a livello del tronco encefalico e del midollo spinale.

La morte di queste cellule avviene gradualmente, nel corso di mesi o anni.

Primi segni quando la perdita progressiva dei motoneuroni supera la capacità di compenso da parte di quelli superstiti.

Progressivo indebolimento muscolare fino alla paralisi neuro-muscolare completa.

Media di sopravvivenza dalla diagnosi: 3 aa.

Epidemiologia ed eziologia

- 40-70 anni, entrambi i sessi
- Incidenza: 2 casi ogni 100.000 individui all'anno
- Sporadica nella quasi totalità dei casi (le forme familiari sono circa il 5% del totale)
- Eziopatogenesi sconosciuta → malattia multifattoriale

Ipotesi eziopatogenetiche più accreditate:

- un danno di tipo *eccitotossico*, dovuto ad un eccesso di Glutammato

- un danno di tipo *ossidativo*, determinato da uno squilibrio tra sostanze ossidanti e sostanze riducenti nel microambiente che circonda i motoneuroni colpiti

Esordio ed evoluzione

- **25% casi: esordio bulbare**
Disartria, disfonia, disfagia

- **75% casi: esordio spinale**
Prima muscoli mani e/o piedi con difficoltà a camminare o correre, oppure incapacità ad eseguire compiti semplici che richiedono destrezza manuale come ad esempio abbottonare la camicia, scrivere o girare una chiave nella serratura associati a ipotrofia muscolare, crampi, fascicolazioni

+

Sintomi per danneggiamento del I motoneurone: spasticità, iper-reflessia, riflessi patologici (segno Babinski).

- **15–45% casi: "effetto pseudobulbare"** che consiste in attacchi di riso o pianto incontrollabile

Nella SLA rimangono integre le funzioni cognitive, sensoriali, sessuali e sfinteriali del paziente.

Materiale consultato

Orphanet Journal of Rare Diseases BioMed Central

Review

Open Access

Amyotrophic lateral sclerosis

Lokesh C Wijesekera† and P Nigel Leigh*†

Table 5: Suggested criteria for non-invasive ventilation (NIV): Provisional European consensus criteria for NIV (European ALS/MND Consortium and European Neuromuscular Centre workshop on non-invasive ventilation in MND, May 2002) [with permission from Leigh et al. 2003]

Symptoms related to respiratory muscle weakness. At least one of	
• Dyspnoea • Orthopnoea • Disturbed sleep (not caused by pain) • Morning headache • Poor concentration • Anorexia • Excessive daytime sleepiness (ESS > 9)	
AND	Evidence of respiratory muscle weakness (FVC ≤ 80% or SNP ≤ 40 cmH2O)
AND	Evidence of EITHER: significant nocturnal desaturation on overnight oximetry OR morning ear lobe blood gas $pCO_2 \geq 6.5$ kPa

ESS, Epworth sleepiness scale

Materiale consultato

AMERICAN ACADEMY OF NEUROLOGY

PRACTICE PARAMETER: THE CARE OF THE PATIENT WITH AMYOTROPHIC LATERAL SCLEROSIS (AN EVIDENCE-BASED REVIEW)

Report of the Quality Standards Subcommittee of the American Academy of Neurology

R.G. Miller, MD; J.A. Rosenberg, MD; D.F. Gelinas, MD; H. Mitsumoto, MD; D. Newman, MD; R. Sufit, MD; G.D. Borasio, MD; W.G. Bradley, DM, FRCP; M.B. Bromberg, MD, PhD; B.R. Brooks, MD; E.J. Kasarskis, MD, PhD; T.L. Munsat, MD; E.A. Oppenheimer, MD; and the ALS Practice Parameters Task Force

J Neurol (2011) 258:359–365
DOI 10.1007/s00415-010-5830-y

REVIEW

Management of respiratory symptoms in ALS

Orla Hardiman

«There are multiple causes of respiratory muscle failure, all of which act to produce a progressive decline in pulmonary function. Diaphragmatic fatigue and weakness, coupled with respiratory muscle weakness, lead to reduced lung compliance and atelectasis. Increased secretions increase the risk of aspiration pneumonia, which further compromises respiratory function. Bulbar dysfunction can lead to nutritional deficiency, which in turn increases the fatigue of respiratory muscles. Early recognition of respiratory decline and symptomatic intervention, including non-invasive ventilation can significantly enhance both quality of life and life expectancy in ALS.»

Dove risiede il problema?

"…the degree to which upper motor neurons are involved is not well established as this is more difficult to measure clinically. Transcranial magnetic stimulation has shown that there may be an upper motor neuron component to ALS-related respiratory symptoms [7, 8]. Notwithstanding, diaphragmatic EMG evidence would suggest that most respiratory symptoms in ALS are primarily a function of lower motor neuron involvement [8]."

"Brainstem involvement of respiratory dysfunction in ALS has not been extensively studied. Recent polysomnographic studies have indicated that hypoventilation can occur in patients with preserved diaphragmatic function during sleep. This hypoventilation is present in both REM and non-REM sleep and is thought to reflect dysfunction of central mechanism in the control of breathing [9]."

…i primi documenti

CHEST®

Official publication of the American College of Chest Physicians

Clinical Indications for Noninvasive Positive Pressure Ventilation in Chronic Respiratory Failure Due to Restrictive Lung Disease, COPD, and Nocturnal Hypoventilation—A Consensus Conference Report

Chest 1999;116;521-534
DOI 10.1378/chest.116.2.521

Cosa cercare?

Table 1 Clinical Symptoms and signs of respiratory impairment in ALS

Symptoms of respiratory dysfunction in ALS
Dyspnoea on minor exertion or talking
Frequent nocturnal awakenings
Excessive daytime sleepiness
Daytime fatigue
Morning headache
Hallucinations
Poor appetite
Poor concentration and/or memory
Mouth dryness
Signs of respiratory dysfunction in ALS
Tachypnoea
Orthopnoea
Use of auxiliary respiratory muscles
Paradoxical movement of the abdomen
Decreased chest wall movement
Weak cough
Sweating
Difficulty clearing secretions
Weight loss

"SNIP carries the advantage that it can be used in patients with bulbar dysfunction, as it does not require a seal around a mouthpiece. A SNIP of < 40 cm H2O correlates with nocturnal hypoxia, and carries a hazard ratio for death within 6 months of 13.6 [20]."

SNIP: sniff nasal inspiratory pressure

Table 2 Criteria for initiation of NIV

Criteria for initiation of NIV in ALS
Symptoms of respiratory dysfunction (Table 1)
FVC <50% predicted or SNP <40 cm H_2O
Nocturnal oxygen desaturation of 90% for at least one cumulative minute
Arterial blood gases: elevated pCO_2

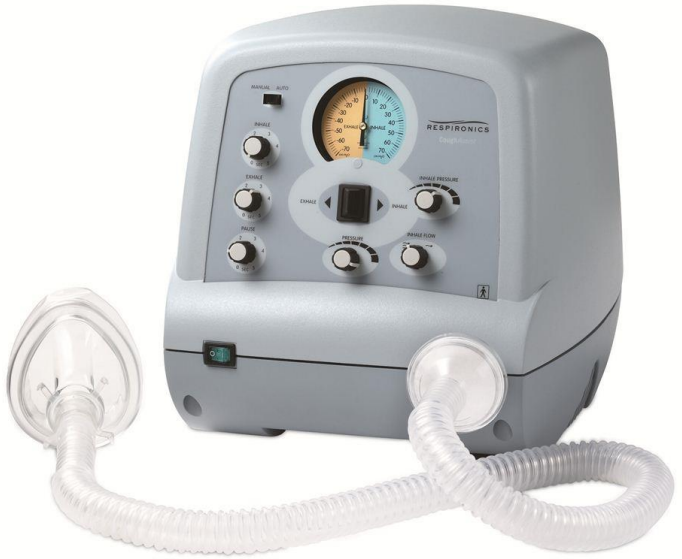
Current evidence suggests that hypoventilation is more common during the REM phase of sleep in patients with diaphragmatic weakness. REM sleep can be often shortened or absent in ALS, leading to sleep disruption and daytime fatigue. There is evolving evidence that periods of hypoventilation may also occur both in REM and non-REM sleep in ALS patients with preserved diaphragmic function, suggesting a disruption of central respiratory control [9], although further studies are warranted to confirm this.

Il problema delle secrezioni

Tenacious secretions should be treated by ensuring adequate hydration, by use of mucolytic agents such as acetylcysteine 200–400 mg tid, or the use of a saline nebulizer with beta-receptor antagonists (e.g. metoprolol or propranolol) ipratropium or theophylline [26].

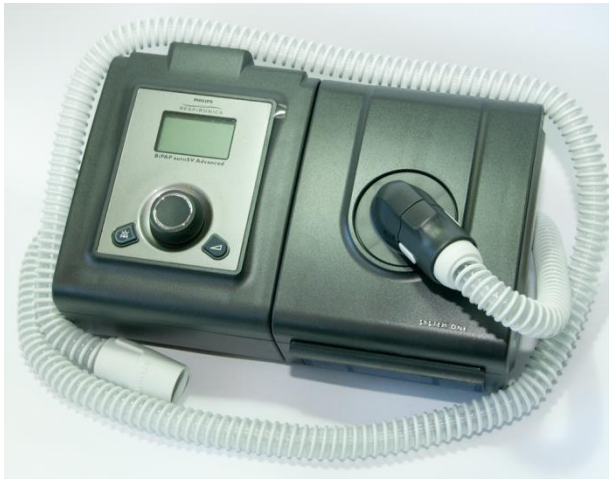
Suctioning is also helpful, and in some instances, a cough insufflator can be of benefit in patients with reduced peak cough expiratory flow (< 2–3 l/s) [27].

Excessive secretions can be treated with amitriptyline or scopolamine patches. When these first line agents are ineffective, botulinum toxin injection of the parotid gland may be helpful, as can irradiation of the salivary glands [26].



Nutrizione e ventilazione

”Gastrostomy should be performed with caution in patients with a vital capacity of< 50%, or a SNIP of< 40 cm H2O, as there is a significant morbidity in this cohort [1, 20, 26, 28]. In this instance, non-invasive ventilation should be initiated prior to gastrostomy insertion [1, 26].”



Problematiche gestionali

"A clear plan for management of respiratory failure should be established, taking into account the fact that routine use of invasive mechanical ventilation at home may be prohibitively expensive in many European health care systems [37]. Moreover, patients contemplating full mechanical ventilation should be aware of the risk of losing all methods of conventional communication, including eye movements, and that they may effectively become ''locked in''. In the absence of advanced technology such as braincomputer interfaces, the wishes of these patients who have become anarthric and incapable of communicating may be difficult to assess. It is, therefore, desirable that the patient's wishes be made known prior to the loss of communication, and a decision to withdraw ventilation be made according to the patient's advance directive.

Opiates or benzodiazepines (where necessary for anxiety) can be used for symptomatic treatment of dyspnoea.

Morphine should be provided in doses of *2.5 mg orally four to six times daily*, followed, if necessary, by morphine s.c. or as an i.v. infusion; start with 0.5 mg/h and titrating as required.

Midazolam *(2.5–5 mg)* or diazepam should be used for nocturnal symptom control and to relieve anxiety. Pain should be managed with opiates.

Neuroleptics can be used for treating terminal restlessness and confusion due to hypercapnia [26]."

Tosse efficace?...il problema dell'ab ingestis

Dysphagia
DOI 10.1007/s00455-015-9687-1

ORIGINAL ARTICLE

Voluntary Cough Airflow Differentiates Safe Versus Unsafe Swallowing in Amyotrophic Lateral Sclerosis

Emily K. Plowman[1,2] · Stephanie A. Watts[2,3] · Raele Robison[1,2] · Lauren Tabor[1,2] · Charles Dion[3] · Joy Gaziano[3] · Tuan Vu[4] · Clifton Gooch[4]

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Tosse efficace?...il problema dell'ab ingestis

"A recent study in 107 hospitalized patients, for example, found that the Clinical Swallowing Evaluation (CSE) identified only 30 % of aspirators confirmed by the gold standard instrumental videofluoroscopic swallowing evaluation (VFSE) [8].

This specific limitation of the CSE is of particular relevance to the ALS patient population, who we have documented have a relatively high incidence of silent aspiration (55 %) [9] coupled with the fact that silent aspiration has been noted to confer a 13-fold increase in the likelihood of pneumonia in dysphagic individuals."

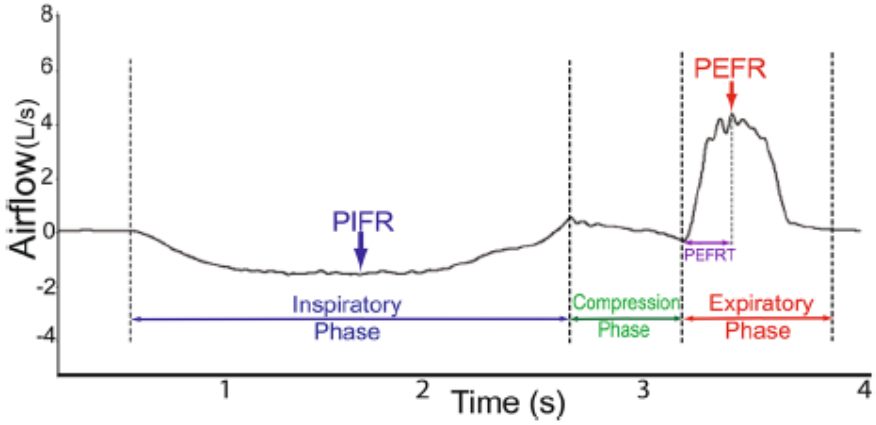
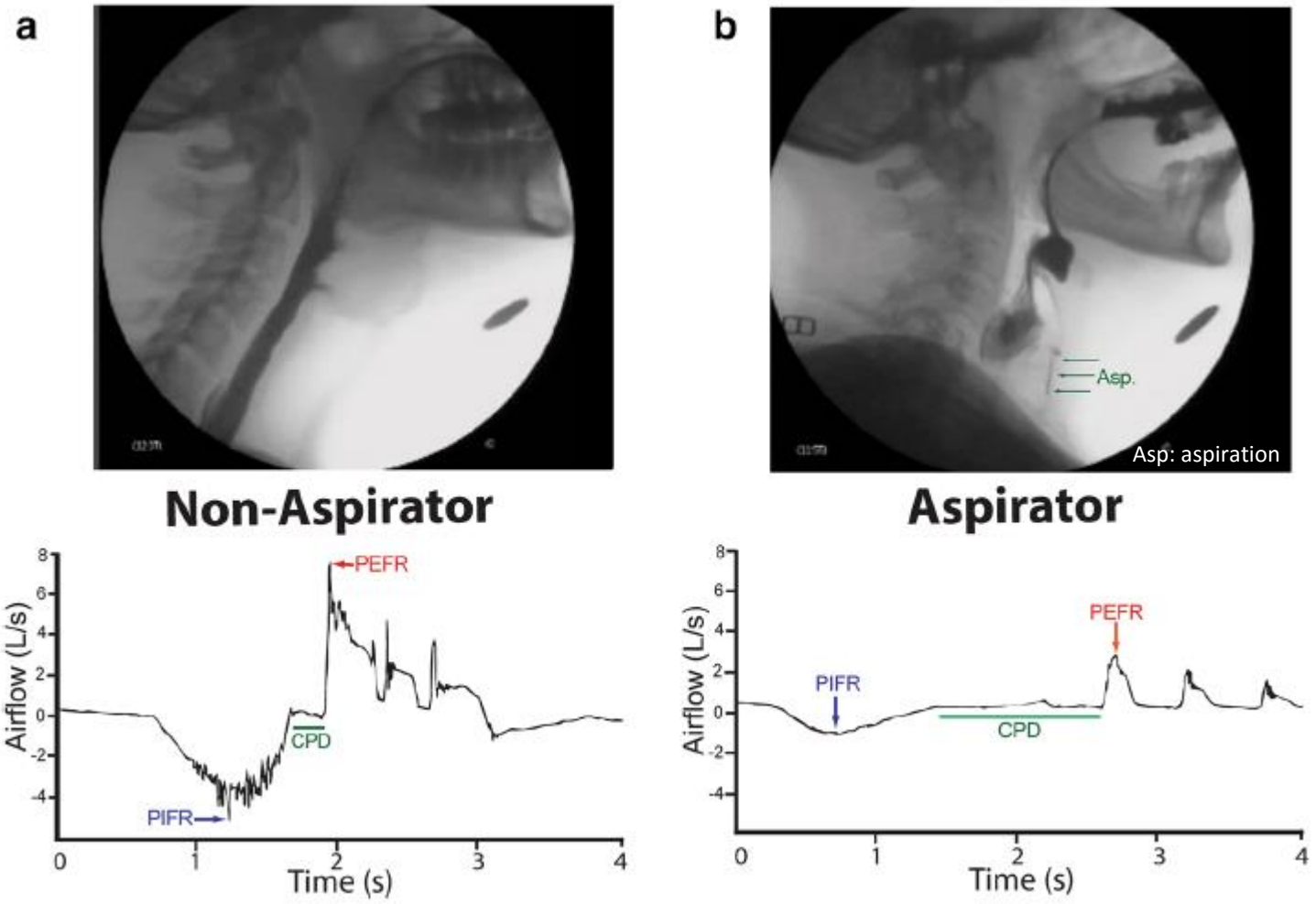


Fig. 1 Example of voluntary cough spirometry waveform depicting derived objective measures. Four temporal measures that include inspiratory phase duration, compression phase duration, expiratory phase duration, and peak expiratory flow rise time (PEFRT) are shown. In addition, measures of peak inspiratory flow rate (PIFR) and peak expiratory flow rate (PEFR) are identified. Cough volume acceleration (CVA) is not depicted but is calculated by dividing PEFRT by PEFR (i.e., CVA = PEFR/PEFRT)



Videofluoroscopic image and voluntary cough airflow waveform examples from an ALS patient who demonstrated safe swallowing (a) and an ALS patient who aspirated without a cough response (b). **The aspirator demonstrated a smaller peak inspiratory flow rate (PIFR), a longer compression phase duration (CPD), and a smaller peak expiratory flow rate (PEFR).**

Tosse efficace?...il problema dell'ab ingestis

Cough volume acceleration (CVA), peak expiratory flow rise time (PEFRT), and peak expiratory flow rate (PEFR) were significantly different between airway safety groups ($p<0.05$) and demonstrated significant discriminant ability to detect the presence of penetration/aspiration.

CVA<45.28 L/s/s, PEFR<3.97 L/s, and PEFRT>76 ms had sensitivities of 91.3, 82.6, and 73.9 %, respectively, and specificities of 82.2, 73.9, and 78.3 % for identifying ALS penetrator/aspirators.

Voluntary cough airflow measures identified ALS patients at risk for penetration/aspiration and may be a valuable screening tool with high clinical utility.

Guidelines

Detailed evidence-based practice guidelines for ALS, which include ventilatory issues, have recently been updated by the European ALS Consortium [26], and by the American Academy of Neurology [1].

Miller RG, Jackson CE, Kasarskis EJ, England JD, Forshew D, Johnston W, Kalra S, Katz JS, Mitsumoto H, Rosenfeld J, Shoesmith C, Strong MJ, Woolley SC (2009) **Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology.** Neurology 73(15):1218–1226

Andersen PM, Borasio GD, Dengler R, Hardiman O, Kollewe K, Leigh PN, Pradat PF, Silani V, Tomik B (2007) EALSC Working Group**. Good practice in the management of amyotrophic lateral sclerosis: clinical guidelines. An evidence-based review with good practice points.** EALSC Working Group. Amyotroph Lateral Scler 8(4):195–213