

# SESSION 10B RESPIRATORY MANAGEMENT

## C93 RESPIRATORY EXERCISES IN AMYOTROPHIC LATERAL SCLEROSIS (REALS)

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*Keywords:* respiratory exercises, delayed-start design, neuroprotection

**Background:** Respiratory insufficiency is the main cause of death in ALS. Non-invasive ventilation and gastrostomy increase survival and quality of life in ALS. Without newer effective pharmacological interventions, it is fundamental to develop programs to improve respiratory function.

**Objectives:** The authors aimed to test a respiratory muscle-training program in ALS.

**Methods:** Inclusion criteria: age 18–75 years, disease duration <18mo, ALS-FRS 25–38, with definite or probable disease, written informed consent. Exclusion criteria: bicipital and flexor digiti muscular strength <4 MRC, weakness of lip sealing, forced vital capacity (FVC) <70%; maximal inspiratory (MIP) and/ or expiratory (MEP) pressures <50%, patients on NIV, gastrostomy, other concomitant diseases such as diabetes and pulmonary diseases, sternocleidomastoid (SCMAmpl) and diaphragmatic (PhrenAmpl) motor amplitudes <1mV or <0.3mV respectively. Patients performed an 8-month respiratory muscle strengthening programme using the “Threshold IMT®”. They were randomized in 2 groups: the efficient load group (G1) and non-efficient load group (G2). However, patients in G2 also performed the exercise with efficient load in the last four months (delayed start study design). Efficient load was individually calculated as 30–40% from MIP and in the first 4 months patients in G2 worked-out with the lowest possible load. Patients were evaluated 3 times, at entry and every 4 months, with ALS-FRS, FVC, MIP and MVV (maximal voluntary ventilation), sniff nasal inspiratory pressure (SNIP), PhrenAmpl and SCMAmpl, VAS for fatigue and dyspnoea, subjective respiratory control feeling, Fatigue Severity Scale (FSS), Epworth’s scale, Functional Independence Measure (FIM), Euro-QoL 5D and Hamilton’s scale.

**Results:** Nineteen patients (13 men, aged 57.7±8.8yrs, 3 bulbar-onset form, 2 definite disease, mean disease duration of 13.2±7.7 months) were included, 4 dropped out due to rapid disease progression. There were no demographic differences between groups at entry. We observed a higher ALS-FRS and MVV decrease in G2 in the first four months. No other differences were found. All patients in both groups described a better voluntary control over respiratory dynamics.

**Discussion and Conclusions:** Exercise is controversial in ALS. Nonetheless, it seems that aerobic exercise at moderate load is related to longer survival and better quality of life. To our knowledge, there has been no specific respiratory exercise programme tested in ALS. In our study, patients in both groups referred a subjective improvement in the voluntary control of the ventilation, as well as a trend for a better outcome in G1 for ALS-FRS and MVV. However, these preliminary results show a trend towards a better outcome for

patients included in G1. Although the completion of this investigation is essential before more definite conclusions, our findings suggest that these studies on respiratory exercise are relevant in ALS.

## C94 HOME INITIATION OF NON-INVASIVE VENTILATION FOR MOTOR NEURONE DISEASE

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*Keywords:* non-invasive ventilation, district general hospital, home initiation

**Background:** The local MND team has been in existence since 1995. Based in a local District General Hospital (DGH), the team provides patient-centred, key worker-led multi-disciplinary team (MDT) care. As the team has developed so has the non-invasive ventilation (NIV) service. The service is unusual in that ventilation is usually initiated in the patients’ homes. The team believes that home initiation of NIV by a DGH based team is at least as effective as initiation in a specialist secondary healthcare setting, and is popular with patients.

**Objectives:** To compare outcomes against published data from the Newcastle NIV study (1).

**Methods:** Retrospective caseload review of 42 patients who had died between 1996 and 31 March 2009 and who had had a trial of NIV was conducted. The case notes were analysed to include all patients who had NIV irrespective of type of presentation. The outcome was mean length of survival from initiation of ventilation to death. Data are also presented for survival of all patients.

**Results:** Bourke reported a survival of 219 days from initiation of ventilation. Our mean length of survival from initiation of NIV was 348 days. Our mean length of survival for all patients from diagnosis was 580 days. Over 90% of patients with MND within the service have NIV initiated at home. This avoids hospital admission for initiation of NIV. Our data indicate that it is safe and effective as mean length of survival is comparable to published data and patients prefer to have NIV initiated at home rather than in hospital. The level of patient satisfaction with the service is also very high.

**Discussion:** We have shown that home initiated NIV in MND is safe and effective over several years. The key factor in that success is the ability to monitor symptoms and detect the early onset of ventilatory failure in an MDT setting, using equipment such as transcutaneous monitoring of CO<sub>2</sub>. The MND MDT is trained to recognize the early symptoms of respiratory failure. Early detection of symptoms is followed up by a team of specialist nursing staff with expertise in respiratory management. The team is based in a District General Hospital but outreach to the primary care setting. The respiratory team monitors patients regularly to optimize ventilatory settings and encourage early use of adjunctive therapies. This may include mechanical cough assistance and early antibiotic therapy.

**Conclusion:** Home initiation of NIV is safe and effective in MND.

**Reference:**

1. Bourke SC, *et al.* Lancet Neurology 2006, 5:140–147

**C95 USUAL INDICATORS OF AMYOTROPHIC LATERAL SCLEROSIS (ALS) DISEASE SEVERITY DO NOT PREDICT OVERNIGHT EFFICACY OF SUBJECTIVELY PRESCRIBED NONINVASIVE POSITIVE PRESSURE VENTILATION**

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Keywords: non-invasive ventilation, forced vital capacity

**Background:** Current guidelines for ALS recommend nocturnal non-invasive positive pressure ventilation (nNIV) for forced vital capacity (FVC) <50% predicted, to prolong survival, sustain respiratory muscle strength and improve sleep quality. nNIV is typically non-objectively prescribed and adjusted. The nocturnal physiologic efficacy of subjective nNIV use in ALS patients has not previously been assessed. Given the challenge of administering nNIV to such patients, we hypothesized that ALS patients commonly have failure of nocturnal oxygenation and ventilation with such nNIV, even when reporting adherence and subjective efficacy.

**Objectives:** To determine the efficacy of subjectively prescribed nNIV in ALS patients reporting adherence and benefit (improved dyspnea and/or sleep quality) with this treatment and ascertain if common measures of disease severity predict nNIV failure.

**Methods:** Twenty consecutive ALS patients reporting successful use of nNIV (>4 h/night, >4 nights/wk and subjective benefit) were prospectively recruited from the Eleanor and Lou Gehrig ALS/MDA Center, and underwent home nocturnal polysomnography (PSG) using their current nNIV regimen. PSG included airflow, NIV pressure, thoracoabdominal effort, ECG and pulse oximetry (SpO<sub>2</sub>). nNIV failure was defined as O<sub>2</sub> desaturation index >4% (ODI4%) ≥5/h recording time; and/or ineffective ventilation time (patient-ventilator asynchrony, central apnea, delivered inspiratory pressure (IPAP) >2cm H<sub>2</sub>O below set IPAP) >5% recording time. Data were analyzed with unpaired t-tests and Fisher's exact test.

**Results:** Twenty patients were studied (6F/14M, mean age 57 ± 10.8, FVC 42.1% predicted ± 16.4, DFS 0.62 ± 0.48). 9 of 20 patients (45%) demonstrated nNIV failure, with mean ± SD nadir SpO<sub>2</sub> = 80 ± 6%, ODI 4 = 6 ± 4/hr, SpO<sub>2</sub> <90% = 6 ± 6% recording time, ineffective ventilation time = 18 ± 16% recording time. nNIV failure and success groups were similar for age (failures 60.6 ± 11.6 years vs 54.4 ± 9.7 years, p = 0.2), FVC at the time of PSG (failures 48 ± 18% predicted vs 38 ± 14%, p = 0.2), ALSFRS-R score at the time of PSG (failures 25 ± 7 vs 22 ± 9, p = 0.5), rate of functional decline (DFS, failures 0.65 ± 0.43 vs 0.60 ± 0.54, p = 0.8), bulbar onset (failures 56% vs 64%, p = 0.9), presence of PEG (failures 33% vs 64%, p = 0.9), level of set IPAP (failures 13 ± 4cm H<sub>2</sub>O vs 12 ± 4 cmH<sub>2</sub>O, p = 0.6), and NIV duration prior to PSG (failures 9 ± 5 months vs. 7 ± 5 months, p = 0.4). 5 subjects who did not meet minimal criteria for nNIV failure

evidenced nadir O<sub>2</sub> saturation of <85% or ventilator double triggering >10 events/hr.

**Discussion and Conclusions:** These data suggest that current nNIV practice is likely not meeting the goals of improving sleep disordered breathing (SDB) or sustaining respiratory muscle strength for ~50% of patients prescribed such therapy. The prevalence of nNIV failure among all patients subjectively prescribed nNIV is likely higher than that seen in this data. Neither degree of disease progression nor impairment appears to predict nNIV success in this setting.

**C96 MULTICENTER STUDY RESULTS OF MOTOR POINT STIMULATION FOR CONDITIONING THE DIAPHRAGM OF PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS/ MOTOR NEURON DISEASE: PRELIMINARY TREND TOWARD SLOWED RESPIRATORY DECLINE AND IMPROVED SURVIVAL**

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Keywords: diaphragm pacing, respiration, surgery

**Background:** The diaphragm pacing system (DPS) is a standardized minimally invasive laparoscopic technique intended to maintain and provide natural diaphragm ventilation. Respiratory insufficiency through diaphragm dysfunction is the major cause of mortality in ALS/MND and presently available therapies are inadequate to address this problem.

**Objectives:** Assess the safety and efficacy of DPS for diaphragm conditioning in ALS/MND.

**Methods:** Prospective, nonrandomized, controlled, multicenter, interventional trial with a lead-in design and 9 month post-implantation treatment period. Prospective efficacy and safety measures were obtained including the rate of decline of pulmonary function, quality of life measurements, adverse event rates and survival or full time tracheostomy with mechanical ventilation.

**Results:** 145 subjects enrolled with 106 implantations from March 2005 to January 2009 (most common reason for not implanting was a drop of FVC below 45% of inclusion criteria). Subject demographics from the first 88 implanted patients are: mean age 54.9 ± 10.3, 71.6% male, 27.9% bulbar onset, ALSRS-r total score 27.8 ± 7.2, riluzole use of 74%, symptom onset to implantation 41.5 months ± 27.1, FVC (% predicted) 61.1 ± 11.8, average pCO<sub>2</sub> 39mm Hg (max = 60), SF 36 average physical of 36, SF 36 average emotional of 53, and non-invasive ventilation use of 82% throughout the study. With a cumulative 1,346 months of device usage (average 1.1 years/patient), safety analysis showed no serious unanticipated adverse device effects with 3 (2.8%) serious adverse events

related to surgical procedure. There were 17 reported respiratory events during the study period, and only one patient stopped pacing. Interim analysis shows a significant ( $p < 0.001$ ) improvement (7%) in ratio of the ALSFRS-R respiratory subscore to the total ALSFRS-r score from implant to treatment. In the subset of subjects with at least 6 months of treatment data and a declining FVC during the lead-in period ( $n = 45$ ), there was a significant reduction in FVC rate of decline ( $p = 0.01$ ), with a paired (treatment to lead-in for each patient) FVC improvement of 1.1% change from 2.7% decline during lead-in to 1.6% decline post implantation. The 30 day survival was 100% (106/106), the 6 month survival was 92% (90/98) and the 12 month survival was 78% (56/72). Using Kaplan-Meier analysis the mean survival is 25.7 months post implant. When analyzing combined DPS and gastrostomy placement subset the 6 month survival was 89% (24/27) and the 12 month survival was 74% (17/23). Respiratory events accounted for 41% of the end events.

**Conclusion:** The DPS system can be safely implanted and utilized in ALS patients. DPS seems to have positive effects in maintaining respiratory function and decreasing respiratory decline in those declining prior to implant. Overall survival and survival with a gastrostomy seems higher than historical comparisons.

#### C97 DIAPHRAGM PACING IN ALS: PRELIMINARY RESULTS SUGGEST SIGNIFICANT SLEEP IMPROVEMENT

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Keywords: respiratory insufficiency, diaphragm, sleep

**Background:** During amyotrophic lateral sclerosis (ALS), respiratory insufficiency and diaphragmatic involvement cause major sleep disturbances. Their correction by non-invasive ventilation (NIV) largely contributes to the improvement in quality of life associated to this therapeutic. It has been suggested that diaphragm pacing (DP) using a laparoscopically implanted device (NeurRx, Synapse, Oberlin, OH, USA) could slow down decline in lung function. To test this hypothesis, a prospective, non randomized, multi-center interventional trial has been conducted among 106 patients at 8 centers. In the subset of patients implanted in Paris, we further tested the hypothesis that DP could maintain diaphragm strength and improve sleep.

**Patients:** 11 patients from the Paris cohort ( $n = 18$ ) had completed 4 months of DP at the time of the present submission; 6 men, 5 women; median age 68 years, 95%CI 63–74; median ALSRS-r total score 34 (29, 40); riluzole 100%; NIV  $n = 5$ ; bulbar onset  $n = 1$ ; median interval between diagnostic and implantation 30 (19,42) months.

**Methods:** In addition to the evaluation of the rate of decline of lung function, quality of life, safety and survival, the Paris patients had measurements of twitch esophageal and trans-diaphragmatic pressures (Pes,tw and Pdi,tw) in response to bilateral anterior magnetic stimulation (BAMPS) and sleep assessments including polysomnographic recordings (PSG) immediately before the implantation and after 4 months of diaphragm stimulation.

**Results:** During the conditioning period, forced vital capacity (FVC) significantly declined. There was no change in its rate of decline as compared to the lead-in period, although none of the patients had to start NIV. Pdi,tw and Pes,tw were markedly altered initially (median 6.7 (4.6, 15.0) cm H<sub>2</sub>O and 2.3 (1.9, 7.0), respectively). In contrast to spirometric variables, they remained unchanged after 4 months. Median sleep efficiency increased from 67 (51, 71)% to 74 (70, 85)% ( $p = 0.02$ ) with a significant reduction in sleep fragmentation (median arousal index from 28 (14, 30) to 13 (10, 21) events/h, ( $p = 0.01$ )). The amount of non REM sleep stage N3, the amount of REM sleep, and sleep latency were unchanged, arguing against a first night effect. In coherence with these results, the patients reported lower Epworth scores after the 4 months pacing period (from 6 (3, 12) to 5 (3, 6),  $p = 0.05$ ).

**Conclusion:** The quality of sleep significantly improved after 4 months of diaphragm pacing in a subset of the Paris cohort of the international DP trial in ALS. This was not associated with a significant reduction in the rate of decline of FVC, but the strength of the diaphragm did not decline during the conditioning period. The mechanisms of the improvement in sleep remain to be elucidated.

#### C98 SURVIVAL IN ALS PATIENTS AFTER TRACHEOSTOMY

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Keywords: tracheostomy, survival, prognosis

**Background:** The most common cause of death in patients with Amyotrophic Lateral Sclerosis (ALS) is respiratory failure due to progressive impairment of the respiratory muscles. The median survival is 36 months in ALS patients who do not receive invasive mechanical ventilation. Little information is reported in the literature about the survival of ALS patients who undergo tracheostomy.

**Objectives:** The aim of our study is to analyze the survival of ALS patients who receive pressure positive ventilation by tracheostomy.

**Methods:** 95 out of 646 ALS patients followed in our Center decided to receive mechanical ventilation by tracheostomy. Long-term follow-up of 85/95 patients was available and was analyzed in the present study. Survival was calculated using Kaplan-Meier analysis.

**Results:** There were 48 males and 37 females. The age of onset ranged from 12–82 years (media 54.81, median 57 years); in 18 patients (21.2%) the disease began before 40 years, in 67 patients (78.8%) after 40. The site of onset was bulbar in 21 patients (24.7%) and spinal in the remaining 64 patients (75.3%). 81 patients had a sporadic ALS, while in 4 patients a family history was present. Dividing sporadic ALS group by clinical phenotype, we observed 62 patients (76.5%) with classic ALS, 18 patients (22.3%) with predominant upper motor neuron phenotype (p-UMN) and 1 (1.2%) with Flail Arm variant. The time from onset of disease to tracheostomy ranged from 6 to 134 months (mean 35.71, median 28 months). Before tracheostomy 24 patients used a NIV, for a mean duration of treatment of 8.84 months (range

1–21 months); only 2 patients used NIV 24 hours/24 before receiving tracheostomy, for 5 and 10 months, respectively. The median survival after tracheostomy was 40 months (95% CI 25.93–54.06 months). Age of onset before 57 years and the time from onset to tracheostomy longer than 28 months were significantly associated with longer survival. After tracheostomy, 10 patients (12%) had a survival longer than 5 years, while only one patient was alive after 10 years (1.2%). 4 patients (4.7%) developed a totally locked-in state after a mean period of 27 months (range 15–48 months) after tracheostomy and 45 months (range 27–69 months) from onset of disease.

**Discussion and Conclusions:** In our series, the median survival of ALS patients receiving tracheostomy is 40 months. Age of onset of the disease and the period of time from onset to tracheostomy are significant prognostic factors. The knowledge of the evolution of ALS after tracheostomy may be helpful in the hard task of end-of-life decisions.

### C99 A POPULATION-BASED STUDY OF TRACHEOSTOMY IN ALS

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*Keywords:* tracheostomy, incidence, outcome

**Objectives:** Respiratory failure is frequent in amyotrophic lateral sclerosis (ALS). Its management is based on mechanical ventilation with non-invasive positive pressure (NIPPV) or

tracheostomy when NIPPV is no longer effective. However, information about the outcome of tracheostomy in ALS is scarce.

**Methods:** We evaluated the clinical characteristics and outcome of tracheostomy in ALS using data from the Piemonte and Valle d'Aosta Register for ALS (PARALS), a prospective epidemiological register collecting all ALS incident cases in two Italian regions.

**Results:** Among the 1260 patients incident in the period 1995–2004, 134 (10.6%) underwent tracheostomy. Young male patients were more likely to be tracheostomized. Site of onset (bulbar vs. spinal) and period of diagnosis (1995–1999 vs. 2000–2004) did not influence the likelihood of being tracheostomized. The mean duration of hospital stay was 52.0 days (SD 60.5). Overall, 27 patients died while still in hospital (20.1%); in-hospital mortality was lower in subjects followed at ALS multidisciplinary centers (13.1% vs. 28.8%;  $p = 0.02$ ). Sixty-five patients (48.5%) were discharged to home, while 42 (31.3%) were admitted to long term care facilities. The median survival time after tracheostomy was 253 days. In the Cox multivariable model the factors independently related to a longer survival were enteral nutrition, age, marital status, and ALS centre follow up.

**Conclusions:** In an Italian epidemiological setting ALS survival after tracheostomy was less than one year. Socio-cultural factors may influence the probability to be tracheostomized, even in a highly socialized health system such as the Italian one.