Amyotrophic Lateral Sclerosis

ISSN: 1748-2968 (Print) 1471-180X (Online) Journal homepage: https://www.tandfonline.com/loi/iafd19

# SESSION 6B EPIDEMIOLOGY

**To cite this article:** (2011) SESSION 6B EPIDEMIOLOGY, Amyotrophic Lateral Sclerosis, 12:sup1, 23-25, DOI: 10.3109/17482968.2011.615502

**To link to this article:** https://doi.org/10.3109/17482968.2011.615502

Published online: 21 Nov 2011.

*Amyotrophic Lateral Sclerosis*, 2011; 12(Suppl. 1): 23–25

informa
healthcare

# SESSION 6B EPIDEMIOLOGY

## C40 EXOGENOUS RISK FACTORS IN ALS: A POPULATION-BASED CASE-CONTROL STUDY

HUISMAN MHB[1], DE JONG SW[1], VAN DOORMAAL PTC[1], VERMEULEN R[2], HEEDERICK D[2], KROMHOUT H[2], SCHELHAAS HJ[3], VAN DER KOOI AJ[4], DE VISSER M[4], VELDINK JH[1], VAN DEN BERG LH[1]

[1]*Department of Neurology, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, Utrecht, The Netherlands,* [2]*Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands,* [3]*Department of Neurology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands,* [4]*Department of Neurology, Amsterdam Medical Center, Amsterdam, The Netherlands*

*Email address for correspondence: m.h.b.huisman-3@umcutrecht.nl*

*Keywords: risk factors, occupation, physical activity*

**Background:** Sporadic amyotrophic lateral sclerosis (ALS) is probably caused by multiple genetic and environmental factors causing motor neuron degeneration. Although environmental risk factors have been extensively studied in ALS, most environmental risk factors are still unknown. Systematic reviews of the literature suggest this may be due to limitations in study design: most risk factor studies had a hospital-based study design, which introduces the risk of referral bias. This source of bias can be eliminated in a population-based case-control study, which enables the provision of class I evidence according to the Armon criteria (1) for exogenous risk factor studies in ALS.

**Objectives:** To determine the association between ALS and multiple exogenous factors: smoking; alcohol; education; medical history; medication use; nutrition; family history; hormonal factors; occupational history; occupational exposures (pesticides, metals, electrical accidents, etc.); physical activity.

**Methods:** A population based study has been performed in the Netherlands between January 2006 and June 2011 (mean population 16,426,273; area 41,528 $km^2$). Patients were ascertained from five sources. Diagnosis was made according to the El Escorial criteria.

700 incident sporadic ALS patients and 2100 controls filled in questionnaires to obtain data about exogenous factors.

**Results:** Multivariate analyses showed an increased risk of ALS in current smokers (OR 1.38; $p = 0.04$). Current smoking was also associated with shorter survival (hazard ratio of 1.51 ($p = 0.02$) adjusted for vital capacity, gender, age and site of onset). Current alcohol consumption was found to be an independent protective factor for ALS (OR = 0.52; $p = 6.6 \times 10^{-5}$), but did not have an effect on survival.

Relatives of sporadic ALS patients had a mildly elevated risk of dementia (recurrence risk λ 1.16; 95% CI: 1.01-1.33). The risk of Parkinson Disease (PD) was not elevated (λ 1.14; 95% CI: 0.83-1.55). A reduced risk of vascular diseases was found in relatives of sporadic ALS patients (stroke: λ 0.94; 95% CI: 0.82-1.07 and myocardial infarction: λ 0.87; 95% CI: 0.76-0.98).

Longest job held in the agricultural sector is associated with an increased risk of developing ALS (OR 1.7; 95% CI: 1.01-3.00, $p = 0.045$) (adjusted for smoking, use of alcohol, and age). Last job held in the agricultural sector is associated with ALS as well (OR 1.8; 95%CI: 1.1-3.1, $p = 0.03$). Subsequently a Job Exposure Matrix (JEM) was used, which enables the linking of occupations to profiles of environmental exposures by providing semi-quantitative assessments of exogenous exposures for each occupation. Mean lifetime occupational exposures to chromium, nickel, diesel motor exhaust, and mine dust were significantly higher in patients compared with controls. Exposure to pesticides was not significantly increased in patients.

Results on the other exogenous factors will be presented, as well as the result of a multivariate analysis including all exogenous risk factors.

**Discussion and conclusions:** Cigarette smoking, occupation in the agricultural sector, and a low level of education are risk factors for ALS. Current smoking is associated with a worse prognosis, alcohol consumption reduces the risk of ALS.

Familial aggregation of ALS, dementia and PD is substantially lower than previously thought. The lowered risk of vascular diseases in relatives of ALS patients supports the view that a beneficial vascular risk profile increases ALS susceptibility.

More risk factors will be analyzed and presented at the symposium. The multivariate analysis, including all exogenous risk factors, will determine which risk factors are independently associated with ALS.

### Reference

1. Armon C. Neuroepidemiology 2003;22:217–28.

## C41 PREMORBID CARDIOVASCULAR FITNESS IS A RISK FACTOR FOR ALS: EVIDENCE FROM RECORD-LINKAGE STUDIES

TURNER M, WOTTON C, TALBOT K, GOLDACRE M

*Oxford University, Oxford, UK*

*Email address for correspondence: martin.turner@clneuro.ox.ac.uk*

*Keywords: fitness, athleticism, cardiovascular risk*

**Background:** Those at risk of developing apparently sporadic ALS have not yet been defined as a population. There is a persistent but anecdotal observation that ALS patients arise from a 'fitter' population, and some have proposed greater physical activity as a risk factor (1). Either way, intuitively such a physical profile might be reflected in a reduced incidence of coronary heart disease (CHD) prior to the development of ALS. The number of individuals and time required for a prospective study of co-morbidities or physical activity in ALS is untenable. Even the most rigorous case-control

ISSN 1748-2968 print/ISSN 1471-180X online © 2011 Informa Healthcare
DOI: 10.3109/17482968.2011.615502

studies suffer from the major issue of recall bias, and have had conflicting results to date (2–4).

**Objectives:** To study the incidence of CHD in relation to the later development of ALS.

**Methods:** A record-linkage study of two large databases of hospital admissions, the Oxford Record Linkage Study (ORLS) and an English national record-linkage dataset of Hospital Episode Statistics was undertaken. The ratio of the rate of ALS in people without a record of CHD, to the rate in people with a record of CHD was calculated, factoring out premature death in the non-CHD and CHD cohorts. Similar analysis for Parkinson's disease (PD) and multiple sclerosis (MS) was undertaken.

**Results:** In the English population, the rate ratio (RR) for ALS in the non-CHD cohort was 1.14 (95% CI 1.05-1.22); for PD it was 0.95 (95% CI 0.93-0.98); and for MS 0.95 (95% CI 0.88-1.04). The ORLS data yielded similar findings.

**Discussion:** Those without a record of CHD were at higher risk of ALS than those with CHD. The higher risk was not found for PD or MS. This provides indirect support for the assertion that ALS arises in a cardiovascularly fitter population. Whilst this might be a result of an altered metabolic or physical activity profile, it could equally reflect distinct motor neuronal network properties associated with improved physical performance in youth, but inherently vulnerable to the stochastic events of ageing.

**Conclusions:** Studies of the genetic, molecular, and neuronal substrates of physical fitness are now a priority for the ultimate goal of the primary prevention of sporadic ALS.

**References**

1. Harwood CA, *et al*. Amyotrophic Lateral Scler 2009 PM:19263258.
2. Scarmeas N, *et al*. Neurology 2002 PM:12221178.
3. Veldink JH, *et al*. Neurology 2005 PM:15668420.
4. Beghi E, *et al*. Amyotroph Lateral Scler 2010 PM: 20433412.

## C42 MAY ALS PHENOTYPE BE CONSIDERED A PART OF THE SPECTRUM OF PARANEOPLASTIC DISEASES?

CHIO A[1,2], CALVO A[1], MOGLIA C[1], MAZZINI L[2], MORA G[3], BERSANO E[1], MANERA U[1], VIGLIANI MC[1,2]

[1]*Department of Neuroscience, University of Torino, Torino, Italy,* [2]*Neuroscience Institute of Torino, Torino, Italy,* [3]*Department of Neurology, University of Eastern Piedmont, Novara, Italy,* [4]*Salvatore Maugeri Foundation, Scientific Institute of Milan, Milano, Italy*

*Email address for correspondence: achio@usa.net*

*Keywords: cancer, risk factor, survival*

**Background:** It is still controversial whether typical ALS in cancer patients can be considered a paraneoplastic disorder.

**Aims:** To determine whether patients with ALS have a higher than expected incidence of cancer and how the co-occurrence of cancer modifies ALS prognosis.

**Methods:** The study population were the 1260 ALS cases incident in Piemonte and Valle d'Aosta in the period 1995-2004. Patients were affected by definite, probable or probable laboratory-supported ALS. Only patients with cancers occurring in the 6 months before and after the onset of ALS were included. The odds ratio of having a cancer in ALS patients was calculated using as reference the incidence rate of cancers in the same area for the period 2004-2006 (www.cpo.it). Odds ratio were calculated by gender and 5-year age-classes.

**Results:** 46 ALS patients had a cancer in the 6 months preceding or following the onset of ALS (11 lung, 10 breast, 7 gastrointestinal tract, and 18 other sites). No differences in the age and site of onset and gender distribution were found between cancer and non-cancer ALS patients. Cancer in ALS was significantly more frequent than expected in both genders (men, OR 2.01; 99% C.I. 1.15-3.28; women 3.43; 1.78-5.95). The higher frequency of cancers in ALS patients was mostly due to lung cancers for both genders (men 4.35, 1.51-9.68; women 4.83, 0.58-14.97) and to breast cancers for women (6.16, 2.29-13.18). Cancer patients had a significantly shorter survival than non-cancer patients (median survival time, 1.8 vs. 2.4 years; $p = 0.01$), but this difference was mostly due to the very short survival of ALS patients with lung cancer (median survival time, 1.0 year).

**Conclusions:** Cancer, predominantly lung and breast cancer, has an incidence significantly higher than expected in ALS population. Our finding suggests a possible correlation between some cases of ALS and cancer. Patients with lung cancer have a worse clinical progression of ALS than other patients.

## C43 EPIDEMIOLOGY OF AMYOTROPHIC LATERAL SCLEROSIS IN THE ISLAND OF IRELAND FROM 1995-2010

BYRNE S[1,2], ELAMIN M[1,2], FITZGERALD T[3], PERRY I[3], LYNCH C[1], DONAGHY C[4], HARDIMAN O[1,2]

[1]*Beaumont Hospital, Dublin, Ireland,* [2]*Trinity College, Dublin, Ireland,* [3]*University College Cork, Ireland,* [4]*Royal Victoria Hospital, Belfast, Northern Ireland*

*Email address for correspondence: suabyrne@hotmail.com*

*Keywords: registry*

**Background:** Population based registries which use multiple methods of ascertainment are held in Ireland and Northern Ireland. The registry in Ireland was established in 1995 and the Northern Irish registry was established in 2005.

**Objectives:** 1) To determine whether the prevalence of ALS in Ireland has changed between 2000 and 2011; 2) To compare epidemiological findings between the two registries for incident cases of ALS diagnosed between January 1st 2005 and December 31st 2010.

**Methods:** Review of incidence, prevalence and survival in a population based cohort collected prospectively. To complete objective two, data mining from existing ALS Registers was carried out.

**Results:** 1) Between 1995 and 2010, 1306 cases of ALS were diagnosed in the Republic of Ireland providing a crude incidence rate of 2.6 per 100,000.

Prevalence data from the Irish Registry for years 2000 and 2010 were compared. Despite the introduction of treatments including non invasive ventilation, the prevalent rates have remained unchanged over a 10 year period.

2) Between 2005-2010, 477 cases of ALS were diagnosed in Ireland and 200 cases were diagnosed in Northern Ireland, giving a crude incidence rate of 2.6 per 100,000 in Ireland and 2.5 per 100,000 in Northern Ireland. Clinical and demographic data

was compared between the two regions. Mean age at onset was 65, and the male to female ratio was 1.15 :1 in both cohorts.35% of patients had bulbar onset disease in both cohorts. The mean duration from first symptom to disease onset was 14 months.

**Conclusion:** Prevalence of ALS remains unchanged, suggesting that the natural history of ALS has not changed over a 10 year period.

Despite differences in health care systems, the incidence, prevalence and clinical features of ALS, and duration from first symptom to diagnosis are identical in the Republic and Northern Ireland. This indicates that both Registers are close to full ascertainment and that delays in ALS diagnosis are unlikely to be influenced by the type of healthcare provided. The only statistically significant difference was the age at onset for females, which was higher in Northern Ireland.