The epidemiology of amyotrophic lateral sclerosis (ALS/MND) in people aged 80 or over

RAEBURN B. FORBES1, SHUNA COLVILLE2, ROBERT J. SWINGLER2 FOR THE SCOTTISH ALS/MND REGISTER

1Department of Neurology, Royal Victoria Hospital, Belfast BT12 6BA, UK
2Department of Neurology, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK

Address correspondence to: R. B. Forbes. Fax: (+44) 28 902 35258. Email: Raeburnforbes@aol.com

Abstract

Objective: to describe the clinical features, incidence, survival and process of care of people with Amyotrophic Lateral Sclerosis/Motor Neurone Disease aged 80 years or more at diagnosis.

Design: prospective, population-based descriptive epidemiological study.


Participants: 135 people aged 80 years or over at diagnosis.

Methods: Descriptive Epidemiology of Amyotrophic Lateral Sclerosis/Motor Neurone Disease in the over 80s. Survival described using Kaplan–Meier curves.

Results: 135 of 1226 cases (11%) were aged 80 years or more. Sixty-seven (50%) had bulbar onset, and 58 (43%) were men. The standardised incidence was 10.2/100,000 (95% CI 7.4–13.1) in men and 6.1/100,000 (95% CI = 4.3–7.6) in women. Median survival from first symptoms was 1.7 years (IQR 1.0–2.8), less than younger patients ($P = 0.0003$; log Rank test). We found evidence of differences in the process of care, as older people were less likely to be prescribed Riluzole (OR 0.12, 95% CI = 0.02–0.89) or be assessed by a neurologist (OR 0.76, 95% CI = 0.67–0.86).

Conclusion: this is the first comprehensive report of the epidemiology of Amyotrophic Lateral Sclerosis/Motor Neurone Disease in older people. Clinical presentation and survival differ from the population as a whole. There is evidence of a different process of care. While this may be to the detriment of their survival, this finding would need to be confirmed by further prospective studies.

Keywords: amyotrophic lateral sclerosis, epidemiology, survival, elderly, ALS/MND, motor neurone disease

Introduction

Amyotrophic lateral sclerosis/motor neurone disease (ALS/MND) is a devastating progressive neurodegeneration. With the exception of some familial cases, its aetiology remains obscure. Epidemiological studies to date have found evidence for a uniform incidence in Western countries where prospective methods of case ascertainment have been used [1]. Yet, there are very few descriptions of the epidemiology of this disease in older people. This is due to the relatively small size of most epidemiological studies, and previous reports in older people were case series [2]. Previous data from the Scottish MND Register highlighted the greater incidence of bulbar onset disease in the over 65s, but there were too few patients aged 80 years or more from whom to make meaningful descriptions of the disease.

We describe 135 people who were diagnosed with ALS/MND at aged 80 years or more from a 10-year prospective, population-based study in Scotland, and compare their clinical, demographic and process of care with younger patients on our register.

Methods

Study population

The Scottish ALS/MND Register is a population-based study which has recorded the clinical details of all Scottish adults diagnosed with ALS/MND since 1 January, 1989. The Register has Scottish multi-centre research ethics committee approval. We identified cases from multiple intersecting sources (i) Referrals from consultant neurologists and neurophysiologists practising in Scotland and Family Care Officers (latterly Nurse Specialists) of the Scottish Motor Neurone Disease Association, (ii) Scottish Morbidity Records (SMR1) of discharges from Scottish Hospitals, and (iii) Mortality Coding from the Office of the Registrar General for Scotland. We used the modified World Federation of Neurology criteria for people diagnosed between 1989–1993 [3] and the El Escorial criteria for people diagnosed from 1994 onwards [4]. Diagnoses were confirmed pathologically in 69 out of 70 autopsies performed in the course of routine care. We recorded symptoms at onset (bulbar, dysarthria or dysphagia;
spinal, limb onset). By convention those with both spinal and bulbar symptoms from onset were classified as bulbar. We took note of any familial cases. We used a record linkage method to identify people who had undergone a percutaneous endoscopic gastroenterostomy (PEG) tube insertion in any Scottish hospital at any time from January 1989 until 31 December, 1999. Using capture recapture methods [5] we have tested ascertainment and shown it to be of the order of 98% complete. An older person was defined as age 80 years or more at the time of diagnosis.

**Incidence**

We estimated crude incidence of ALS/MND with the 1994 mid-year estimate of the Scottish population [6]. To facilitate comparisons with future reports we standardised using the direct method [7] to the 1990 US population estimate (previously used to make international comparisons of ALS/MND incidence). We calculated 95% confidence intervals for standardised incidence using appropriate methods [8].

**Survival analysis**

We performed univariate analyses using Kaplan–Meier methods to compare survival between those aged 80 and over with those <80 years of age.

**Results**

**Demographic features**

We diagnosed 1226 cases of ALS/MND between 1 January, 1989 and 31 December, 1998, of which 135 (11%) were aged 80 or over. Of these 135, 58 were men (43%). Sixty-seven (50%) had bulbar onset disease, 60 (44%) had spinal onset and 8 (3%) were unclassified due to incomplete or ambiguous case records. Females accounted for 47 of 67 (70%) bulbar onset cases, while 30 of 57 (53%) spinal onset were males. A pure lower motor neurone syndrome was recorded in 25 (19%) cases, and only one older person had a family history of the condition.

The median survival in older people was 20 months from onset, with a median time from onset to diagnosis of 10 months. An average patient with ALS/MND in this age group survives <1 year from diagnosis.

**Incidence**

The overall crude incidence was 7.5 cases per 100,000 (95% CI = 6.3–8.9) (Table 1).

Standardised to the US 1990 population, the incidence was 7.3/100,000 (95% CI = 5.8–8.8) overall, 10.2/100,000 (95% CI = 7.3–13.1) in men and 6.1/100,000 (95% CI = 4.3–7.9) in women. There were 12 prevalent cases on 31 December, 1998 (five cases per 100,000 95% CI = 2.5–8.7).

There were 5 nonagenarians diagnosed in the entire decade of study. Two were men, and the longest survivor was a women who lived for 9 months from onset. None of these five patients received Riluzole or had a PEG tube inserted. A nonagenarian with spinal onset, who was assessed by a neurologist, subsequently had a post mortem examination which confirmed ALS/MND pathology. The other nine autopsies in the over 80s were consistent with ALS/MND.

**Process of care**

Only one person over 80 at diagnosis was prescribed Riluzole. The first of 12 PEG tube procedures was performed in 1994. Eighty older patients (59%) had been assessed by a neurologist, 39 (30%) were not managed by neurologists and the degree of involvement in another 11 (8%) patients was unclear.

**Comparisons with people aged <80 years at diagnosis**

Table 2 summarises the main demographic and clinical parameters for those aged 80 and over (n = 135) with those aged <80 years at diagnosis (n = 1091). In the older people, women are numerically over-represented, but the actual standardised incidence is greater in older men. Bulbar onset disease is more likely in older people (OR 1.5 95% CI = 1.3–1.8) but there is no difference in the incidence of pure lower motor neurone syndromes. Median survival is less in older people (P = 0.0003, log rank test). There appears to be a considerable difference in the process of care, with fewer prescriptions of Riluzole and fewer patients being assessed by neurological specialists. There did not appear to be any difference in the rate of PEG tube usage.

### Table 1. Crude and standardised incidence of ALS/MND, Scotland 1989–1998, except where specified

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Cases observed</th>
<th>Crude incidencea per 100,000 (95% CI)</th>
<th>Standardised incidenceb per 100,000 aged 80 years or over (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>108</td>
<td>0.4 (0.2–0.3)</td>
<td>0.3 (0.1–0.2)</td>
</tr>
<tr>
<td>50–59</td>
<td>207</td>
<td>4.2 (3.2–3.7)</td>
<td>3.6 (2.4–2.9)</td>
</tr>
<tr>
<td>60–69</td>
<td>388</td>
<td>8.6 (7.0–7.8)</td>
<td>7.7 (5.7–6.7)</td>
</tr>
<tr>
<td>70–79</td>
<td>386</td>
<td>12.1 (9.9–10.9)</td>
<td>10.2 (7.6–8.8)</td>
</tr>
<tr>
<td>80–84</td>
<td>104</td>
<td>12.0 (8.1–9.9)</td>
<td>10.3 (6.0–7.9)</td>
</tr>
<tr>
<td>85–90</td>
<td>26</td>
<td>7.1 (3.2–4.9)</td>
<td>7.2 (2.7–4.5)</td>
</tr>
<tr>
<td>≥90</td>
<td>5</td>
<td>5.5 (0.7–2.3)</td>
<td>5.1 (0.3–1.7)</td>
</tr>
<tr>
<td>Ireland 1995–1997</td>
<td>135</td>
<td>7.3 (5.8–8.8)</td>
<td>6.1 (4.3–7.9)</td>
</tr>
</tbody>
</table>

a1994 mid-year Scottish population estimate

b1990 US Census population
Table 2. Comparison of clinical features, process of care and survival of people with ALS/MND in Scotland 1989–1998

<table>
<thead>
<tr>
<th>Age at Diagnosis of ALS/MND</th>
<th>Statistical test</th>
</tr>
</thead>
<tbody>
<tr>
<td>280 years</td>
<td>&lt;80 years</td>
</tr>
<tr>
<td>Cases observed</td>
<td>130</td>
</tr>
<tr>
<td>Males</td>
<td>53</td>
</tr>
<tr>
<td>Females</td>
<td>77</td>
</tr>
<tr>
<td>Bulbar</td>
<td>65</td>
</tr>
<tr>
<td>Spinal</td>
<td>57</td>
</tr>
<tr>
<td>LMN*</td>
<td>25</td>
</tr>
<tr>
<td>Mixed UMN-LMN</td>
<td>98</td>
</tr>
<tr>
<td>Riluzole</td>
<td>1</td>
</tr>
<tr>
<td>None</td>
<td>129</td>
</tr>
<tr>
<td>Neurology</td>
<td>80</td>
</tr>
<tr>
<td>Non-neurology</td>
<td>39</td>
</tr>
<tr>
<td>PEG</td>
<td>12</td>
</tr>
<tr>
<td>None</td>
<td>118</td>
</tr>
<tr>
<td>Post mortem</td>
<td>10</td>
</tr>
<tr>
<td>None</td>
<td>120</td>
</tr>
<tr>
<td>Median survival from onset (years)</td>
<td>1.69 (IQR 1.00–2.80)</td>
</tr>
<tr>
<td>Time from onset to diagnosis (years)</td>
<td>0.79 (IQR 0.42–1.50)</td>
</tr>
</tbody>
</table>

LMN = Pure lower motor neurone syndrome; UMN-LMN = Mixed upper motor and lower motor neurone syndrome; PEG = Percutaneous endoscopic gastroenterostomy.

Discussion

This summary of ALS/MND epidemiology in people aged 80 or over is the most comprehensive to date. We found evidence of differences in clinical presentation, survival and process of care compared with younger people with this degenerative disorder.

Bulbar onset disease accounted for at least half of all presentations in this age group and a minority had spinal onset ALS/MND, which is the reverse to the pattern in a population as a whole, irrespective of age at diagnosis. Other large population-based studies consistently find that 30–40% have bulbar onset disease [1, 9]. Older and younger people had similar frequencies of pure lower motor neurone syndromes. Pure lower motor neurone syndromes are important as they may be mimicked by potentially treatable inflammatory disorders such as multi-focal motor neuropathy with conduction block, chronic inflammatory demyelinating polyradiculoneuropathy and inflammatory muscle disease [10–12]—all more prevalent in older people.

It is well known that increasing age at onset predicts worse survival from ALS/MND [13, 14] and this would appear to be true of older patients in Scotland where the duration of ALS/MND in older people is around 5 to 6 months shorter than the average (Table 2). The cause of reduced survival is unclear. It is possible that age-related depletion or degeneration of the motor neurone pool may predispose to ALS/MND but we have no way of testing this hypothesis at present. The higher frequency of bulbar onset may be relevant because this is an independent predictor of poor prognosis in most survival analyses [15–17]. Older patients may have associated conditions, e.g. pulmonary disease, which reduce survival, but it was difficult to collect information about co-morbid conditions in this series. Our data provide some evidence that the process of care for older-people with ALS/MND is quite different from that experienced by younger patients, but it is difficult to know if these explain the difference in survival.

The most striking observation is the low rate of riluzole prescription in older patients. This drug is the only therapy which has ever been shown to modify the natural history of ALS/MND, particularly bulbar onset disease [18, 19]. Studies indicate that Riluzole is tolerated in people with ALS/MND aged over 75 years [20] and the drug is licenced for use in the European Union. However, at the time of the study, many health boards in Scotland were unwilling to make this expensive drug available because of controversy concerning cost utility. This policy may account for the lower prescription rates in the elderly. The National Institute of Clinical Excellence in England and Wales and the Health Technology Board of Scotland have since recommended use for ALS/MND patients and prospective studies will be required to see if prescription rates increase.

Specialist care by a neurologist is probably important, as the differential diagnosis of ALS/MND includes potentially treatable inflammatory diseases, but this older group of patients were less likely to be assessed by a specialist. This may be explained by the relative lack of neurologists in Scotland (<1 per 200,000 population for most of the study period). We would advise that specialist advice is sought when the diagnosis is suspected, and guidelines for patient management are now available [21].

PEG tubes are increasingly used to circumvent feeding difficulties experienced by patients with neurogenic dysphagia, although evidence of benefit is based upon case series and is conflicting [22–24]. In our population, the frequency of PEG tube use was similar to that of younger patients, but one might argue that PEG tube usage should be greater in a population with more bulbar onset disease.

Summary

In a population-based study, we describe ALS/MND in 135 people aged ≥80 years at diagnosis, and show that there are differences in clinical presentation, survival and process of care
care compared with younger patients. Some of these differences in process of care may contribute to the adverse outcomes observed in older people, but evidence should be sought from further prospective evaluations of the process of care.

**Key points**
- The incidence of ALS/MND increases with age.
- Older people with ALS/MND are more likely to have bulbar onset disease.
- Older people with ALS/MND are less likely to see a neurological specialist or be prescribed disease modifying treatment.

**Funding**
The study was funded by the Scottish Motor Neurone Disease Association.

**Conflicts of Interest**
RF has received financial support from Aventis plc (manufacturers of Riluzole) to assist with attendance at a scientific conference. Aventis plc also provided some library support.

**References**


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