Received: 29 June 2020 | Revised: 25 September 2020 | Accepted: 24 October 2020

DOI: 10.1111/ane.13370

ORIGINAL ARTICLE

WILEY

End-of-life care in amyotrophic lateral sclerosis: A comparative registry study

Eva Eljas Ahlberg[1] | Bertil Axelsson[2]

[1]Department of Surgery, Östersund Hospital, Östersund, Sweden

[2]Unit of Clinical Research Centre Östersund, Umeå University, Umeå, Sweden

Correspondence
Eva Eljas Ahlberg, Palliative Care Unit, Department of Surgery, Östersund Hospital, SE-831 83 Östersund, Sweden.
Email: ahlbergeva7@gmail.com

Abstract

Background: Amyotrophic lateral sclerosis (ALS) is a fatal disease requiring palliative care. End-of-life care has been well studied in patients with incurable cancer, but less is known about the quality of such care for patients with ALS.

Aim: To study whether the quality of end-of-life care the last week in life for patients dying from ALS differed compared to patients with cancer in terms of registered symptoms, symptom management, and communication.

Design: This retrospective comparative registry study used data from the Swedish Registry of Palliative Care for 2012–2016. Each patient with ALS (n = 825) was matched to 4 patients with cancer (n = 3,300).

Results: Between-group differences in assessments for pain and other symptoms were significant ($p < 0.01$), and patients with ALS had fewer as-needed injection drugs prescribed than patients with cancer. Patients with ALS also had dyspnea and anxiety significantly more often than patients with cancer. There was no significant difference in communication about transition to end-of-life care between the two groups. Patients dying from ALS received artificial nutrition on their last day of life significantly more often than patients with cancer.

Conclusions: The results indicate that patients with ALS receive poorer end-of-life care than patients dying from cancer in terms of validated symptom assessments, prescription of as-needed drugs, and timely cessation of artificial nutrition. Educational efforts seem needed to facilitate equal care of dying patients, regardless of diagnosis.

KEYWORDS
amyotrophic lateral sclerosis, palliative care, quality indicators, terminal care

1 | INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a fatal disease, with degeneration of upper and lower motor neurons and a high burden of symptoms not unlike that of cancer.[1] Supportive interventions including multidisciplinary care and optimization of symptom treatments have improved quality of life for these patients and palliative care remains the cornerstone of ALS management.[2-10]

Cancer is the dominant diagnosis in specialized palliative care, but ALS has traditionally been the main non-cancer diagnosis admitted to specialized palliative care. Compared to cancer, relatively few studies, often with a small number of patients, have focused on the end-of-life phase in patients with ALS.[11-22] Palliative care should be provided according to need, regardless of diagnosis. Previous studies have shown that patients with non-malignant conditions such as heart disease, dementia, and stroke are more likely to have unmet palliative care needs than patients with cancer.[23-26] No study has previously addressed this issue for subjects with ALS.

The objectives of this study were [1] to investigate whether end-of-life care and symptom prevalence differed in the last week of

life between patients dying from ALS and those dying from cancer and [2] to learn more about place of death for patients with ALS in Sweden.

2 | METHODS

This was a retrospective comparative registry study using data from the Swedish Registry of Palliative Care (SRPC).

The SRPC, started in 2005, is a national quality register for end-of-life care for all deaths in Sweden.[27] The register has been evaluated, validated, and revised.[28,29] Data are registered post-mortem by health care staff in a 30-question web-based end-of-life questionnaire (ELQ) that focuses on the last week of life. All questions must be answered for the form to be submitted, ensuring no missing data. This study focused on some of the quality indicators defined by the Swedish National Board of Health and Welfare.[30]

2.1 | Primary research question

Did the proportions of patients with ALS and those with cancer differ in validated assessments for pain and other symptoms in the last week of life?

2.2 | Secondary research questions

Did the proportions of patients and next of kin with documented communication about transition to end-of-life care differ between patients with ALS and those with cancer?

Did the proportions of patients using artificial nutrition at the time of death differ between the two diagnostic groups?

Were patients with ALS prescribed as-needed injection drugs differently to those with cancer?

Did the prevalence of various symptoms in the last week of life differ between patients with ALS and patients with cancer?

What place of death was registered for patients with ALS?

2.3 | Ethics statement

This study conforms to the principles of the Helsinki declaration, and the Regional Ethics Committee in Umeå had no objections to the research (2018/14-31).

2.4 | Power analysis

To detect a numerical 10 percentage difference in the proportions between the studied diagnostic groups with a level of significance of $p < 0.01$ and power of 0.8, the study would require about 600 patients per group. To get a sufficient sample, we chose data on all patients with ALS and cancer who were registered in the SRPC during 2012–2016.

2.5 | Study population

Patients who had neurological disease as the main cause of death in the SRPC database in 2012–2016 were linked using unique personal identification numbers to the Swedish Cause-of-Death Register at the Swedish National Board of Health and Welfare. Patients with the diagnosis ALS (ICD G12.2) reported as the main or underlying cause of death were included and data were immediately anonymized by removing names and personal identification numbers.

Patients reported to the SRPC during 2012–2016 who had ALS as the main or underlying cause of death in the Cause of Death Register were included in the study sample. The deaths had to be registered as "expected." Patients with cancer reported as the main or underlying cause of death in the SRPC during the same period were chosen as controls.

Exclusion criteria for both groups were patients with more than one registered underlying cause of death and patients who, according to the SRPC data, had lost their ability to communicate for a month or more before death (Figure 1).

Places of end-of-life care were categorized as general home care, specialized palliative home care, short-term and permanent-stay nursing home, hospital, and hospice/specialized palliative in-ward unit.

A professional statistician matched each patient with ALS (n = 825) to 4 patients with cancer (n = 3,300), according to place of end-of-life care, gender, age, and county in Sweden (21 different counties). Chi2-test, and when appropriate Fisher's exact test, was used for differences in proportions of categorical variables. The statistics were done as 2-sided tests with $p < 0.01$ considered statistically significant. All analyses were performed using SPSS version 24.

3 | RESULTS

The Swedish Cause-of-Death Register listed 1599 patients with ALS in 2012–2016. A total of 101 321 patients with cancer and 1116 patients with ALS were registered in the SRPC database during the same period for a coverage ratio of 70% in ALS. A total of 825 deaths from ALS (Figure 1) and 3300 deaths from cancer (50.5% men, 49.5% women) were included according to study criteria. The mean age was 70.7 for ALS group and 70.8 for the control group (Table 1).

Patients with ALS were found to have a lower probability than those with cancer of being assessed for pain: 27.9% versus 43.2%, $p < 0.001$ (Table 2). The proportion of patients with ALS who were assessed for other symptoms on a validated scale (16.7%) was also significantly lower than patients with cancer (21.5%), $p < 0.01$.

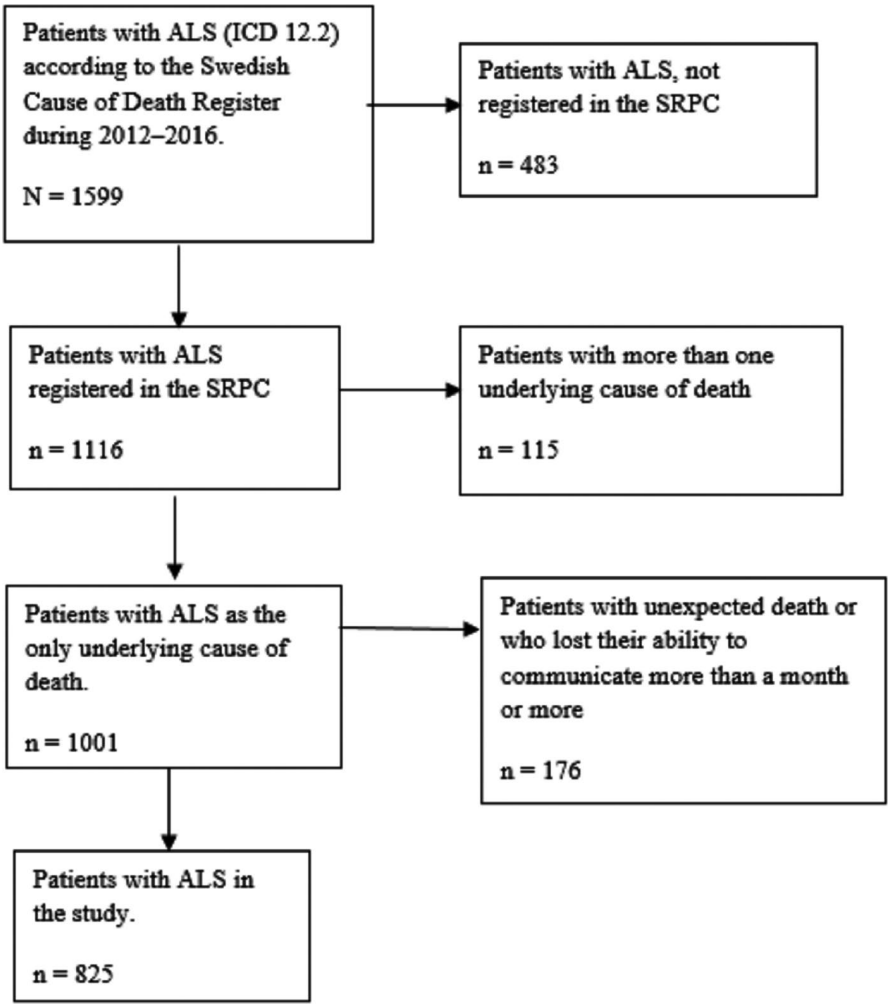

FIGURE 1 Inclusion of patients with ALS in the study population.

There were no significant differences between the two groups regarding communication about transition to end-of-life care with patients and next of kin. Patients dying from ALS received artificial nutrition significantly more often than patients with cancer on their last day of life (39.5% vs. 14.8%, $p < 0.001$).

Patients with ALS were less likely than those with cancer to have injection drugs prescribed as needed, and the greatest difference in injection drugs for nausea and pain (Table 2).

There were between-groups differences in symptoms (Figure 2), although all six symptoms were reported in both groups. More patients with ALS than with cancer had dyspnea (57.5% vs. 23.0%) and anxiety (64.6% 53.5%, $p < 0.001$). Patients with cancer, on the other hand, had more pain, confusion, and nausea ($p < 0.001$). About half (49.7%) of patients with ALS were reported to have pain versus 82.5% of patients with cancer.

Of the 1116 patients dying from ALS registered in SRPC during the study period, 307 (28%) died at home, and 206 of these (67%) had support from specialized palliative home care; 371 (34%) died in hospital and 187 (16%) in hospice or on a specialized palliative ward (Figure 3). Patients with ALS were a little less likely to have support from specialized palliative than patients with cancer (35% vs 40%, Figure 4).

4 | DISCUSSION

To continue the improvement of palliative care of patients with neurological diseases there is a need for further studies of the specific diseases [13,14] The study by Ozanne et al.[14] with data from the SRPC indicates high symptom burden and a clear need for improvement of the palliative care in the last week for patients with neurological diseases, including ALS. This large population-based register study is the first to compare some of the key indicators of quality of end-of-life care between patients with ALS and patients with cancer, regardless of level of care. An essential part of palliative care is to assess symptoms and continually evaluate symptom management. The Swedish guidelines from the National Board of Health and Welfare[30] set target levels for several of the quality indicators, which are documented in the SRPC. For example, pain should be assessed for all patients. In this study, symptoms were assessed with validated instruments in only 27.9% of patients with ALS. Even in patients with cancer, who are well-known to suffer pain, only 43.2% were assessed on a validated pain scale. This is far from the goal, and there is definitely potential for improvement. There was also a significant between-group difference in

TABLE 1 Demographic data of the study population.

Variables	ALS *n* = 825 (%)	Cancern =3,300 (%)
Age		
0–54	66 (8.0)	264 (8.0)
55–64	138 (16.7)	552 (16.7)
65–74	304 (36.8)	1216 (36.8)
75–84	244 (29.6)	976 (29.6)
85+	73 (8.8)	292 (8.8)
Gender		
Female	408 (49.5)	1632 (49.5)
Male	417 (50.5)	1668 (50.5)
Time for loss of ability to communicate		
Retained ability	198 (24.0)	389 (11.8)
Hours	301 (36.5)	1047 (31.7)
Day/days	271 (32.8)	1659 (50.3)
Week/weeks	55 (6.7)	205 (6.2)

assessments of other symptoms, but the difference was less than 10%, so the clinical value of this result is more uncertain. About 80% of the patients in both groups had no symptom assessment (other than pain) on a validated scale within the last week. One reason could be that patients very near death are too tired or have communicative difficulties that make symptom evaluation challenging. It was not possible to get information about for example bulbar onset, hand weakness or ventilation support out of the SRPC, factors that could affect the ability to communicate. Although there is lacking information about the exact number, very few patients with ALS were on invasive ventilation in Sweden during the years 2012–2016.

And as shown in Table 1, 93.3% of the patients with ALS in this study had retained their ability to communicate up to less than a week before their death; therefore, it should have been possible to assess their symptoms. Clearly, the need remains for educational interventions to improve symptom assessments, regardless of diagnosis and place of end-of-life care, to make the palliative care more equal, and to upgrade its quality.

Communication with patients and families is an important part of palliative care. Previous studies comparing end-of-life care for patients with non-malignant diseases and patients with cancer have shown differences in communication about transition to end-of-life care, with poorer outcomes for patients with non-malignant diseases.[24-26] In contrast, in this study, there was no significant difference in documented break-point communication between patients with ALS and those with cancer. This lack of difference may be due either to ALS patients' traditionally getting more specialized palliative care than those with other non-malignant diseases or to the fact that ALS is considered a progressive disease with a short prognosis from the time of diagnosis. Communicating about the severity and prognosis of the disease is an established and integrated part of care, and staging points such as the introduction of feeding tubes or non-invasive ventilation can prompt end-of-life discussions.[31]

TABLE 2 Comparison of quality indicators for patients with ALS and patients with cancer.

Variables	ALS *n* = 825	%	Cancer *n* = 3,300	%	*p*-value
Pain assessment with validated scales					
Yes	230	27.9	1426	43.2	<0.001
No	535	64.8	1687	51.1	
Unknown	60	7.3	187	5.7	
Symptom assessment (other than pain) with validated scales					
Yes	138	16.7	709	21.5	0.002
No	619	75.0	2289	69.4	
Unknown	68	8.2	302	9.2	
End-of-life discussion with patient					
Yes	603	73.1	2504	75.9	0.104
No	129	15.6	473	14.3	
Unknown	93	11.3	323	9.8	
End-of-life discussion with next of kin					
Yes	671	81.3	2740	83.0	0.093
No	83	10.1	267	8.1	
Unknown	69	8.4	256	7.8	
Had no next of kin	2	0.2	37	1.1	
Artificial nutrition supply during last day in life					
Yes	326	39.5	490	14.8	<0.001
No	485	58.8	2786	84.4	
Unknown	14	1.7	24	0.7	
Individual injection prescription for symptom relief					
Pain					
Yes	729	88.4	3188	96.6	<0.001
No	91	11.0	107	3.2	
Unknown	5	0.6	5	0.2	
Rattles					
Yes	720	87.3	2999	90.9	0.003
No	98	11.9	287	8.7	
Unknown	7	0.8	14	0.4	
Anxiety					
Yes	725	87.9	3044	92.2	<0.001
No	91	11.0	242	7.3	
Unknown	9	1.1	14	0.4	
Nausea					
Yes	564	68.4	2811	85.2	<0.001
No	242	29.3	462	14.0	
Unknown	19	2.3	27	0.8	

In this study, 39.5% of patients with ALS had parenteral fluid or nutrition supply on their last day of life versus 14.8% in the cancer group. The last is consistent with a study by Martinsson et al.[26] and may reflect adequate care, but it could also be due to difficulties in

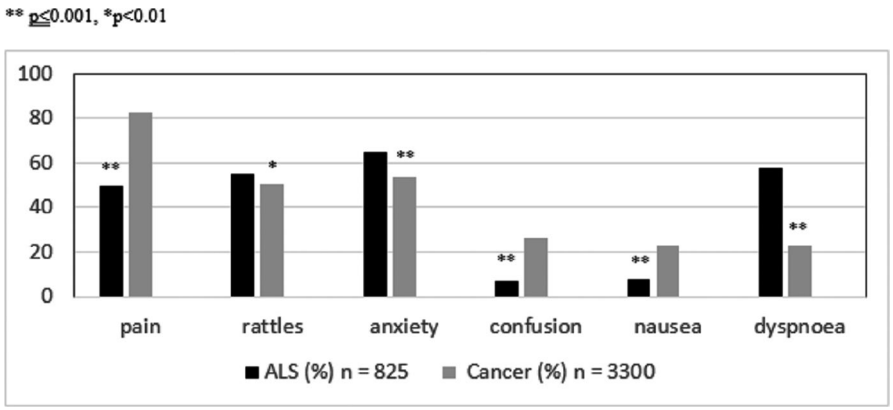

FIGURE 2 Symptom prevalence during the last week in life.

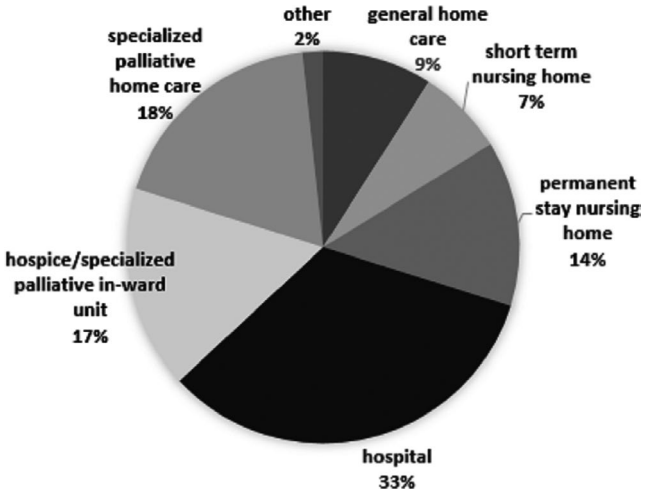

FIGURE 3 Place of end-of-life care (death) for patients with ALS (*n* = 1,116) registered in SRPC during the years 2012–2016.

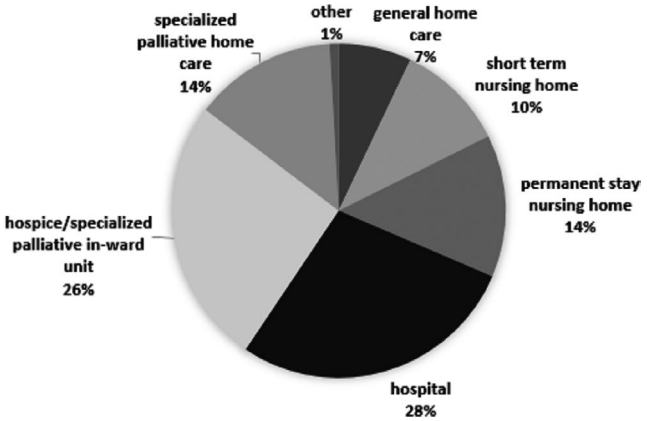

FIGURE 4 Place of end-of-life care (death) for patients with cancer (*n* = 101,321) registered in SRPS during the years 2012–2016.

decision-making and the uncertainty of diagnosing imminent death in patients with ALS. The Swedish national guidelines for palliative care recommend that intravenous fluids and nutrition should be used only rarely for patients with a short expected survival.[32] An earlier study has shown that dyspnea occurs more often when patients with mixed diagnoses have intravenous fluids or nutrition in their last days of life; it is not unlikely to be a worsening factor for patients with ALS, too.[33] Further studies are needed to identify prognostic factors in the final days of life to find the best treatment and the optimal time to decrease and finally withdraw therapies such as nutrition and antibiotics as they become inappropriate.

Prescriptions of necessary injection drugs for pain were statistically significantly less for patients with ALS than for patients with cancer (88.4% vs 96.6%) who were prescribed closer to the National Board of Health and Welfare's target level of >98%.[30] There is a possibility that patients with a PEG in place at time of death to a greater extent receive their drugs enterally. Patients with ALS also were less likely to be prescribed injection drugs against nausea, possibly because of their lower prevalence of nausea. (Figure 2). The lower frequency of as needed medication in ALS patients may partly be affected by difficulties to express needs, because of weakness and bulbar symptoms but as 93.3% were reported to have retained their ability to communicate, we assume that this has not been a substantial confounder in this study. It could be secondary to the caregivers lacking understanding of the symptom load and importance of symptom assessment in patients with ALS.

Both groups of patients were reported to have had high symptom loads. Anxiety followed by dyspnea was the most frequently registered combination of symptoms in patients dying from ALS. Neudert et al. investigated the terminal phase of 121 patients with ALS by telephone interviews with the relatives. They concluded that the majority died peacefully (around half of the patients died at home).[16] In contrary to our study, only 20–30% were reported to have dyspnea and 6–8% anxiety and restlessness.[16] In an earlier study by Ganzini et al.[34] caregivers reported that 56% of patients with ALS had dyspnea, similar to the findings in this study (57.5%), but only 30% were reported to have anxiety in the last month of life compared with the 64.6% in our study who had anxiety in the last week. This difference may be due to the different timeframe (last week vs. last month) or differences in the patient cohorts.

Pain with ALS worsens patients' quality of life and is underestimated as a clinical problem. It is poorly identified and can be a clinical challenge due to its numerous pathophysiological mechanisms.[35]

A noteworthy result was that almost half the patients with ALS were reported to have pain, but only 27.9% were assessed on a validated pain scale. This could raise questions about the validity of the registration. Earlier studies with smaller number of patients have shown a prevalence of pain in a wide range between 15 and 80%.[36-40]

A prior study[34] indicated that 10% of patients with ALS were reported to have confusion the last month in life. This is in line with our findings that 7% of patients with ALS were reported as confused the last week of life compared with 26.1% of those with cancer ($p < 0.001$). Whether or not ALS patients had other symptoms, not asked in the end-of-life questionnaire, but of greater impact, is a question still to be answered. An earlier study by Chochinov et al.[19] showed that patients with ALS reported more dignity-related distress, such as feeling like a burden, feeling a loss of control, and feeling weak and fatigued than other non-cancer populations. Those parameters were not open to investigation in this study. Further studies on patients' subjective experiences are needed to increase our knowledge about other end-of-life symptoms in patients with ALS.

In this study, the most common place of death for patients with ALS was in hospital, followed by home with support from specialized palliative home care, in line with the results from Ozanne et al, another study from the SRPC.[14] In a study from Taiwan[41] most patients with ALS died in a medical facility in contrast to Italy[42] and southwest China,[43] where most patients died at home. In a Spanish study,[44] 56.1% of 1035 patients with ALS died in a hospital and 30.4% died at home, which is more similar to our findings. Disparities between countries are likely due to both cultural and structural differences.

4.1 | Methodological considerations/ strengths and limits

First, this study was observational and retrospective in design, which means its results should be regarded more as hypothesis generating. There might be a selection bias in the SPRC with a preference for units particularly interested in palliative care. The coverage is nearly 100% in the Swedish Cause-of-Death Register, but is less in the SRPC. Another disadvantage of a registry study is the limited background information available such as ethnicity, comorbidity, and socioeconomic status, which might have affected the results of the study.

In addition, the questionnaires are completed retrospectively and might not always be accurate, so recall bias could affect the results. All symptoms are registered by staff, and so might differ from patients' subjective experiences. Another limitation is that only six predefined symptoms are available to register in the ELQ. Other important symptoms may thus be omitted.

We chose patients with cancer as the comparative group for patients with ALS as if they represent a kind of "gold standard" for palliative care. Previous studies have shown that patients with cancer receive better end-of-life care than patients with other diagnoses,[24-26] but the clinical relevance of that might be debated. Of course, there are differences between patients dying from ALS and patients dying from cancer, but the suffering and the burden of symptoms can be high in both groups, justifying equality in palliative care.

The validity of the ELQ has been evaluated repeatedly, which lends strength to the study. A limitation is that these validation studies have been performed in a specialized palliative care,[28,29] but not in other healthcare settings. There is a possibility that staff at specialized palliative care units interpret questions differently from staff at other healthcare units. To eliminate this confounding factor, the patients were matched according to place for end-of-life care in this study.

Palliative care is not the same or equally available across Sweden. A strength of this study was our matching of each patient with ALS with 4 patients with cancer, according not only to gender, age, and place of end-of-life care, but also to the different counties in Sweden to reduce this confounding factor.

This study is to our knowledge it is the largest yet published in terms of the number of patients with ALS. Our results may be valid for the Swedish setting, but differences in health care and end-of-life care between countries may limit generalizability to other countries.

5 | CONCLUSION

Our results indicate that patients with ALS may receive poorer end-of-life care than patients with cancer in terms of assessments of pain and other symptoms and prescription of as-needed injection drugs. Artificial nutrition at time of death was much more common in patients with ALS than those with cancer. Anxiety and dyspnea followed by pain were the most common symptoms during the last week in life in patients with ALS. There is a need for more studies and educational interventions to improve the quality of end-of-life care and to make it more equal, regardless of diagnosis and level of care.

ACKNOWLEDGEMENTS

The authors wish to thank Björn Tavelin (statistician) for his valuable help and comments.

CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data used in this study can be received from the Swedish Registry of Palliative Care.

ORCID

Eva Eljas Ahlberg https://orcid.org/0000-0003-0388-5521

REFERENCES

1. Foster LA, Salajeghej MK. Motor neuron disease: pathophysiology, diagnosis, and management. *Am J Med*. 2019;*132*(1):32-37.

2. Andersen PM, Abrahams S, Borasio GD, de Carvalho M, Chio A, Van Damme P. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)—revised report of an EFNS task force. *Eur J Neurol*. 2012;*19*(3):360-375.
3. Oliver DJ. Palliative care for patients with motor neuron disease: current challenges. *Degener Neurolo Neuromuscul Dis*. 2016;*6*:65-72.
4. Hogden A, Foley G, Henderson RD, James N, Aoun SM. Amyotrophic lateral sclerosis: improving care with a multidisciplinary approach. *J Multidiscip Healthc*. 2017;*10*:205-215.
5. Cheng HWB, Chan KY, Chung YKJ, et al. Supportive & palliative interventions in motor neuron disease: what we know from current literature? *Ann Palliat Med*. 2018;*7*(3):320-331.
6. Ng L, Khan F, Young CA, Galea M. Symptomatic treatments for amyotrophic lateral sclerosis/motor neuron disease. *Cochrane Database Syst Rev*. 2017;1:CD011776.
7. Ng L, Khan F. Multidisciplinary care for adults with amyotrophic lateral sclerosis or motor neuron disease. *Cochrane Database Syst Rev*. 2009;4:CD007425.
8. Martin S, Trevor-Jones E, Khan S, et al. The benefit of evolving multidisciplinary care in ALS: a diagnostic cohort survival comparison. *Amyotroph Lateral Scler Frontotemporal Degener*. 2017;*18*:569-575.
9. Van den Berg JP, Kalmijn S, Lindeman E, et al. Multidisciplinary ALS care improves quality of life in patients with ALS. *Neurology*. 2005;*65*:1264-1267.
10. Borasio GD. The role of palliative care in patients with neurological disease. *Nat Rev Neurol*. 2013;*9*:292-295.
11. Borasio GD, Volts R. Palliative care in amyotrophic lateral sclerosis. *J Neurology*. 1997;*244*(Suppl 4):S11-S17.
12. Oliver DJ. The quality and care of symptom control-the effects on the terminal phase of ALS/MND. *J Neurol Sci*. 1996;*139*(suppl):134-136.
13. Oliver DJ, Borasio GD, Caraceni A, et al. A concensus review on the development of palliative care for patients with chronic and progressive neurological disease. *Eur J Neurol*. 2016;*23*:30-38.
14. Ozanne A, Sawatsky R, Håkansson C, et al. Symptom relief during last week of life in neurological diseases. *Brain Behav*. 2019;*9*:e01348.
15. Connolly S, Galvin M, Hardiman O. End-of-life management in patients with amyotrophic lateral sclerosis. *Lancet Neurol*. 2015;*14*:435-442.
16. Neudert C, Oliver D, Wasner M, Borasio GD. The course of the terminal phase in patients with amyotrophic lateral sclerosis. *J Neurol*. 2001;*248*:612-616.
17. Cheng HWB, Chan OMI, Chan CHR, Chan WH, Fung KS, Wong KY. End-of-life characteristics and palliative care provision for patients with motor neuron disease. *Am J Hosp Palliat Care*. 2018;*35*(6):847-851.
18. Bentley B, O'Connor M. The end-of life experiences of people with motor neuron disease: family carers' perspectives. *J Palliat Med*. 2016;*19*(8):857-862.
19. Chochinov HM, Johnston W, McClement SE, et al. Dignity and distress towards the end of life across four non-cancer populations. *PLoS One*. 2016;*25*:1-13.
20. Rudnicki S, McVey AL, Jackson CE, Dimachkie MM, Barohn RJ. Symptom management and end of life care. *Neurol Clin*. 2015;*33*:889-908.
21. Karam CHY, Paganoni S, Joyce N, Carter GT, Bedlack R. Palliative care issues in amyotrophic lateral sclerosis: an evidenced-based review. *Am J Hosp Palliat Med*. 2016;*33*:84-92.
22. Burkhardt C, Neuwirth C, Sommacal A, Andersen PM, Weber M. Is survival improved by the use of NIV and PEG in amyotrophic lateral sclerosis (ALS)? A post-mortem study of 80 patients. *PLoS One*. 2017;*12*:e0177555.
23. Tiirola A, Korhonen T, Suurakka T, Lehto JT. End-of-life care of patients with amyotrophic lateral sclerosis and other nonmalignant disease. *Am J Hosp Palliat Med*. 2017;*34*:154-159.
24. Brännström M, Hägglund L, Furst CJ, Boman K. Unequal care for dying patients in Sweden. A comparative registry study of deaths from heart disease and cancer. *Eur J Cardiovasc Nurs*. 2012;*11*:454-459.
25. Eriksson H, Milberg A, Hjelm K, Friedrichsen M. End of life care for patients dying from stroke. A comparative registry study of stroke and cancer. *PLoS One*. 2016;*11*:e0147694.
26. Martinsson L, Lundström S, Sundelöf J. Quality of end-of-life care in patients with dementia compared to patients with cancer: a population-based registry study. *PLoS One*. 2018;*13*(7):e0201051. https://doi.org/10.1371/journal.pone.0201051
27. Lundström S, Axelsson B, Heedman P-A, Fransson G, Fürst C-J. Developing a national quality register in end-of-life care: the Swedish experience. *Palliat Med*. 2012;*26*:313-321.
28. Martinsson L, Heedman P-A, Lundström S, Fransson G, Axelsson B. Validation study of an end-of-life questionnaire from the Swedish Register of Palliative Care. *Acta Oncol*. 2011;*50*:642-647.
29. Martinsson L, Heedman P-A, Lundström S, Axelsson B. Improved data validity in the Swedish Register of Palliative Care. *PLoS One*. 2017;*12*(10):e0186804.
30. Socialstyrelsen [National Board of Health and Welfare]. Nationella riktlinjer-Palliativ vård i livets slutskede-Målnivåer för indikatorer [National guidelines-palliative end-of-life care-goal levels for indicators]. Stockholm: Socialstyrelsen; 2017. Swedish.
31. National institute for Health and Care Excellence. NICE Guidance on Motor Neurone disease; 2016. NICE. www.nice.org.nk/NG42. Accessed February 24, 2016.
32. Regionala cancercentrum i samverkan [Regional Cancer Centre in Collaboration]. Nationellt vårdprogram palliativ vård i livets slutskede [National guidelines palliative end-of-life care]. Regionala cancercentrum i samverkan; 2016. Swedish.
33. Fritzon A, Tavelin B, Axelsson B. Association between parenteral fluids and symptoms in hospital end-of-life care: an observational study of 280 patients. *BMJ Support Palliat Care*. 2013;*5*(2):160-168.
34. Ganzini L, Johnston WS, Silviera MJ. The final month of life in patients with ALS. *Neurology*. 2002;*59*:428-431.
35. Ishida N, Hongo S, Kumano A, et al. Relationship between pain and functional status in patients with amyotrophic lateral sclerosis: a multicenter cross-sectional study. *J Palliat Med*. 2018;*21*(5):588-591.
36. Lopes LCG, Galhardoni R, Silva V, et al. Beyond weakness: characterization of pain, sensory profile and conditioned pain modulation in patients with motor neuron disease: a controlled study. *Eur J Pain*. 2018;*22*:72-83.
37. Pizzimenti A, Aragona M, Onesti E, Inghilleri M. Depression, pain and quality of life in patients with amyotrophic lateral sclerosis: a cross-sectional study. *Funct Neurol*. 2013;*28*:115-119.
38. Hanisch F, Skudlarek A, Berndt J, Kornhuber ME. Characteristics of pain in amyotrophic lateral sclerosis. *Brain Behav*. 2015;*5*:e00296.
39. Stephens HE, Lehman E, Raheja D, et al. Pain in amyotrophic lateral sclerosis: patient and physician perspectives and practices. *Amyotroph Lateral Scler Frontotemporal Degener*. 2016;*17*:21-29.
40. Rivera I, Ajroud-Driss S, Casey P, et al. Prevalence and characteristics of pain in early and late stages of ALS. *Amyotroph Lateral Scler Frontotemporal Degener*. 2013;*14*:369-372.
41. Tsai C-P, Chang B-H, Lee CT-C. Underlying cause and place of death among patients with amytrophic lateral sclerosis in Taiwan: a population-based study, 2003–2008. *J Epidemiol*. 2013;*23*(6):424-428.
42. Spataro R, Lo Re M, Piccoli F, La Bella V. Causes and places of death in Italian patients with amyotrophic lateral sclerosis. *Neurologica*. 2010;*122*:217-223.

43. Yang R, Huang R, Chen D, et al. Causes and places of death of patients with amyotrophic lateral sclerosis in Southwest China. *Amyotroph Lateral Scler*. 2011;*12*(3):206-209.
44. Domínguez-berjón MF, Esteban-Vasallo MD, Zoni AC, Gènova-Maleras R, Astray-Mochales J. Place of death and associated factors among patients with amyotrophic lateral sclerosis in Madrid (Spain). *Amyotrophic Lateral Scler Frontotemporal Degener*. 2016;17:62-68.

How to cite this article: Eljas Ahlberg E, Axelsson B. End-of-life care in amyotrophic lateral sclerosis: A comparative registry study. *Acta Neurol Scand*. 2020;00:1–8. https://doi.org/10.1111/ane.13370