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ORIGINAL COMMUNICATION

Euthanasia and physician-assisted suicide in amyotrophic lateral sclerosis: a prospective study

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Abstract The objective of this study is to determine if quality of care, symptoms of depression, disease characteristics and quality of life of patients with amyotrophic lateral sclerosis (ALS) are related to requesting euthanasia or physician-assisted suicide (EAS) and dying due to EAS. Therefore, 102 ALS patients filled out structured questionnaires every 3 months until death and the results were correlated with EAS. Thirty-one percent of the patients requested EAS, 69 % of whom eventually died as a result of EAS (22 % of all patients). Ten percent died during continuous deep sedation; only one of them had explicitly requested death to be hastened. Of the patients who requested EAS, 86 % considered the health care to be good or excellent, 16 % felt depressed, 45 % experienced loss of dignity and 42 % feared choking. These percentages do not differ from the number of patients who did not explicitly request EAS. The frequency of consultations of professional caregivers and availability of appliances was similar in both groups. Our findings do not support continuous deep sedation being used as a substitute for EAS. In this prospective study, no evidence was found for a relation between EAS and the quality and quantity of care received, quality of life and symptoms of depression in patients with ALS. Our study does not support the notion that unmet palliative care needs are related to EAS.

Keywords Depression · Euthanasia · Physician-assisted death · Palliative care

Introduction

The majority of the patients who request EAS have cancer [22]. Patients with amyotrophic lateral sclerosis (ALS), however, are a well-known and frequently used example in case studies [2] and television broadcasts on euthanasia. ALS is characterized by progressive degeneration of motor

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neurons and the clinical hallmarks are progressive limb weakness, respiratory failure and bulbar palsy [19]. The majority of patients die within 5 years after onset of the disease, usually due to respiratory insufficiency [6].

Since there is no cure for ALS; specialized palliative care is the best treatment available [20]. We examined retrospectively the actual end-of-life practices performed in patients with ALS over the periods 1994–1998 [32] and 2000–2005 [15] and found that 20 % died as a result of EAS, a percentage which was said to be unacceptably high [7]. In relation to this, the quality and availability of palliative care in The Netherlands has been questioned [16]. It is suggested that identifying patients with a wish for EAS early on in the course of their illness will enable an intervention and that intensive palliative treatment will reduce the interest in euthanasia [7].

In view of these grave concerns and the relatively high proportion of EAS in ALS patients in The Netherlands, we performed a prospective study on factors that may influence the attitude towards EAS and a final decision for EAS in ALS patients. The objective of this study is to determine if quality of care, depression, quality of life, coping style, and characteristics of the disease of ALS patients are related to requesting EAS and dying as a result of EAS.

Methods

Study design

Participating patients completed questionnaires every 3 months until death. The follow-up consisted of a selection of the questionnaires that were used at baseline. The follow-up questionnaires that were completed closest to the patient's death were used for the analyses. When the patient died, the treating physician filled in a questionnaire in which end-of-life practices and received requests were documented.

All physician questionnaires were self-administered. The patients self-administered all except three questionnaires (ALSFRS-r, CIDI, MMSE). If the patient was physically unable to fill in a questionnaire that was supposed to be self-administered, a trained interviewer helped the patient complete all the questionnaires at home.

Participants

One hundred and ninety-two ALS patients were selected through the three national referral centers for amyotrophic lateral sclerosis (University medical center of Utrecht, University medical center of Amsterdam, the Radboud university medical center of Nijmegen). All patients were diagnosed with probable or definite ALS [3], understood the Dutch language, could communicate at least "yes" and "no", were not dependent on tracheotomy with mechanical ventilation, did not have a severe cognitive impairment, had no clinical diagnosis of frontotemporal dementia, had a life expectancy of 6 months or less and ultimately died during the study. Life expectancy estimates were based on clinical appraisal by a neurologist specialized in ALS and a forced vital capacity of less than 60 % [18]. One hundred and thirty-six (71 %) of the 192 selected patients agreed to participate. Seventeen of these patients left the study early, because they felt too tired. Three patients developed severe cognitive impairment and fourteen patients survived the period until closure of the study and were, therefore, excluded. All included patients ($n = 102$) died from October 2003 to March 2008. The 56 non-responders and the 34 patients who dropped out or who were excluded from the study did not differ with regard to sex, age or site of onset of the disease from the 102 participants.

Characteristics of patients

Demographic and disease characteristics were collected from the patients' medical files. Stage of disease was assessed using the revised ALS functional rating scale (ALSFRS-r) [4]. The patients' symptoms were measured using a structured questionnaire based on the format applied in a nationwide survey [23].

We examined how the patient coped using the Utrecht Coping List (UCL) [21, 26]. The Mini Mental State Examination (MMSE) was performed to test for severe cognitive impairment [5].

End-of-life practices

The questions for the physicians on end-of-life practices were based on the questionnaire of the nationwide survey containing medical end-of-life practices [23]. In these questions we avoided the terms "euthanasia", "physician-assisted suicide" and "sedation", because their connotations are too varied. Instead, we used wording that describes more closely actual medical practice, permitting us to classify the answers in the categories defined here. Euthanasia was defined as the administration of drugs with the explicit intention of ending the patient's life, at the patient's explicit request. Physician-assisted suicide was defined as the prescription or supplying of drugs with the explicit intention of enabling the patient to end his or her own life. Continuous deep sedation (CDS) was defined as the administration of drugs to keep the patient in deep sedation or coma until death.

If a physician reported more than one end-of-life practice, only the practice considered to have the greatest potential to influence the hastening of a patient's death was

included in the analysis [23]. The practices in order of decreasing influence were: (1) EAS, (2) withholding or withdrawing medical treatment with the explicit intention of hastening death, (3) intensified alleviation of pain or symptoms while taking into account the possible hastening of death, and (4) withholding or withdrawing medical treatment while taking into account the possible hastening of death. CDS was not categorized under end-of-life practices, but was treated as a separate practice [23]. We chose to categorize CDS differently from "the intensified alleviation of pain or symptoms while taking into account the possible hastening of death", because the explicit goal of CDS is to remedy otherwise untreatable symptoms and not to hasten death.

Symptoms of depression and quality of life

In end-stage patients with ALS, symptoms of a depression according to the DSM-IV may overlap with symptoms of ALS, which may result in an over-estimation of depression [17]. We, therefore, used a short version of the Composite International Diagnostic Interview (CIDI) and the Hospital Anxiety and Depression Scale (HADS) which does not include questions on somatic symptoms and which has also been used in previous studies [1, 11]. A HADS symptom of depression score of 11 or more is considered to be an indication of a possible depression and an anxiety score of 10 or more as an indication of anxiety [8]. The CIDI is positive for 'depression' if the patient had depressive feelings or diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day for a minimum of two consecutive weeks. Finally, depressive symptoms were assessed by asking the patients: have you felt depressed during the last 3 months [13]?

Quality of life was measured using the 40-item ALS assessment questionnaire (ALSAQ-40) on a five-point scale [14].

Characteristics of care

We used the patient version of the Palliative Outcome Scale (POS) to assess quality of care characteristics [10]. All questions on received care, as shown in Online Appendix Table 5, were assessed using a structured questionnaire based on a previous ALS study on quality of care [29].

Statistical analysis

Chi-square test was used to analyze differences between the patients who explicitly requested EAS and those who did not. Fisher's exact test was used when cells had an expected frequency of less than five. For differences in continuous variables, the Mann–Whitney U test was used to calculate significance. The above analyses were also performed for patients who actually died as a result of EAS and those who did not. The 11 patients who suddenly died unexpectedly were excluded from these analyses as they were not able to opt for EAS [23].

All tests were two-sided, and a p value of less than 0.05 was considered to indicate statistical significance. Missing values ranged from 0 to 10.

Results

Characteristics of patients

The characteristics of the 102 participants are presented in Table 1. Thirty-two patients (31 %) explicitly approached their physician with a request for EAS between one and 72 weeks prior to their death (median 9 weeks). There were no significant differences in the stage of disease, experienced symptoms or coping styles between patients who explicitly requested EAS and those who did not.

End-of-life practices

Table 2 presents the end-of-life practices that were actually performed, showing that 22 percent of the patients died as a result of EAS. Ten percent died during continuous deep sedation, which was in conjunction with 'intensified alleviation of symptoms' or 'withholding medical treatment' in nine patients. One patient received artificial fluids and nutrition during sedation. Only one of the ten patients who died during continuous deep sedation had made an explicit request for EAS.

Table 3 presents the outcome of the 32 patients who explicitly approached their physician with a request for EAS. Ten patients' requests were not acted upon because four patients died before EAS could be performed, four died during the decision-making process, and two withdrew their request.

Symptoms of depression and quality of life

No significant differences in the quality of life and depressive symptoms were found between patients who explicitly requested EAS and those who did not (Table 4). About one in six patients fulfilled criteria for depression according to the CIDI in both groups. Patients who scored 11 or more on the HADS depression subscale reported that they felt less eager when looking forward to joyous events than they had prior to becoming ill (100 %), and that they felt (far) less happy about things they used to enjoy (96 %). The majority within this group reported that they could

Table 1 Patients' characteristics

Variable median (range)	Explicit request for EAS		*p* value
	No ($n = 70$)	Yes ($n = 32$)	
Demographic characteristics			
Gender (%)			0.79
Female	37	34	
Male	63	66	
Place of death (%)			0.79
Nursing home or hospice	21	16	
Hospital	17	10	
Home	62	74	
Disease characteristics			
Site of onset (%)			0.45
Bulbar	36	28	
Spinal	64	72	
Age at onset (years)	61 (33–82)	62 (40–80)	0.66
Survival time (years)	2.8 (0.8–7.4)	2.8 (0.4–6.4)	0.82
Diagnosis (%)			
Sporadic ALS	96	100	0.55
Familial ALS	4	0	
Stage of disease			
ALSFRS-r[a]	21 (4–45)	20 (7–36)	0.60
Symptoms in last 3 months of study (%)			
Fatigue	85	77	0.35
Pain	38	39	0.93
Vomiting	7	7	1.0
Immobility	72	71	0.91
Dependency	85	90	0.75
No chance of improvement	64	74	0.32
Fear of choking	41	42	0.93
Feeling a burden on family	51	65	0.21
Suffering without improvement	36	42	0.58
Futile suffering	16	16	0.97
Loss of dignity	52	45	0.61

[a] A higher score on the ALS functional rating scale (ALSFRS-r) reflects a healthier stage of disease

Table 2 End-of-life practices in 102 patients

End-of-life practices	*n* (%)
Unexpected sudden death	11 (11)
No end-of-life practices	21 (20)
Total end-of-life practices performed	70 (69)
Euthanasia	21
Physician-assisted suicide	1
Ending of life without explicit request by patient	0
Intensified alleviation of symptoms	32
Withholding or withdrawing medical treatment	16
Continuous deep sedation[a]	10 (10)

Unexpected sudden death, no end-of-life practices and total end-of-life practices performed add up to 100 %

[a] Continuous deep sedation has been provided in conjunction with intensified alleviation of symptoms or withholding medical treatment; patients are, therefore, also included in these categories

Table 3 Practices in 32 patients who explicitly requested euthanasia or physician-assisted suicide

	n
End-of-life practices performed	
Euthanasia	21
Physician-assisted suicide	1
Intensified alleviation of symptoms, because	
Patients went through the decision-making process but died before euthanasia could be performed	4
Patient died during decision-making process	1
Withholding or withdrawing medical treatment, because	
Patients withdrew request	2
Patient died during decision-making process	1
No end-of-life practice, because patients died during decision-making process	2

Table 4 Symptoms of depression and quality of life in 102 patients

Variable median (range)	Explicit request for EAS		*p* value
	No ($n = 70$)	Yes ($n = 32$)	
Symptoms of depression			
HADS[a]; total score	14 (1–42)	13 (1–28)	0.83
Anxiety score	5 (1–21)	6 (0–14)	0.90
Depression score	8 (1–21)	7 (1–20)	0.65
Anxiety score ≥10 %	19	13	0.45
Depression score ≥11 %	26	28	0.80
Depressed according to patient (%)	18	16	0.78
CIDI[b]; depression (%)	16	13	0.77
Quality of life			
ALSAQ-40[c]; total score	106 (12–156)	103 (46–157)	0.87
Mental score	15 (0–36)	17 (0–37)	0.57
Physical score	91 (12–120)	89 (39–120)	0.79

[a] A higher HADS score reflects more symptoms of depression. A HADS symptoms of depression score of 11 or more is considered an indication of a possible depression and an anxiety score of 10 or more as an indication of anxiety

[b] CIDI is positive for depression if the patient was depressed and/or had diminished interest or pleasure in all, or almost all activities most of the day, nearly every day for a minimum of two consecutive weeks

[c] A higher ALSAQ-40 score reflects a lower quality of life

rarely appreciate a good book, TV- or radio show (70 %). Patients who scored 10 or more on the HADS anxiety subscale reported they frequently felt anxious (94 %) and they panicked suddenly (94 %).

In total, 17 patients (1 in 6) thought of themselves as being depressed; 10 of them were treated with antidepressants. Of the other seven, two patients had not yet discussed their symptoms with a physician, two were offered treatment but refused it, and two consulted a social worker but did not wish to visit a psychologist. One patient did not receive any treatment, but wished to consult a psychologist or social worker. This patient did not explicitly request EAS. Forty-seven percent of the patients who thought of themselves as being depressed were also classified as depressed according to the CIDI.

Characteristics of care

The care received from professional caregivers and the available aids and appliances was usually reported as adequate (Online Appendix Table 5). At the last measurement prior to death, 84 % of all patients thought that the health care in general was good or excellent (86 % of patients with explicit EAS request, $p = 0.30$). One patient within this group reported the care received to be very poor. This was a 75-year-old, married woman, who lived in a nursing home. She was not able to walk or speak, had difficulties swallowing, was short of breath, and explicitly requested EAS. While the physicians were still involved in the decision-making process, she died of a myocardial infarction. She received care from a rehabilitation physician, dietician, occupational therapist, social worker and the nursing home caregivers. The patient scored 18 on the HADS depression subscale, she did not receive antidepressants nor did she visit a psychologist, but she indicated that she did not want to do so. Nor did she want artificial administration of fluids and nutrients to compensate for her swallowing difficulties.

Three other patients regarded the aids and appliances as being very poor. The main source of dissatisfaction was their wheelchair. They reported that they received the wheelchairs too late and that they were not adequate. Two of these three patients scored eleven or more on the HADS depression subscale and one scored ten or more on the HADS anxiety subscale, but none of them requested EAS.

Seventy-one percent of the patients were satisfied with the frequency of the consultations of all professional caregivers (Online Appendix Table 5). At the last visit prior to death, patients had expressed a wish for more frequent consultations from the primary care physician (10 %), the rehabilitation physician (10 %) or more assistance at home with personal care (11 %).

Performing EAS

The reported associations in Tables 1, 4 and 5 were also calculated for the 21 patients who actually died as a result of EAS and those who died without EAS (not shown). We could not find a significant difference or trend between these two groups in any of the quality of life or care items,

symptoms of depression, coping style or characteristics of the disease.

Discussion

The frequency of EAS is consistent with previous retrospective studies on EAS in patients with ALS in The Netherlands, performed in the periods 1994–1999 and 2000–2005, and therefore, suggest a stable proportion of EAS in this population even though ALS care in general has improved during this period [24, 28, 32]. In 2005, the national Dutch study on end-of-life practices showed that the general EAS proportion decreased and that continuous deep sedation increased, suggesting that continuous deep sedation may be used as a substitute for EAS by physicians [25, 31]. The findings of our prospective study do not support continuous deep sedation being used as a substitute for EAS in ALS, as only one of ten patients who died during continuous deep sedation had explicitly requested death to be hastened. According to the treating physician of the patient who explicitly requested EAS, the sedation was performed without appreciating the possibility of hastening death.

In a recent, prospective survey on the attitudes towards hastened death in Germany and Switzerland which included 66 ALS patients, half of the patients could imagine asking for assisted suicide or euthanasia and 14 % expressed a current wish to hasten death at baseline which did not change at follow-up measurements. The wish to hasten death was predicted by depression, anxiety, loneliness, perceiving to be a burden to others, and a low quality of life. A comparison with our results is difficult as, in contrast to our study, the data could not be related to the actual act of hastening death, a difference in use of the HADS scoring system and because of the differences in the legal system in different countries. This is reflected by their finding that none of the patients talked to their physician about their wish to hasten death; this would be unusual in The Netherlands [27].

Our finding that patients who explicitly requested EAS received the same care and were just as satisfied with their care as patients who did not explicitly request EAS is in accordance with a Belgian study. A large, retrospective study of 1,690 non-sudden deaths in Belgium showed no indication that EAS is performed more often among patients who do not use multidisciplinary palliative care services [30]. In our study, 84 % of all patients in end-stage ALS reported that their health care in general was good or excellent. This agrees well with the findings in the North American ALS CARE project, which reported that 89 % of the patients with ALS were satisfied with their medical care. Most of these patients were, however, at an earlier stage of the disease, having been diagnosed within the previous 6 months [9].

As expected, the prevalence of depression according to the CIDI was higher in our study than the average percentage of depression in the last 12 months in a general population (6.6 %) [12]. We did not find an association between depressive symptoms and EAS, which is in accordance with a study on attitudes towards assisted suicide in Oregon (USA) [8]. Our results contrast, however, with another American study, in which patients with ALS who expressed the wish to die were more likely to meet criteria for depression [1]. Nevertheless, the authors of this last study decided that caution is needed in concluding that the desire to hasten dying in end-stage ALS is simply a feature of depression, since depression in end-stage disease is difficult to separate from existential suffering which leads patients to question why they should continue to live.

Strengths of this study are the longitudinal, prospective design, the high response rates, the decreased chance of socially acceptable answers to questions due to the open culture towards EAS in The Netherlands, and the availability of information on actually performed EAS instead of the often-used wish to hasten death. A limitation of our study is that we did not identify a possible clinical depression with the help of a psychiatrist or psychologist. Another limitation was that five patients were included in this study and also in our previous retrospective study of 2000–2005 [15]. We believe that the impact of this overlap is small when analyzing changes in EAS in time. Especially as none of these five patients requested EAS or received EAS. Another limitation is that, although we were able to include a relatively large number of end-stage ALS patients in this prospective study, the number of patients who explicitly requested EAS or who died as a result of EAS limits the statistical power to detect determinants of EAS.

However, the results on care received, symptoms of depression and quality of life of patients who explicitly requested EAS and those who did not, do not show any trend towards a consistent association.

A relatively high number of patients with ALS explicitly ask their physician for EAS and receive EAS. Our study does not support the notion that unmet palliative care needs are related to EAS. Further research on determinants of EAS may focus more on intrinsic values, psychological and social factors; 84 % of all patients reported that their health care in general was good or excellent. Nevertheless, although not related to EAS, our study shows that there are shortcomings in the provision of care. For example, the considerable percentage of patients who fear choking (>40 %) contrasts sharply with the actual frequency of choking in the end stage of ALS and with our finding that death is considered to be peaceful in more than 94 % of

ALS patients in The Netherlands [15]. This emphasizes the need for adequate and timely patient information regarding symptoms and palliative care in the final stage of the disease.

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Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical standard This study was approved by the local ethics committee of University Medical Center Utrecht and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients, or their legal representatives if the patient was unable to consent, signed the informed consent in the telestroke group prior to their inclusion in the study.

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