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ORIGINAL ARTICLE

Patients' self-perceived burden, caregivers' burden and quality of life for amyotrophic lateral sclerosis patients: a cross-sectional study

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Aims and objectives. This study surveys the quality of life of amyotrophic lateral sclerosis patients and the factors associated with amyotrophic lateral sclerosis patients' self-perceived burden and their caregivers' burden.

Background. Burdens of patients with amyotrophic lateral sclerosis and their caregivers in Chinese population are largely unknown.

Design. A cross-sectional study was conducted among 81 pairs of amyotrophic lateral sclerosis patients and their caregivers.

Methods. Amyotrophic lateral sclerosis patients' self-perceived burden and caregivers' burden were assessed by the Self-Perceived Burden Scale and Zarit-Burden Interview, respectively. Quality of life of amyotrophic lateral sclerosis patients was measured using the World Health Organization Quality of Life-Bref. The amyotrophic lateral sclerosis Functional Rating Scale-Revised questionnaire was used to estimate patients' physical function.

Results. Both patients and caregivers reported a mild to moderate burden. The World Health Organization quality of life-Bref scores were decreased in respondents with lower amyotrophic lateral sclerosis Functional Rating Scale-Revised, higher Self-Perceived Burden Scale and higher Zarit-Burden Interview scores. Self-Perceived Burden Scale scores were associated with patients' knowledge of amyotrophic lateral sclerosis, respiratory function and female sex. Zarit-Burden Interview scores were associated with caregivers' age, patients' motor function and out-of-pocket payment.

Conclusion. With increase in amyotrophic lateral sclerosis patients' self-perceived burden and caregivers' burden, quality of life of amyotrophic lateral sclerosis patients decreased. Female patients, who had known more about the disease, and those with severe respiratory dysfunction were subject to higher self-perceived burden. Older caregivers and caregivers of patients with severe motor dysfunction and more out-of-pocket payment experienced more care burdens.

What does this paper contribute to the wider global clinical community?

- With increase in amyotrophic lateral sclerosis (ALS) patients' self-perceived burden (SPB) and caregivers' burden, quality of life (QOL) of ALS patients decreased.
- There is an urgent demand to expand medical insurance coverage to cover ALS in China and other developing countries. Long and adequate supports are needed for relieving caregivers' burden.
- Corresponding mental care is likely to be not only required, but also essential to improve QOL for ALS patients.

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Relevance to clinical practice. Our study suggests that paying more attention to female amyotrophic lateral sclerosis patients might benefit patients in China or other South-East Asian countries under the Confucian concept of ethics. There is an urgent demand to expand medical insurance coverage to cover amyotrophic lateral sclerosis in China and other developing countries. Long and adequate supports are needed for relieving caregiver's burden. To improve the quality of life of patients, relieving the patients' SBP and caregivers' burden is likely to be not only required, but also essential.

Key words: amyotrophic lateral sclerosis, caregiver burden, medical insurance, nursing, psychosocial care, quality of life, self-perceived burden

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Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease that involves upper and lower motor neurons in the brain and spinal cord. It is characterised by progressive muscular atrophy and has an average survival of 3–5 years from onset due to respiratory failure (Kiernan *et al.* 2011). The aetiology of the disease remains unclear. There is no effective treatment for ALS to date. This study provides an understanding of burden and its relevant factors among ALS patients and their caregivers and quality of life (QOL) of ALS patients in China.

Background

Neurologists provide symptomatic treatment to prolong the survival time and improve QOL of ALS patients (Creemers *et al.* 2014, Hwang *et al.* 2014). Compared with the general population in German, QOL was found to be significantly reduced in ALS patient cohort except for 'bodily pain', and the QOL of ALS patients could be influenced by depression and physical impairment (Körner *et al.* 2015). Several studies indicated that weight loss (Körner *et al.* 2013), oropharyngeal dysphagia (Paris *et al.* 2013) and pain (Pizzimenti *et al.* 2013) would negatively impact on the QOL of ALS patients. ALS patients become severely disabled and dependent within months or a few years after symptoms onset, which is not only painful and distressful to the patients, but also burdensome to their caregivers (Chiò *et al.* 2005, 2006, Gauthier *et al.* 2007).

The feeling of being a burden, that is self-perceived burden (SPB), is posited as a multidimensional construct that arises from the care recipient's feelings of dependence and the frustration and worry, which may lead to feel guilty and responsible for the caregiver's hardship (Cousineau *et al.* 2003). High SPB could affect cancer patients' preferences for palliative care to avoid further burdening their caregivers (Lee *et al.* 2015). Among ALS patients, being a burden was a prevalent feeling as disease progression (Mora *et al.* 2012). A cross-sectional survey found that SPB was significantly correlated with the physical function of ALS patients (Chiò *et al.* 2005); however, this association was not identified in another longitudinal study (Gauthier *et al.* 2007). Some studies found SPB of ALS patients was also correlated with patients' depression and caregivers' burden (Chiò *et al.* 2005, Gauthier *et al.* 2007).

Caregiver's burden includes the caregiver's health, psychological well-being, finances, social life and the relationship between the caregiver and the patient (Zarit *et al.* 1980). In Savundranayagam's opinion, caregiver's burden is a multidimensional construct that includes stress burden (tension and anxiety), relationship burden (changes in dyadic relationships) and objective burden (time infringements) (Savundranayagam *et al.* 2011). A study on 140 patients (Lillo *et al.* 2012) reported that 48% of ALS caregivers had high levels of burden. Another study (Goldstein *et al.* 2006) reported that ALS caregivers' psychological distress (mood, burden and strain) increased significantly over time. A Japanese study showed that the ALS caregivers' burden was higher than the burden observed for other intractable neurological diseases such as Parkinson's disease, spinocerebellar degeneration and multiple system atrophy (Miyashita *et al.* 2009), although a Germany study found the caregiver's burden of ALS was lower than the burdens observed for dementia, mixed neuropsychiatric diseases and internal-geriatric diseases (Hecht *et al.* 2003). ALS caregivers' burden has been reported to be influenced by a passive coping style of the caregiver, anxiety and feeling less supported by

the ALS team, and physical disability and emotional well-being of ALS patients (Creemers *et al.* 2015) (Pagnini *et al.* 2011), and neurobehavioral symptoms of patients (Chiò *et al.* 2010, Cui *et al.* 2015) (Lillo *et al.* 2012). The ALS function score of ALS patients may also be important for the caregivers' burden (Chiò *et al.* 2005, Rabkin *et al.* 2009, Pagnini *et al.* 2010).

Amyotrophic lateral sclerosis patients' SPB and caregiver burden have been drawing increasingly attention with more relevant studies conducted in developed countries or regions. However, few studies had been conducted in developing countries. There are several works that focused on the prognosis (Gil *et al.* 2009), treatment (Dubrovsky & Sica 1999), epidemiology (Dubrovsky & Sica 1999, Bucheli *et al.* 2014) and economic cost (Bucheli *et al.* 2013) of ALS in South America, but only one Chinese study referred to caregivers' burden (Cui *et al.* 2015). We therefore performed a cross-sectional study to survey the factors associated with ALS patients' SPB and their caregivers' burden, the relationship between ALS patients' SPB and their caregivers' burden, and QOL of ALS patients in a Chinese population.

The study

Aim

The aim of this study was to explore the QOL of ALS patients and the relevant factors associated with burdens of ALS patients and their caregivers.

Design

This cross-sectional survey involves both ALS patients and their caregivers. The definition of cross-sectional survey is described as a type of observational study that involves the analysis of data collected from a population, or a representative subset, at one specific point in time.

Participants

Considering that there was lack of exact epidemiological data about ALS in China, and ALS was orphan disease with very low incidence (2·16/100,000 in Europe) (Kiernan *et al.* 2011), we chose not less than five times the values for multiple linear regression model in our design (14*5 = 70) as our sample size based on statistical experience. Finally, a total of 81 patients with ALS who were seen at the Department of neurology of West China Hospital of Sichuan University in south-west China between March 2015–September 2015 were interviewed consecutively enrolled for this cross-sectional study. All patients were diagnosed with probable, or definite ALS according to the revised criteria of El Escorial. Clinically definite ALS is defined on clinical evidence alone by the presence of upper motor neuron, as well as lower motor neuron signs, in the bulbar region and at least two spinal regions or the presence of upper motor neuron signs and lower motor neuron signs in three spinal regions; clinically probable ALS is defined on clinical evidence alone by upper motor neuron and lower motor neuron signs in at least two regions with some upper motor neuron signs necessarily rostral to (above) the lower motor neuron signs for ALS (Brooks *et al.* 2000). Patients with other severe neurological diseases, and severe psychiatric disorders were excluded. The caregiver was one of the patient's family members who lived with the patient more than one month and had the responsibility for the largest component of the patients' informal care. Professional caregivers or who earn money from the care provided were excluded.

Data collection

Data were collected by two trained senior nurses through face-to-face interviews at department of neurology. In addition to demographic information, both the patients and his/her caregivers were interviewed separately with several self-rating questionnaires. To clarify the impact of age on the patient's SBP and caregiver's burden, patients/caregivers were classified into two groups (low 45 years and over 45 years) based on the description of a previous study (Yuan *et al.* 1997, Turner *et al.* 2012), for individual who was below 45-year-old usually regarded as a young adult, while the one who was beyond 45 was regarded as a middle-aged or elderly individual in China. In addition, patients were also classified into two groups including young onset (younger than 45 years) and late onset (older than 45 years) based on a previous study (Turner *et al.* 2012).

Severity of ALS patients

The severity of ALS was evaluated with the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) questionnaire (Cedarbaum *et al.* 1999), which contains 12 items (0–48 scores). The factors of ALSFRS-R correspond to (1) fine motor: coordinated, mostly upper, limb motions (e.g. writing, feeding, dressing and turning), (2) bulbar function (e.g. speech, swallowing, salivation), (3) gross motor: less finely controlled activities (e.g. turning, dressing, walking, climbing) and (4) respiratory function (e.g. dyspnoea, orthopnoea, respiratory insufficiency) (1996, Cedarbaum *et al.* 1999). As there were lapped items between fine motor and gross motor (turning and dressing), we combined these two as

one dimension (motor function). Higher scores indicate better function. To facilitate clinical interpretation of findings, ALSFRS-R scores were categorised into three stages of severity: mild (37–48), moderate (25–36) and severe (0–24), as previously suggested (Kimura *et al.* 2006, Kollewe *et al.* 2008, Mioshi *et al.* 2012, Chen *et al.* 2014). The internal consistency (Cronbach's alpha) of ALSFRS-R and its subdomains (bulbar, motor and respiration) in our study were 0·88, 0·83, 0·83 and 0·77, respectively.

QOL of ALS patients

The QOL of each patient was evaluated with the Chinese version of the World Health Organization Quality of Life-Bref (WHOQOL-BREF) questionnaire, which is equivalent across different countries and the outcome assessed by it is comparable (Hao *et al.* 2006). It contains 26 items and four subdomains including physical domain (e.g. pain, energy, sleep, mobility, activity of daily living, medicine dependence, work ability), psychological domain (e.g. positive feelings, think, esteem, body and appearance, negative feelings, spirit), social domain (e.g. relationship, social support, sexual life) and environment domain (e.g. safety, housing condition, finance, medicine service, information, leisure, environmental condition, transportation). Each domain score is transformed to reflect a 0–100 scale, and the total scores are the summation of the scores for each domain (a high score corresponds to a favourable QOL). The internal consistency (Cronbach's alpha) of Chinese version of WHOQOL-BREF was 0·85 (Hao *et al.* 2006), while the internal consistency (Cronbach's alpha) of the whole scale and its subdomains in our study was 0·81, 0·79, 0·80, 0·76 and 0·79, respectively.

SPB of ALS patients

The ALS patients' SPB was measured with the Chinese version of Self-Perceived Burden Scale (SPBS) (Wu & Jiang 2010), which contains 10 items and scores range from 0–50. The 10 items were selected based on one single, general burden factor (Cousineau *et al.* 2003). Higher scores indicate high SPB. To estimate how severe self-perceived burden did patients feel, SPBS scores were categorised into four stages: none to little (≤19), mild to moderate (20–29), moderate to severe (30–39) and severe (≥40), as previously suggested (Xu *et al.* 2011, Fang *et al.* 2013). The internal consistency (Cronbach's alpha) of Chinese version of SPBS was 0·91 (Wu & Jiang 2010), while the internal consistency (Cronbach's alpha) of SPBS in our study was 0·93.

Caregiver burden of ALS caregivers

The caregiver's burden was evaluated using the Chinese version of Zarit-Burden Interview (ZBI) scale (Zarit *et al.* 1980, Wang *et al.* 2006), which contains 22 items and scores range from 0–88. Higher scores indicate high caregiver burden. We divided caregiver's burden into four grades, namely severe burden (61–88), moderate to severe burden (41–60), mild to moderate burden (21–40) and little or no burden at <21 based on the description of a previous study (Zarit & Zarit 1987). We did not divide caregivers' strain into personal strain and role strain based on different domains as there is lack of an ideal frame that covers all items (Whitlatch *et al.* 1991, Lai 2007). The internal consistency (Cronbach's alpha) of Chinese version of ZBI was 0·87 (Wang *et al.* 2006), while the internal consistency (Cronbach's alpha) of ZBI in our study was 0·92.

Ethical considerations

All participants were informed before enrolment and given a written informed consent form for the study under a protocol approved by the Ethics Committee of West China Hospital of Sichuan University (Ethical code: 243).

Data analysis

SPSS version 19.0 (SPSS, Inc, Chicago, IL, USA) was used to analyse the data. Before we conducted statistical analyses, we constructed the quantile–quantile plot and the Kolmogorov–Smirnov test to examine the distribution of the data and found that continuous variables, including WHOQOL-BREF score, ALSFRS-R score, SPBS scores, age range of patients and caregivers, and onset age of patients, were normally distributed. Continuous values were shown as mean ± standard deviation (SD). Comparisons of patients' SPB and caregivers' burden regarding different demographic and clinical variables, such as age, sex, patients' age of onset, patients' site of onset, patients' physical function, education-level employment status, marital status, caregivers' relationship to patients, family income, payment method, caregivers' health condition, patients' self-care ability and knowledge of disease, were analysed using independent *t*-tests or one-way analysis of variance (ANOVA). A multiple linear regression model with a stepwise approach was used to analyse the association between the factors measured among the patients and caregivers, motor function of the patients, caregiver burden and patients' SPB. Collinearity statistics was conducted to judge whether the collinear relation existed between the factors and a variance inflation factor (the reciprocal of tolerance) of 10 (equivalent to a tolerance level of 0·10) was used as rules of thumb to indicate excessive or serious multicollinearity (O'brien 2007). p-values < 0·05 (two-sided) were considered statistically significant.

Results

One hundred and seven patients met the diagnostic criteria of the study, and we excluded four caregivers refused to participate, seven patients lived alone, 13 patients attended our clinic without their informal primary caregiver, and two pairs did not complete the survey. Finally, a total of 81 pairs including 55 definite patients and 26 probable patients who completed the questionnaires were analysed.

Clinical features of ALS patients and caregivers

The general characteristic of ALS patients and their caregivers are listed in Table 1. The sex ratio of the patients was 49:32 (male:female). The mean age of patients was 52·7 ± 12·2 years, the mean disease duration was 17·8 ± 14·9 months, and the mean score of ALSFRS-R was 36·5 ± 8·6. Twenty-six (32·1%) patients had early age of onset, and 12 (14·8%) patients had bulbar onset. The mean age of caregivers was 47·5 ± 14·5 years. The sex ratio of the caregivers was 26:55 (male: female).

SBP of ALS patients

The mean SPBS score of all patients was 25·7 ± 10·8 (Table 1). Twenty-seven (33·3%) patients bore little or no burden, 25 (30·9%) patients bore mild to moderate burden, 18 (22·2%) patients bore moderate to severe burden, and 11 (13·6%) patients bore severe burden (Table 2). Female patients' SPBS scores were significantly higher than male patients ($p < 0·05$). Patients with mild impairment had significantly lower SPB than those with severe impairment ($p < 0·05$). Patients with a high educational level had significantly higher SPBS scores than patients with a low educational level ($p < 0·05$). Patients with better knowledge of ALS had significantly higher SPBS scores than patients with poor knowledge of the disease ($p < 0·05$). No significant differences in patients' SPBS score were found between subgroups in terms of age, age of onset, onset forms, employment status, total family income, patients' payment methods and marital status.

Caregiver burden of ALS caregivers

The mean ZBI score of the caregivers was 26·8 ± 15·1 (Table 1). Twenty-nine (35·8%) caregivers bore little to no burden, 37 (45·7%) caregivers bore mild to moderate burden, 13 (16·0%) caregivers bore moderate to severe burden, and two (2·5%) caregivers bore severe burden (Table 2). Caregivers of patients with high ALSFRS-R scores had significantly lower ZBI than caregivers of patients with low ALSFRS-R scores ($p < 0·05$). ZBI scores in caregivers younger than 45 years were significantly lower than that in whom over 45 years ($p < 0·05$). Caregivers who paid out-of-pocket expenses for their patients had significantly higher ZBI scores than caregivers whose patients had medical insurance ($p < 0·05$). Caregivers whose patients were unable to care for themselves completely reported significantly higher ZBI scores than caregivers whose patients were able to care for themselves whether partially or completely ($p < 0·05$). No significant differences in caregivers' ZBI scores were found between subgroups regarding sex, employment status, family income, knowledge of the disease and marital status.

Quality of life of ALS patients

The QOL of ALS patients is presented in Table 3. Patients with high ALSFRS-R scores had significantly higher WHOQOL-BREF scores than patients with lower ALSFRS-R scores ($p < 0·05$), especially in the physical and psychological domains. There were no significant differences in the scores of the social and environment domains of WHOQOL-BREF among patients with different ALSFRS-R score groups. Patients with high SPBS scores and whose caregivers bore more burdens had low WHOQOL-BREF scores, particularly in the physical and psychological domains ($p < 0·05$).

Multiple linear regression models of SPBS and ZBI

The multiple regression analysis models indicated that the patients' SPB was associated with the knowledge of the disease, respiratory function and sex of patients ($p < 0·05$, Table 4). The multiple regression analysis models indicated that the burden of ALS caregivers was associated with age of caregiver, motor function of patients and payment method (Table 5).

Discussion

This study firstly investigates patients' SPB and QOL, and their caregivers' burden in a Chinese ALS population. In this study, both ALS patients and their caregivers experienced mild to moderate burden, which is consistent with the findings of several studies among Caucasian patients (Chiò *et al.* 2005, Gauthier *et al.* 2007, Pagnini *et al.* 2010, 2011, Kowal *et al.* 2012, Qutub *et al.* 2014), but inconsistent with a study that found that ALS caregivers had moderate to severe burden (Kim *et al.* 2011). Patients in our study experienced mild or moderate burden perhaps because they were in the early or middle stages of the disease.

Table 1 Demographic, clinical features and SPBS of ALS patients and demographic features and ZBI of their caregivers

	Patients (n = 81)	SPBS (Mean ± SD)	*p*-value	Caregivers (n = 81)	ZBI (Mean ± SD)	*p*-value
Age (years)	52·73 ± 12·17			47·52 ± 14·46		
Gender (male: female)	49:32			26:55		
Disease duration (months)	17·82 ± 14·91			/		
Patients' age of onset (years)	47·5 ± 14·5			/		
Patients' ALSFRS-R	36·53 ± 8·56			/		
Age (years)						
<45	22 (27·2%)	28·23 ± 12·17	0·08	38 (46·9%)	23·61 ± 12·63	0·02*
≥45	59 (72·8%)	24·69 ± 10·22		43 (53·1%)	27·00 ± 15·56	
Gender						
Female	32 (39·5%)	29·09 ± 10·62	0·02*	55 (67·9%)	26·98 ± 15·18	0·90
Male	49 (60·5%)	23·41 ± 10·45		26 (32·1%)	26·50 ± 15·30	
Patients' age of onset (years)						
<45	26 (32·1%)	28·50 ± 11·91	0·10	/	25·81 ± 13·34	0·68
≥45	55 (67·9%)	24·31 ± 10·10		/	27·31 ± 15·99	
Patients' site of onset						
Bulbar	12 (14·8%)	23·75 ± 10·99	0·51	/	27·75 ± 15·95	0·82
Limb	69 (85·2%)	25·99 ± 10·84		/	26·67 ± 15·09	
Patients' ALSFRS-R						
Mild (≥37)	46 (56·8%)	23·17 ± 11·05	<0·003*	/	19·89 ± 10·97	<0·001*
Moderate (25–36)	27 (33·3%)	26·56 ± 8·71		/	34·56 ± 15·44	
Severe (≤24)	8 (9·9%)	36·88 ± 9·13		/	40·63 ± 13·85	
Education level						
Primary or Below	22 (27·2%)	20·73 ± 10·28	0·04*	17 (21·0%)	25·24 ± 18·43	0·74
Secondary	46 (56·8%)	27·41 ± 10·53		39 (48·1%)	26·31 ± 13·72	
Higher education or above	13 (16·0%)	27·77 ± 10·88		25 (30·9%)	28·72 ± 15·23	
Employment status						
Employed	43 (53·1%)	25·70 ± 10·77	0·97	24 (29·4%)	30·04 ± 16·41	0·22
Unemployed	38 (46·9%)	25·61 ± 11·03		57 (70·4%)	25·47 ± 14·49	
Marital status						
Married	77 (95·1%)	25·31 ± 10·93	0·21	74 (91·4%)	27·38 ± 15·26	0·83
Single	4 (4·9%)	32·25 ± 5·74		7 (8·6%)	20·86 ± 13·50	
Relationship to patients						
Spouse	/	28·38 ± 16·40	0·07	55 (67·9%)	23·50 ± 11·67	0·18
Other	/	23·50 ± 11·67		26 (32·1%)	28·40 ± 16·37	
Total family income (RMB, ¥)						
≤1000	18 (22·2%)	29·72 ± 9·66	0·10	18 (22·2%)	28·17 ± 17·32	0·95
1001–3000	36 (44·4%)	22·56 ± 10·92		36 (44·4%)	27·11 ± 15·75	
3001–6000	21 (25·9%)	26·62 ± 11·40		21 (25·9%)	25·48 ± 14·06	
≥6001	6 (7·4%)	28·67 ± 7·63		6 (7·4%)	25·83 ± 9·91	
Patients' payment way						
Out-of-pocket	31 (38·3%)	23·94 ± 10·89	0·26	/	31·03 ± 15·04	0·04*
Insurance or other ways	50 (61·7%)	26·72 ± 10·75		/	24·22 ± 14·73	
Caregivers' health condition						
Well	/	24·08 ± 10·61	0·42	39 (48·1%)	24·33 ± 13·31	0·41
Average	/	27·44 ± 10·65		34 (42·0%)	27·12 ± 14·15	
Poor	/	25·75 ± 12·77		8 (9·9%)	37·75 ± 23·19	
Patients' self-care ability						
Required no assistance	/	23·36 ± 11·04	0·38	22 (27·2%)	17·00 ± 9·63	<0·001*
Required some assistance	/	25·84 ± 10·53		43 (53·1%)	27·81 ± 14·98	
Required Completely assistance	/	28·31 ± 11·32		16 (19·8%)	37·69 ± 13·85	

In our study, female patients had a higher SPB than male patients, which is inconsistent with two other western studies (Chiò *et al.* 2005, Gauthier *et al.* 2007). In eastern countries, women are responsible for the majority of domestic work, including care for their children and parents-in-law under the Confucian concept of ethics (Hashizume

Table 1 (continued)

	Patients (n = 81)	SPBS (Mean ± SD)	*p*-value	Caregivers (n = 81)	ZBI (Mean ± SD)	*p*-value
Knowledge of disease						
Good	25 (30·9%)	30·76 ± 9·28	0·003*	38 (46·9%)	28·29 ± 16·04	0·58
Average	28 (34·6%)	25·82 ± 11·27		28 (34·6%)	24·39 ± 12·73	
Poor	28 (34·6%)	20·93 ± 9·80		15 (18·5%)	27·67 ± 17·22	

ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; SPBS, Self-Perceived Burden Scale; ZBI, Zarit-Burden Interview. Mean ± SD: Mean and standard deviation.
*Significant difference.

Table 2 Degree of patients' self-perceived burden and caregivers' burden

Degree	Patient, *n* (%)	SPBS (Mean ± SD)	Caregiver, *n* (%)	ZBI (Mean ± SD)
None to little burden	27 (33·3)	13·63 ± 3·30	29 (35·8)	11·21 ± 4·44
Mild to moderate burden	25 (30·9)	24·36 ± 2·02	37 (45·7)	29·49 ± 5·70
Moderate to severe burden	18 (22·2)	34·89 ± 2·45	13 (16·0)	48·23 ± 5·34
Severe burden	11 (13·6)	43·00 ± 3·07	2 (2·5)	65·00 ± 5·66

SPBS, Self-Perceived Burden Scale; ZBI, Zarit-Burden Interview. Mean ± SD: Mean and standard deviation.

2000, Kao & McHugh 2004, Koh & Koh 2008). Depending on others' care leads women to feel significant guilty and psychological burden. Therefore, healthcare providers in China should pay more attention on the SPB of ALS patients, especially for female patients. It is challenging for neurologists and nurses all over the world to decide whether or not, when and how to introduce an ALS diagnosis to patients (McCluskey *et al.* 2004, Schellenberg *et al.* 2014). In western countries, patients have the right to receive accurate and easily understood information about their diagnosis, treatment and prognosis, while, under the Chinese special cultural background, Chinese physicians appeared to give far greater weight to family preferences in medical decision-making (Feldman *et al.* 1999). To avoid the death strike for patients, Chinese doctors prefer to give the information about diagnosis of a serious disease to the family member firstly. Of course, the patients have the rights to know the truth. If they desire to know the condition of the disease, the doctors will tell them the truth, but Chinese doctor feel it is better to let his/her family member tell them at a proper time. In addition, from what we have seen, ALS caregivers in China usually do not want neurologist or nurses to inform patients the diagnosis and the prognosis of ALS. In the present study, we found that patients with a higher education or who were more knowledgeable about the disease, particularly the prognosis of the disease, had an increased SPB. Some studies have found that SPB might affect patients' medical decisions, including decisions for treatment, advance directives and place to receive care, especially at their end-of-life care (McPherson *et al.* 2007, Winter & Parks 2012, Lee *et al.* 2015). Therefore, hiding the truth of diagnosis of ALS temporarily or long term appropriately might be a benefit way to prevent Chinese ALS patients from losing hope or the will to fight the disease. In addition, patients with severe respiratory dysfunction had an increased burden, which is consistent with a study that found a significantly correlation between ALS patients' SPB and their physical impairment (Chiò *et al.* 2005), but inconsistent with another study (Gauthier *et al.* 2007).

Additionally, we found that caregivers reported lower care burden if they had a higher total family income or their patients had medical insurance, which is not identified in previous studies. The inconsistent findings may be due to reliable health insurance systems and the higher income levels of developed countries or regions (Kaub-Wittemer *et al.* 2003, Goldstein *et al.* 2006, Qutub *et al.* 2014). In Korea, 44·8% of the direct medical costs is carried by ALS patients themselves, and the remaining costs were paid by the government (Oh *et al.* 2015). However, the cost of riluzole in South America varies from $600–$1,600 per month and is seldom covered by a government subsidy (Bucheli *et al.* 2013). In China, the cost of riluzole treatment (the cost is more than $700 per month) for ALS has not yet been included in the healthcare coverage, which is really expensive compared with the average income of Chinese inhabitant. If one family member had severe diseases that would cost a lot of money, the whole family would pay for the medicine bill together, thought it could empty their bank accounts. It is an urgent demand to expand medical insurance coverage to cover ALS in

Table 3 Quality of life of ALS patients

	WHOQOL-BREF (Mean ± SD)				
	Physical	Psychological	Social	Environment	Total
ALSFRS-R					
Total (n = 81)	49·12 ± 18·35	59·16 ± 18·10	67·80 ± 12·27	58·49 ± 14·09	234·56 ± 51·25
Mild (*n* = 46)	57·38 ± 16·52	64·31 ± 16·87	70·65 ± 11·49	61·62 ± 15·03	253·96 ± 50·19
Moderate (*n* = 27)	42·06 ± 13·77	54·32 ± 15·72	63·54 ± 12·55	55·32 ± 10·14	215·91 ± 35·39
Severe (*n* = 8)	25·45 ± 10·36	45·83 ± 23·04	64·20 ± 12·62	51·17 ± 16·45	185·99 ± 51·61
p-value	<0·001*	0·005*	0·054	0·054	<0·001*
SPBS					
Total (n = 81)	49·12 ± 18·35	59·16 ± 18·10	67·80 ± 12·27	58·49 ± 14·09	234·56 ± 51·25
Little to no burden (*n* = 27)	59·92 ± 19·01	70·67 ± 15·13	72·22 ± 13·67	63·77 ± 15·41	266·60 ± 52·22
Mild to moderate (*n* = 25)	44·86 ± 16·30	55·56 ± 16·12	64·33 ± 11·67	56·00 ± 12·23	227·39 ± 45·52
Moderate to severe (*n* = 18)	43·65 ± 13·56	55·50 ± 18·80	68·98 ± 9·82	59·20 ± 13·95	220·69 ± 40·88
Severe (*n* = 11)	41·23 ± 17·88	45·08 ± 12·89	62·88 ± 10·78	58·48 ± 14·09	199·19 ± 40·88
p-value	0·002*	<0·001*	0·056	0·032*	<0·001*
ZBI					
Total (n = 81)	49·12 ± 18·35	59·16 ± 18·10	67·80 ± 12·27	58·49 ± 14·09	234·56 ± 51·25
Little to no burden (*n* = 29)	58·25 ± 15·89	64·66 ± 18·25	71·55 ± 11·47	59·91 ± 16·07	254·37 ± 49·27
Mild to moderate (*n* = 37)	47·59 ± 17·09	60·25 ± 16·57	67·79 ± 11·65	61·15 ± 11·98	236·78 ± 46·65
Moderate to severe (*n* = 13)	36·26 ± 16·93	48·72 ± 14·47	60·26 ± 13·67	51·44 ± 9·34	196·68 ± 39·41
Severe (*n* = 2)	28·57 ± 20·23	27·08 ± 8·84	62·50 ± 5·89	34·38 ± 17·68	152·53 ± 40·83
p-value	0·001*	0·003*	0·043*	0·011*	<0·001*

WHOQOL-BREF, World Health Organization Quality of Life-BREF; ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; SPBS, Self-Perceived Burden Scale; ZBI, Zarit-Burden Interview. Mean ± SD: Mean and standard deviation.
*Significant difference.

Table 4 Multiple linear regression model of patients' self-perceived burden

							Collinearity statistics				
Model	Variable	*B*	SE	Std.B	*t*	*p*-value	Tolerance	VIF	Adjusted R^2	*F*	*p*-value
1	Constant	16·01	2·95		5·42	<0·001*			0·125	12·48	0·001*
	Patients' knowledge of disease	4·92	1·39	0·37	3·53	0·001*	1·00	1·00			
2	Constant	19·505	3·21		6·07	<0·001*			0·176	9·53	<0·001*
	Patients' knowledge of disease	4·79	1·35	0·36	3·55	0·001*	0·99	1·00			
	Patients' gender	−5·39	2·23	−0·25	−2·41	0·018*	0·99	1·00			
3	Constant	37·79	8·28		4·56	<0·001*			0·223	8·63	<0·001*
	Patients' knowledge of disease	4·19	1·34	0·32	3·14	0·002*	0·96	1·03			
	Patients' gender	−5·22	2·17	−0·24	−2·41	0·019*	0·98	1·00			
	ALSFRS-R-R	−1·55	0·65	−0·24	−2·38	0·020*	0·96	1·04			

Excluded Variables: Model 1: ALSFRS-R-M, ALSFRS-R-R, ALSFRS-R-B, ZBI, patients' age, patients' gender, patients' education; Model 2: ALSFRS-R-M, ALSFRS-R-R, ALSFRS-R-B, ZBI, patients' age, patients' education; Model 3: ALSFRS-R-M, ALSFRS-R-B, ZBI, patients' age, patients' education.
Regression Equation: $Y_1 = 37{\cdot}79 + 4{\cdot}19X_1 - 1{\cdot}55X_2 - 5{\cdot}22X_3$.
Y_1 = SPBS; X_1 = Patients' knowledge of disease; X_2 = Respiratory function of ALSFRS-R; X_3 = Patients' gender (male = 1 while female = 0).
B = Unstandardised Coefficients; SE = Standard Error; Std.B = Standardised Coefficients; VIF = Variance Inflation Factor; Adjusted R^2 = Adjusted Coefficient of Determination. ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; ALSFRS-R-B, patients' bulbar function; ALSFRS-R-M, patients' motor function; ALSFRS-R-R, patients' respiratory function; SPBS, Self-Perceived Burden Scale; ZBI, Zarit-Burden Interview.
*Significant difference.

Table 5 Multiple linear regression model of caregivers' burden

Model	Variable	*B*	SE	Std.B	*t*	*p*-value	Collinearity Statistics		Adjusted R^2	*F*	*p*-value
							Tolerance	VIF			
1	Constant	48·96	4·29		11·42	<0·001*			0·266	30·01	<0·001*
	ALSFRS-R-M	−1·41	0·26	−0·53	−5·48	<0·001*	1·00	1·00			
2	Constant	52·28	4·50		11·63	<0·001*			0·296	17·79	<0·001*
	ALSFRS-R-M	−1·38	0·25	−0·52	−5·48	<0·001*	0·99	1·00			
	Payment	−6·03	2·91	−0·20	−2·08	0·03*	0·99	1·00			
3	Constant	43·36	6·27		6·92	<0·001*			0·322	13·66	<0·001*
	ALSFRS-R-M	−1·40	0·25	−0·52	−5·67	<0·001*	0·99	1·00			
	Payment	−5·93	2·85	−0·19	−2·08	0·04*	0·99	1·00			
	Caregivers' age	0·19	0·10	0·19	−2·01	0·03*	0·99	1·00			

Excluded variables: Model 1: ALSFRS-R-R, ALSFRS-R-B, payment, patient's self-care ability, caregivers' age, SPBS; Model 2: ALSFRS-R-R, ALSFRS-R-B, patient's self-care ability, caregivers' age, SPBS; Model 3: ALSFRS-R-R, ALSFRS-R-B, patient's self-care ability, SPBS.
Regression equation: $Y_2 = 43{\cdot}36 + 0{\cdot}19X_4 - 1{\cdot}40X_5 - 5{\cdot}93X_6$.
Y_2 = ZBI; X_4 = Age of caregiver; X_5 = ALSFRS-M; X_6 = Payment.
B = Unstandardised Coefficients; SE = Standard Error; Std.B = Standardised Coefficients; VIF = Variance Inflation Factor; Adjusted R^2 = Adjusted Coefficient of Determination. ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; ALSFRS-R-B, patients' bulbar function; ALSFRS-R-M, patients' motor function; ALSFRS-R-R, patients' respiratory function; SPBS, Self-Perceived Burden Scale; ZBI, Zarit-Burden Interview.
*Significant difference.

China and other developing countries. Caregivers in our study were younger than caregivers in western countries (Burke *et al.* 2015, Creemers *et al.* 2015, Hsieh *et al.* 2015, Tramonti *et al.* 2015, Pagnini *et al.* 2016) but older than caregivers in another Chinese study (Cui *et al.* 2015). A previous study has showed that younger ages corresponded with higher ZBI scores (Qutub *et al.* 2014). On the contrary, older caregivers reported more care burden than young caregivers in our study. We speculate that this phenomenon could be occurring for two reasons as follows. Firstly, people are more likely to experience physical decline as they get older, making it unable to cope with care work. Additionally, many Chinese people (≥45 years old) are in the position of having to support their old parents along with their kids, taking care of a patient is no doubt an enormous burden. It is necessary to help middle-aged and older caregivers with long and strong support. Although our results revealed that the employment status of the ALS caregivers was not related to caregiver burden, a previous study found that those who maintained employment (Qutub *et al.* 2014) had a higher caregiver burden. Our study found that caregivers' educational level and sex were not correlated with caregiver burden, which is consistent with several other studies (Hecht *et al.* 2003, Qutub *et al.* 2014). Besides, our data also showed caregivers burden increased with the severity of the disease. Research has indicated that as the disease progressed, functional impairment increased which required more demands for caregiving (as reflected in the length of caregiver per day) due to poor self-care (Qutub *et al.* 2014), which is undoubtedly a large burden for caregivers. Our findings are consistent with several studies (Hecht *et al.* 2003, Adelman *et al.* 2004, Chiò *et al.* 2005, Gauthier *et al.* 2007, Pagnini *et al.* 2010, Watermeyer *et al.* 2015) but are inconsistent with other studies, which found that there is no significant correlation between the physical function of ALS patients and the caregiver burden (Goldstein *et al.* 2006, Rabkin *et al.* 2009, Kim *et al.* 2011, Lillo *et al.* 2012, Qutub *et al.* 2014).

- In the current study, we found that patients' QOL got worse as the disease progressed, which is consistent with the findings of several previously established studies (Olsson Ozanne *et al.* 2011, Creemers *et al.* 2014). In particular, we found that the physical and psychological domains of QOL decreased with disease progression, indicating that urgent effective treatment and nursing care are needed for improving the QOL of ALS patients, as ALS patients depend on others more as the disease progresses (Qutub *et al.* 2014). So far, physical deterioration was probably not reversible; hence, to improve the QOL of patients, corresponding psychosocial care are likely to be not only required, but also essential. Furthermore, we found that patients' QOL declined as their SPB and caregivers' burden increased, indicating that when patients reported much more feeling of being a burden, or caregivers' burden reported higher care burden, in the

meanwhile, patients tended to live a worse life. In addition, a recent study found that early intervention with an assistive communication device seems to have a positive impact on QOL and gives patients the opportunity to improve skills for communication in later disease stages (Londral *et al*. 2015). However, these assistive communication devices are usually too expensive for ALS family, which may increase the burdens of ALS patients and their caregivers. Therefore, there is an urgent demand to expand medical insurance coverage to cover the disease of ALS in China and other developing countries to relieve the burdens of patients and their givers, thereby improving the QOL of ALS patients.

Limitations

The following describes the limitations of this study. First, the cross-sectional design does not allow a definitive conclusion for causation to be drawn. Second, all of the patients and caregivers were recruited from one ALS centre, and final-stage patients were not recruited because they were mostly homebound. This recruitment procedure caused selection bias, which may have influenced the results. Third, all of the patients in the current study came from a single tertiary referral centre, which may lead to another selective bias. Finally, although the sample size was enough for statistical analysis, it is relatively small for exploring a subset of other correlations. Further multicenter longitudinal study with lager sample may help to verify our study.

Conclusions

With increase in ALS patients' SPB and caregivers' burden, patients' QOL decreased. Female patients with more knowledge of the disease and those with severe respiratory dysfunction were subject to higher SPB. Caregivers of patients with severe motor impairments and more out-of-pocket payment experience increased burden. These results provide a baseline for SPB, caregiver burden and QOL and may inform innovative and improved methods to assist families affected by ALS.

Relevance to clinical practice

The results of this study suggest hiding the diagnosis of ALS from ALS patients was a common phenomenon in China, because the caregivers hope their loved one do not lose hope or the will to fight the disease. Female patients generally tended to have more SPB than male patients, which prompted to paying more attention to female patients in China or other South-East Asian countries under the Confucian concept of ethics. In addition to the community for their love and care, ALS families need substantial help, such as expanding medical insurance coverage to cover ALS in China and other developing countries, and long and adequate material support is needed for relieving ALS caregiver burden. To improve the QOL of patients, relieving the patients' SBP and caregivers' burden is likely to be not only required, but also essential.

Contributions

Study design: DG, HS, RY; data collection and analysis: DG, RO, XM, LZ, QW, XC, YL; and manuscript preparation: DG, RO, HS, RY.

Conflict of interest

The authors declare that they have no conflict of interests.

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