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【 ORIGINAL ARTICLE 】

Contradictory Responses to the COVID-19 Pandemic in Amyotrophic Lateral Sclerosis Patients and Their Families and Caregivers in Japan

Masaru Yanagihashi[1], Tatsuki Sugisawa[2], Masaaki Fuchimoto[3], Yuuichi Saotome[4], Keiko Onozawa[3], Yukinori Matsumoto[5], Kota Bokuda[6], Junya Ebina[1], Mari Shibukawa[1], Takehisa Hirayama[1], Yoshitaka Murakami[7], Naohiro Washizawa[4], Satoru Ebihara[2] and Osamu Kano[1]

Abstract:

Objective The coronavirus disease 2019 (COVID-19) pandemic has resulted in a shortage of medical resources, including ventilators, personal protective equipment, medical staff, and hospital beds. We investigated the impact of COVID-19 in amyotrophic lateral sclerosis (ALS) patients, their families, caregivers, and medical experts.

Methods We conducted a nationwide ALS webinar about COVID-19 in May 2020 and sent a questionnaire to those enrolled.

Results A total of 135 participants (31 ALS patients; 23 families and caregivers of ALS patients; 81 medical experts) responded to this cross-sectional self-report questionnaire. The results showed that tracheostomy and invasive ventilation (TIV) was used in 22.6% of ALS patients, whereas 77.4% of ALS patients were not under TIV. Among non-TIV patients (n=24), 79.2% did not want TIV in the future. However, 47.4% of non-TIV patients not wanting a tracheostomy in advanced stages replied that they would want an emergency tracheostomy if they developed COVID-19-related pneumonia. These results suggest that ALS patients may be receptive to emergency treatments for reasons other than ALS. In addition, approximately half of the ALS patients agreed with the policy of not ventilating the elderly or ALS patients in case of a ventilator shortage. Furthermore, compared with medical experts, few ALS patients reported that the chance for ALS patients to obtain work was higher due to the increasing availability of remote work.

Conclusions This survey indicates that the COVID-19 pandemic might be associated with increased distress about access to care and work, inducing contradictory responses and potential hopelessness among ALS patients.

Key words: amyotrophic lateral sclerosis (ALS), COVID-19, percutaneous endoscopic gastrostomy, tracheostomy and invasive ventilation, webinar

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[1] Department of Neurology, Toho University Faculty of Medicine, Japan, [2] Department of Rehabilitation Medicine, Toho University Graduate School of Medicine, Japan, [3] Emergency and Critical Care Center, Toho University Omori Medical Center, Japan, [4] Nutrition Therapy Center, Toho University Omori Medical Center, Japan, [5] Department of Community Medical Support Center, Toho University Omori Medical Center, Japan, [6] Department of Neurology, Tokyo Metropolitan Neurological Hospital, Japan and [7] Department of Medical Statistics, Toho University Faculty of Medicine, Japan

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Correspondence to Dr. Osamu Kano, osamu.kano@med.toho-u.ac.jp

Introduction

The coronavirus disease 2019 (COVID-19) is a pandemic that threatens to overwhelm the global health infrastructure. The reported symptoms of COVID-19 include upper and lower respiratory tract infections, ranging from mild to severe, and a possibility for fatal outcomes (1). Hospitals have reported a shortage of key equipment, including ventilators and personal protective equipment for medical staff needed to care for critically ill patients with the disease.

Amyotrophic lateral sclerosis (ALS) is a progressive, incurable, and fatal neurodegenerative disease with an average life expectancy of 3 to 5 years after its onset (2, 3). While there is no treatment to stop its progression, a tracheostomy with invasive ventilation (TIV) can prolong the survival (4). The choice to perform a TIV is challenging because although it allows the patients to survive with increasing paresis, the disease eventually renders patients dependent on family and/or caregivers and ultimately may lead to a locked-in state with the inability to communicate. Therefore, TIVs are performed for only 4-8% of ALS patients in the USA, 5.2% of ALS patients in northern Europe (5-7), and about 30% of ALS patients in Japan (8). The most difficult situation for ALS patients with an impaired respiratory function (and also for their families and caregivers) is when they suffer from pneumonia and require endotracheal intubation. Though the decision to perform the procedure depends on the remaining respiratory function, once endotracheal intubation is completed, extubation becomes difficult, and the endotracheal tube may not be able to be permanently removed. It is thus easy to understand why ALS patients and their families, including their caregivers, might feel anxious during the COVID-19 pandemic. However, there have been few studies on ALS patients' experiences during the COVID-19 pandemic (9-11).

To investigate the impact of COVID-19 on ALS patients, their families, their caregivers, and medical experts, we sent a questionnaire to those enrolled in an ALS webinar (organized by one of the authors of this study) and analyzed the data.

Materials and Methods

We hold a yearly nationwide event named "ALS Café" for ALS patients, their families, and caregivers in an ALS multidisciplinary clinic at Toho University Omori Medical Center. However, we postponed the event this year because of the COVID-19 pandemic. Instead, we held a nationwide webinar in May 2020, for three hours. The total number of connections to the webinar with communication equipment was 294; therefore, we speculate that more than 300 participants viewed our webinar. The topics of this event were nutrition therapy, respiratory care, rehabilitation, and social resource support by ALS multidisciplinary care staff. All topics covered information regarding COVID-19. At the end of this program, we discussed the topics with all staff present and answered questions regarding ALS and COVID-19 that were submitted via email. In addition, we conducted a survey on matters related to the webinar using Google Forms. We asked ALS patients about their current treatment, such as riluzole, edaravone, noninvasive ventilation (NIV), TIV, mechanical cough assist, communication tools, gastrostomy feeding tube, nasogastric tube, rehabilitation, hybrid assistive limb (HAL$^{®}$; cyborg-type robot suit), and living conditions. We also asked patients about their anxieties and concerns regarding COVID-19 and their ideas regarding future medical treatment methods and medical procedures, such as ventilation, tracheostomy, and gastrostomy.

OpenEpi [Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health (www.OpenEpi.com), updated April 6, 2013, accessed January 15, 2021] was used for the statistical analysis. The differences in the distribution among ALS patients, families and caregivers, and medical experts were compared using a chi-squared test (two-sided). The significance level was set at a p value of 5%.

The research in this questionnaire survey was approved by the Ethics Committee of Toho University Omori Hospital, Tokyo, Japan. The procedures were conducted in accordance with the Declaration of Helsinki.

Results

A total of 135 participants, including 31 ALS patients, participated in this cross-sectional self-report questionnaire (Table 1). All responses were classified by respondent type [ALS patients, families and caregivers of ALS patients (F&Cs), and medical experts (MEs)] and summarized. MEs included doctors, nurses, pharmacists, rehabilitation therapists, and care managers. Regarding the age of respondents, respondents indicated their age group instead of their actual age for privacy protection. ALS patients in their 60s were the largest age group and made up 38.7% of the respondents. There was a statistically significant difference in the distributions between 3 groups with respect to age ($p<0.001$). Among ALS respondents, 64.5% were men, but the proportion of women was higher than that of men among F&Cs and MEs. Most ALS patients lived with family or caregivers (83.9%). The proportion of ALS patients who needed care was 71.0%, and that of patients who had regular hospital visits was 51.6%. The frequency of patients receiving treatments of riluzole and edaravone was 77.4% and 45.2%, respectively. The proportion of patients with a percutaneous endoscopic gastrostomy (PEG) was 29.0%. In addition, noninvasive ventilation was used by 12.9% of the patients, and 77.4% were not under TIV. Among non-TIV patients (n=24), 79.2% of them reported they did not want TIV in the future. Mechanical cough assist was used by 22.6% of ALS patients, and 77.4% of ALS patients received rehabilitation. In the past, 22.6% of ALS patients had received HAL$^{®}$ treatment.

Table 1. **Demographics of Amyotrophic Lateral Sclerosis (ALS) Patients, Families and Caregivers of ALS Patients, and Medical Experts.**

	ALS patients (n=31)	Families and caregivers of ALS patients (n=23)	Medical experts (n=81)	p value#
Age, years (%)				<0.001
20-29	3.2	8.7	6.2	
30-39	3.2	8.7	32.1	
40-49	12.9	26.1	40.7	
50-59	19.4	26.1	17.3	
60-69	38.7	26.1	2.5	
70-79	19.4	4.3	1.2	
80-89	3.2	0	0	
Gender, M/F (%)	64.5 / 35.5	34.8 / 65.2	46.9 / 53.1	0.08
Living condition (%)				
Alone	16.1			
With family or caregivers	83.9			
Independence (%)				
Self-reliant	29.0			
Needs care occasionally	25.8			
Needs care at all times	45.2			
Medical care (%)				
Hospital visit	51.6			
Home care* only	12.9			
Hospital visit and home care	35.5			
Riluzole (%)	77.4			
Edaravone (%)				
Under medication in hospital	12.9			
Under medication at home	32.3			
Never	54.8			
Percutaneous endoscopic gastrostomy (PEG) (%)	29.0			
Noninvasive ventilation (%)				
Intermittent use	3.2			
All-night use	3.2			
All-day use	6.5			
Never	87.1			
Tracheostomy and invasive ventilation (TIV) (%)				
In use	22.6			
Not in use	77.4			
- Do not want TIV#, n=24 (%)	79.2			
Mechanical cough assist (%)	22.6			
Rehabilitation (%)				
Hospital visit	12.9			
Home care	51.6			
Hospital visit and home care	12.9			
Never	22.6			
Hybrid assistive limb® treatment (%)				
Treated	22.6			
Never	77.4			

*home care: doctors, rehabilitation staff and nurses visit residents

#: p value<0.05 is considered significant (two-sided Chi-squared test)

Questionnaire regarding COVID-19 infection

Although none of the respondents were infected with COVID-19 at the time they responded to the survey, more than 80% were worried about COVID-19 infection (Table 2). Similarly, over 80% were concerned about the infection of family members, caregivers, and colleagues. The percentage of patients who canceled or postponed hospital visits due to the COVID-19 epidemic was 25.8%, while 61.3% were able to attend such visits as usual. Conversely, only 3.2% of ALS patients cancelled or postponed home-visit nursing. In addition, 74.2% of ALS patients, 95.7% of F&Cs, and 88.9% of MEs were reportedly at risk of medical disruption due to the COVID-19 pandemic. Anxiety about

Table 2. Questionnaire Study of COVID-19 Infection.

	ALS patients (n=31)	Families and caregivers of ALS patients (n=23)	Medical experts (n=81)	p value[#]
COVID-19 infection (%)	0	0	0	
COVID-19 infection of family, caregiver, or co-workers (%)	0	0	4.9	
Concern about contracting COVID-19 (%)				0.57
Very much	48.4	65.2	43.2	
So much	32.3	17.4	39.5	
Same as before	9.7	8.7	12.4	
Not much	6.5	8.7	3.7	
None	3.2	0	1.2	
Concern about infection among family, caregivers, or co-workers (%)				0.30
Very much	38.7	69.6	51.9	
So much	45.2	30.4	38.3	
Same as before	9.7	0	7.4	
Not much	6.5	0	2.5	
None	0	0	0	
Hospital visits (%)				
Cancellation or postponement	25.8			
As usual	61.3			
No hospital visit	12.9			
Home-visit nursing care (%)				
Cancellation or postponement	3.2			
As usual	51.6			
No home care	45.2			
Concern about poor medical care (%)				0.04
Very much	38.7	69.6	37.0	
So much	35.5	26.1	51.9	
Same as before	12.9	4.4	8.6	
Not much	9.7	0	2.5	
None	3.2	0	0	
Concern about cancellation or postponement of PEG (%)	n=22	n=11		0.178
Very much	4.6	18.2		
So much	27.3	36.4		
Same as before	13.6	36.4		
Not much	18.2	0		
Never	9.1	0		
Do not want PEG	27.3	9.1		
Concern about cancellation or postponement of tracheostomy (%)	n=5	n=2		0.55
Very much	20.0	50.0		
So much	20.0	50.0		
Same as before	20.0	0		
Not much	40.0	0		
Never	0	0		
Urgent tracheostomy due to COVID-19 infection[a] (%)	n=19	n=15		0.41
Want tracheostomy	47.4	33.3		
Do not want tracheostomy	52.6	66.7		
The most important medical resource (%)				0.02
Personal protective equipment	16.1	13.0	39.5	
Ventilator	19.4	30.4	22.2	
Medical staff & hospital beds	64.5	56.5	38.3	
The policy that introducing a ventilator does not apply to the elderly because of a shortage of ventilators (%)				0.80
Agree	48.4	39.1	44.4	
Disagree	51.6	60.9	55.6	
The policy that performing TIV does not apply to ALS patients because of a shortage of ventilators (%)				0.02
Agree	48.4	43.5	23.5	
Disagree	51.6	56.5	76.5	
The impact of the pandemic on ALS patients due to the increase in remote work opportunities (%)				<0.001
Produces a chance for work	38.7	21.7	64.2	
Remains the same	58.1	69.6	22.2	
Less chance for work	3.2	8.7	13.6	

PEG: percutaneous endoscopic gastrostomy, TIV: tracheostomy and invasive ventilation

[a] asked of patients, families, and caregivers who indicated that they did not want a tracheostomy

Some percentages in the table might not add up to 100% due to rounding.

#: p value <0.05 is considered significant (two-sided Chi-squared test) not being able to undergo PEG or possibly postponing the procedure was reported by 31.9% of ALS patients and 54.6% of F&Cs.

Among ALS patients who had not undergone TIV but wished to have surgery in the future, 40.0% of them and 100.0% of F&Cs were concerned about the cancellation or postponement of surgery. Furthermore, 33.3% of F&Cs and 47.3% of ALS patients who had not undergone TIV and did not want to have surgery in the future reported their wish for the patient to undergo a TIV if they developed pneumonia due to COVID-19.

When participants were asked which medical resources had the highest priority if medical resources became depleted, medical staff and hospital beds were cited by most ALS patients (64.5%) and F&Cs (56.5%), while personal protective equipment was cited most often by medical experts (39.5%). If there was a shortage of ventilators, 48.4% of ALS patients, 39.1% of F&Cs, and 44.4% of MEs agreed with the policy of not using ventilators for the elderly. Similarly, 48.4% of ALS patients and 43.5% of F&Cs agreed with the policy of not using ventilators for ALS patients in case of a shortage. In response to the question of whether the outbreak of COVID-19 would increase the number of people remote working and the opportunities for ALS patients to play an active role in the future, 38.7% of ALS patients, 21.7% of F&Cs, and 64.2% of MEs answered positively. Four questionnaire items showed significant differences in the distribution between 2 or 3 groups: concern about poor medical care ($p=0.04$), the most important medical resource ($p=0.02$), the policy that performing TIV does not apply to ALS patients because of a shortage of ventilators ($p=0.02$), and the impact of the pandemic on ALS patients due to the increase in remote work opportunities ($p<0.001$).

Discussion

Although this study's sample of ALS patients was small, the age, gender ratio, living conditions, and proportion receiving riluzole therapy, PEG, NIV, and TIV introduction were similar to those reported in a previous epidemiology study conducted in Japan (8). The average age of the onset for ALS was around 60 years old. It was expected that caregivers would often be partners, and there was no marked age difference among the respondents (3). In contrast, most MEs were in their 20-40s, showing a significant difference. The man-to-woman ratio of the patients was exactly the opposite of that of the caregivers, which was presumed to be mainly due to the care provided by husbands and wives.

According to a previous report, an infectious disease outbreak like the COVID-19 pandemic can cause emotional distress and anxiety, even in people not at high risk of getting sick (12, 13). When examining ALS patients exclusively, scores for depression, anxiety, and self-awareness during the COVID-19 outbreak were higher than before the outbreak. In addition, the depression, anxiety, and self-awareness scores of ALS patients were worse than those of caregivers (10). Previous research has indicated that, in ALS patients and their caregivers, anxiety, and depression were closely associated with one another but not with a physical disability or disease duration (14). In the present study, over 80% of respondents were worried that they or the people around them might become infected with COVID-19. Concerns of poor medical care were the greatest in the F&C group, presumably due to high anxiety regarding COVID-19 infection.

Of note, half of the non-TIV patients who did not want a tracheostomy in advanced stages of their ALS reported that they would want an emergency tracheostomy if they developed COVID-19-related pneumonia. Furthermore, one-third of F&Cs reported wanting a tracheostomy performed under these conditions. These results may indicate that ALS patients and F&Cs are particularly receptive to emergency invasive treatments for reasons other than ALS. These intentions were reflected in their responses to the importance of medical resources, and it was speculated that ALS patients and F&Cs were more concerned about having medical staff and beds than personal protective equipment after COVID-19 infection.

However, about half of ALS patients agreed with the policy of not ventilating the elderly or ALS patients in case of a ventilator shortage. The pros and cons were similar among the three groups, but there were many dissenting opinions among MEs regarding refusal to ventilate ALS patients due to a ventilator shortage. This suggests that they felt that ventilators should not be refused to be given to such patients based on ethical reasons.

Furthermore, compared with MEs, fewer ALS patients and F&Cs reported that the chance for ALS patients to obtain work was increased due to the increased availability of remote work. Remote work is also difficult for some ALS patients to perform; however, the lower expectations in patients and F&Cs than in MEs may have been due at least in part to a correlation with distress in both groups, as indicated by a previous study (14).

The findings from the present survey suggest that the COVID-19 pandemic might be associated with increased distress regarding access to care and work, inducing contradictory responses and potential hopelessness among ALS patients. Since we conducted this questionnaire at the ALS Café, which was conducted for the first time in this instance, there are no data to use to compare the distress before and during the pandemic. In the future, we will compare distress by conducting regular questionnaires via Webinar and examine the effects of COVID-19.

In summary, it is more important than ever for ALS medical staff to pay attention to the psychological distress of ALS patients and their F&Cs, and they should consider that these patients may actually wish to receive TIV if they suffer from COVID-19-related pneumonia.

The authors state that they have no Conflict of Interest (COI).

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References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet **395**: 497-506, 2020.
2. Swinnen B, Robberecht W. The phenotypic variability of amyotrophic lateral sclerosis. Nat Rev Neurol **10**: 661-670, 2014.
3. Kano O, Iwamoto K, Ito H, et al. Limb-onset amyotrophic lateral sclerosis patients visiting orthopedist show a longer time-to-diagnosis since symptom onset. BMC Neurol **13**: 19, 2013.
4. Hayashi N, Atsuta N, Yokoi D, et al. Prognosis of amyotrophic lateral sclerosis patients undergoing tracheostomy invasive ventilation therapy in Japan. J Neurol Neurosurg Psychiatry **91**: 285-290, 2020.
5. Vender RL, Mauger D, Walsh S, Alam S, Simmons Z. Respiratory systems abnormalities and clinical milestones for patients with amyotrophic lateral sclerosis with emphasis upon survival. Amyotroph Lateral Scler **8**: 36-41, 2007.
6. Qadri S, Langefeld CD, Milligan C, Caress JB, Cartwright MS. Racial differences in intervention rates in individuals with ALS: a case-control study. Neurology **92**: e1969-e1974, 2019.
7. Tollefsen E, Midgren B, Bakke P, Fondenes O. Amyotrophic lateral sclerosis: gender differences in the use of mechanical ventilation. Eur J Neurol **17**: 1352-1357, 2010.
8. Atsuta N, Watanabe H, Ito M, et al. Age at onset influences on wide-ranged clinical features of sporadic amyotrophic lateral sclerosis. J Neurol Sci **276**: 163-169, 2009.
9. Andrews JA, Berry JD, Baloh RH, et al. Amyotrophic lateral sclerosis care and research in the United States during the COVID-19 pandemic: challenges and opportunities. Muscle Nerve **62**: 182-186, 2020.
10. De Lucia N, Ausiello FP, Spisto M, Manganelli F, Salvatore E, Dubbioso R. The emotional impact of COVID-19 outbreak in amyotrophic lateral sclerosis patients: evaluation of depression, anxiety and interoceptive awareness. Neurol Sci **41**: 2339-2341, 2020.
11. Consonni M, Telesca A, Dalla Bella E, Bersano E, Lauria G. Amyotrophic lateral sclerosis patients' and caregivers' distress and loneliness during COVID-19 lockdown. J Neurol **268**: 420-423, 2021.
12. Wang C, Pan R, Wan X, et al. Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) epidemic among the general population in China. Int J Environ Res Public Health **17**: 2020.
13. Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. Lancet **395**: 912-920, 2020.
14. Chen D, Guo X, Zheng Z, et al. Depression and anxiety in amyotrophic lateral sclerosis: correlations between the distress of patients and caregivers. Muscle Nerve **51**: 353-357, 2015.

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