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Evaluation of Pulmonary Function Test in Patients with Amyotrophic Lateral Sclerosis and its Correlation with Disease Symptoms

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ABSTRACT

Introduction: Amyotrophic lateral sclerosis (ALS) is a neurogenic progressive disease that leads to muscle atrophy. The purpose of this study was to evaluate pulmonary function test (PFT) in patients with ALS and its correlation with ASL symptoms.

Materials and Methods: This cross-sectional study was performed on 32 ALS patients at Ghaem Hospital, Mashhad, Iran. All patients filled out a demographic form and underwent body plethysmography to determine forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), and FEV1/FVC indexes based on their gender and age. Blood samples were also collected to analyze atrial blood gas (ABG) and the levels of oxygen and carbon dioxide. Finally, the data were analyzed by using SPSS20 software.

Results: The mean age of the patients was 61.66±13.6 years. The prevalence of ALS was higher in females than in males. The study of the symptoms of the disease (87.1%) of the patients in the study was motor disorder, (0.31%) swallowing disorder, (48.0%) cough and shortness of breath and (40.0%) speech impairment. The results showed that there was a significant relationship between hypercarbia and night oxygen saturation , which the hypercarbia abundance was higher among patients whose night oxygen saturation was SO2 <90. But there was no significant relationship between hypercarbia and hypoxemia with symptoms of the disease.. Other results showed that the FEV1 test with swallowing disorder (P = 0.01) and cough and shortness of breath (P = 0.02) the results of FVC test with swallowing disorder (P = 0.01) and cough and shortness of breath (P = 0.02) and Also, there was a significant relationship between FEV1 / FVC test with swallowing disorder (P = 0.01) and cough and shortness of breath (P = 0.01) so that, With the normalization of the Pulmonary Function Test and the improvement of the patients , the symptoms of the disease also decreased.

Conclusion: Overall, the results indicate that early detection of pulmonary involvement in patients with ALS can lead to interventions such as oxygen therapy and reduce symptoms and help improve their quality of life.

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Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that affects the upper and lower motor neurons (1). The ALS is the most common neuromuscular disease worldwide that annually affects 1-2 per 100,000 people (1). This disease can be seen as a sporadic or familial condition, which mostly affects males at the age of 40-70 years (1). There is no definite diagnostic tool for ALS; accordingly, the diagnosis of this disease is mainly accomplished based on its clinical features (2). The EI Escorial criteria are among the commonly used diagnostic criteria for ALS (3).

The primary symptoms of ALS include muscular atrophy and weakness, including involuntary muscle fasciculation, as well as muscle cramp and rigidity. Muscular weakness may present as limb weakness, slurred speech, and nasal speech (4-6). The progression of the disease results in difficulty in movement, dysphagia, and speech problems, as well as spasticity and hyperreflexia (4).

Respiratory muscle weakness results in impaired pulmonary function, which is a common feature of ALS, followed by respiratory failure and death (7). Respiratory involvement begins with decreased vital capacity and forced expiratory volume (7). Respiratory failure due to respiratory muscle weakness or pneumonia is the most common cause of death in ALS patients (1). The ALS has no definite treatment and the treatments are mainly symptomatic (8). In case of respiratory involvement, such therapeutic approaches as intermittent positive pressure ventilation, bilevel positive airway pressure, and biphasic cuirass ventilation can be applied for the patients (8).

Regarding the importance of pulmonary function test (PFT) in the management and prognosis of ALS, the present study was conducted to assess the role of PFT among patients with ALS and the relationship between pulmonary function parameters and ALS symptoms.

Materials and methods

This cross-sectional study was conducted on patients with ALS referring to Ghaem Hospital in Mashhad, Iran, for 15 months (data collection from July 2016 to December 2017). The study population was selected using the convenience sampling technique. The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences Mashhad, Iran (registration code: 5018).

Study population

The ALS diagnosis was made by neurologists based on the EI Escorial criteria (3). A total of 32 patients with mild to moderate ALS were identified. All patients were informed about the aim and procedure of the study by the researcher. They were then asked to sign an informed consent form if they were willing to participate in the study. All patients agreed to participate and signed the consent form.

Technical information

A demographic questionnaire and clinical form was filled out by all patients. This form covered such data as age, gender, time of the onset of symptoms, neurological symptoms, respiratory symptoms, time interval between the diagnosis of the disease and first PFT, medical history, and smoking status. All patients underwent PFT in the Respiratory Clinic based on body plethysmography to assess forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), and FEV1/FVC. The values were then interpreted based on age and gender. The assessment of atrial blood gas (ABG) and blood levels of oxygen and carbon dioxide was accomplished by collecting blood samples (1 cm^3) from the subjects.

Statistical analysis

The data were presented using descriptive statistics, including mean and standard deviation for the continuous variables and frequency and percentage for the categorical variables. The assessment of the relationship between the study variables was performed using the Chi-square test. Furthermore, Fisher's exact test was used to analyze the qualitative variables. The data were analyzed in the SPSS software, version 20. P-value smaller than 0.05 was considered statistically significant.

Results

A total of 32 patients, including 15 males (46.9%) and 17 females (53.1%), participated in this study. The mean age of the patients was 61.96±13.06 years. Table 1 presents the demographic characteristics and laboratory findings of the patients. Asthma was present in 2 (6.3%) patients as a comorbid respiratory condition. Out of the 32 patients, 7 (21.9%) cases were not able to perform the FVC test; furthermore, 23 (71.9%) patients failed to perform the maximum inspiratory pressure and maximum expiratory pressure tests.

Table 1. Demographic and laboratory characteristics of the study population

Variable		Frequency (%)
Age (year)	30-40	2 (6.3%)
	41-50	3 (9.4%)
	51-60	10 (31.3%)
	61-70	8 (25.0%)
	>70	9 (28.1%)
Time interval between the first PFT and primary diagnosis	No tests	13 (40.6%)
	At the time of diagnosis	9 (28.1%)
	<1 month from diagnosis	1 (3.1%)
	<1 year from diagnosis	5 (15.6%)
	>1 year from diagnosis	4 (12.5%)
History of a previous PFT		2 (6.3%)
Repeated PFT during study period		5 (15.6%)
Smoking		5 (15.6%)
Comorbid respiratory diseases		2 (6.3%)
Hypercarbia		16 (50%)
Oxygen saturation (day)	<90	0 (0.0%)
	>90	32 (100.0%)
Oxygen saturation (night)	<90	19 (59.4%)
	>90	13 (40.6%)
Oxygen administration	No	17 (53.1%)
	Nocturnal oxygen	8 (25.0%)
	Oxygen therapy	5 (15.6%)
	BIPAP	2 (6.3%)

PFT: pulmonary function test, BIPAP: bi-level positive airway pressure

Table 2 lists the PFT results in the participants. According to this table, 26 (81.3%) patients cooperated in PFT, while 6 (18.8%) failed to cooperate.

Table 2. Results of pulmonary function test in the study population

Variable		Frequency (%)
MIP	>70%	2 (6.3%)
	≤70%	7 (21.9%)
MEP	>70%	3 (9.4%)
	≤70%	6 (18.8%)
FEV1	Abnormal	12 (37.5%)
	Normal	13 (40.6%)
FVC	Abnormal (<50%)	7 (21.9%)
	Normal (>50%)	18 (56.3%)
FEV1/FVC	Abnormal	2 (6.3%)
	Normal	23 (71.9%)

MIP: maximum inspiratory pressure, MEP: maximum expiratory pressure, FEV1: forced expiratory volume in 1 sec, FVC: forced vital capacity

The symptoms of the patients are illustrated in Figure 1. Treatment was performed for all patients; however, 5 (15.6%) patients died during the course of data collection. Among the patients with hypercarbia, 13 (81.2%) cases had nocturnal oxygen saturation below 90%, while 3 (18.8%) subjects had oxygen saturation above 90%. The results indicated a significant relationship between hypercarbia and nocturnal oxygen saturation (P=0.01). The relationship between PFT and ALS symptoms is presented in Table 3. The FEV1 and FVC showed a significant relationship with dysphagia (P=0.01 each) and cough and dyspnea (P=0.02 each). Similarly, FEV1/FVC was significantly correlated with dysphagia (P=0.01) and cough and dyspnea (P=0.01; Table 3).

Table 3. Relationship between disease symptoms and study variables

Variable	Hypoxemia		Hypercarbia		FEV1		FVC		FVE1/FVC	
	Frequency (%)	P-value	Frequency (%)	P-value	Frequency (%)	P-value	Frequency (%)	P-value	Frequency (%)	P-value
Motor involvement	16 (84.2%)	0.40	13 (86.7%)	0.60	9 (75.0%)	0.20	9 (75.0%)	0.20	1 (50.0%)	0.10
Dysphagia	6 (33.3%)	0.50	7 (43.8%)	0.10	1 (9.1%)	0.01**	2 (18.2%)	0.01**	0 (0.0%)	0.01**
Cough and dyspnea	9 (64.3%)	0.07	7 (58.3%)	0.20	5 (55.6%)	0.02*	5 (55.6%)	0.02*	2 (100.0%)	0.01**
Speech problems	7 (41.2%)	0.50	6 (42.9%)	0.50	5 (41.7%)	0.08	5 (41.7%)	0.08	1 (50.0%)	0.10

FEV1: forced expiratory volume in 1 sec, FVC: forced vital capacity
* Significant at α=0.05 based on Fisher's exact test
** Significant at α=0.01 based on Fisher's exact test

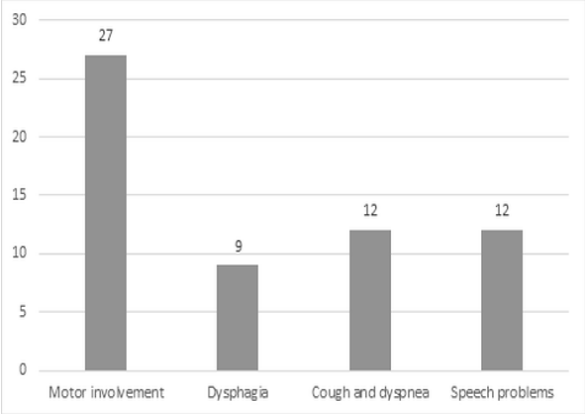

Figure 1. Frequency of symptoms among the study population

Discussion

The findings of this study revealed that the mean age of the patients with the diagnosis of ALS was 61.96±13.06 years, which is in line with the previous reports (8-11). In this study, ALS was most frequently diagnosed in females (53.1%), which is in contrast with the findings of the previous studies (10-12). The discrepancy between the findings of the present research and those of the previous studies might be due to the small sample size of this study.

This study revealed that hypercarbia was present in 50% of the patients while all patients had oxygen saturation above 90% during the daytime, 59.4% of them had oxygen saturation below 90% at night. This study also found a significant relationship between hypercarbia and nocturnal oxygen saturation. Similarly, in a study performed by Prell et al. (2016), a relationship was observed between dyspnea and reduced oxygen saturation (13). It was also found that ALS patients with hypoventilation had significantly lower nocturnal oxygen saturation. Regarding this, such interventions as oxygen therapy and nasal intermittent positive pressure ventilation can help improve the quality of life and pulmonary complications, thereby affecting the longevity of ALS patients (13-16).

Based on the findings of the current study, both FEV1 and FVC demonstrated a significant relationship with dysphagia and cough/dyspnea, indicating that patients with normal PFT had fewer complaints. In a study, the survival of ALS patients increased with the improvement of PFT results, and FVC was considered as a risk factor for ALS survival (17). Similarly, in another study, FEV1 and FVC were lower in ALS patients at the time of diagnosis, compared to those in healthy individuals (18, 19).

It is recommended to assess PFT in all ALS patients upon diagnosis in order to determine the risk of mortality and morbidity and improve the quality of life and longevity in ALS patients (20, 21). Based on the evidence, PFT has a high sensitivity and specificity in the diagnosis of respiratory involvement in ALS. The findings of this study provided further evidence regarding the importance of PFT in the management and diagnosis of ALS.

One of the limitations of this study was the implementation of data collection in only one center, which can limit the generalizability of the findings to the whole ALS population. Furthermore, due to the limitation in time and the rarity of the disease, small sample size was investigated in this study. It is recommended to perform multicenter longitudinal studies with larger sample size to better evaluate the respiratory risk factors for morbidity and mortality in ALS patients.

Conclusion

The PFT can be used as a cheap and easily accessible diagnostic tool for the early detection and management of respiratory involvement in ALS.

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Conflicts of interest

The authors declare that there is no conflict of interest.

References

1. Gruis KL, Lechtzin N. Respiratory therapies for amyotrophic lateral sclerosis: a primer. Muscle Nerve. 2012; 46:313-31.
2. van der Gr aaff MM, Sage CA, Caan MW, Akkerman EM, Lavini C, Majoie CB, et al. Upper and extra-motoneuron involvement in early motoneuron disease: a diffusion tensor imaging study. Brain. 2011; 134:1211-28.
3. Brooks BR, Miller RG, Swash M, Munsat TL. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord. 2000; 1(5):293-9.
4. Moosavi-Movahedi AA, Golchin AR, Nazari KK, Chamani J, Saboury AA, Bathaie SZ, Tangestani-Nejad S. Microcalorimetry, energetics and binding studies of DNA–dimethyltin dichloride complexes. Thermochim Acta. 2004; 414:233-41.
5. Haidet-Phillips AM, Hester ME, Miranda CJ, Meyer K, Braun L, Frakes A, et al. Astrocytes from familial and sporadic ALS patients are toxic to motor neurons. Nat Biotechnol. 2011; 29:824-8.
6. Noh EJ, Park MI, Park SJ, Moon W, Jung HJ. A case of amyotrophic lateral sclerosis presented as

oropharyngeal Dysphagia. J Neurogastroenterol Motil. 2010; 16:319-22.
7.Galvin M, Gaffney R, Corr B, Mays I, Hardiman O. From first symptoms to diagnosis of amyotrophic lateral sclerosis: perspectives of an Irish informal caregiver cohort-a thematic analysis. BMJ Open. 2017; 7:e014985.
8. Nicholson TT, Smith SB, Siddique T, Sufit R, Ajroud-Driss S, Coleman JM 3rd, et al. Respiratory pattern and tidal volumes differ for pressure support and volume-assured pressure support in amyotrophic lateral sclerosis. Ann Am Thorac Soc. 2017; 14:1139-46.
9.Chamani J, Heshmati M. Mechanism for stabilization of the molten globule state of papain by sodium n-alkyl sulfates: spectroscopic and calorimetric approaches. J Colloid Interface Sci. 2008; 322:119-27.
10.Tobin K, Gilthorpe MS, Rooney J, Heverin M, Vajda A, Staines A, et al. Age-period-cohort analysis of trends in amyotrophic lateral sclerosis incidence. J Neurol. 2016; 263:1919-26.
11. Ingre C, Roos PM, Piehl F, Kamel F, Fang F. Risk factors for amyotrophic lateral sclerosis. Clin Epidemiol. 2015; 7:181-93.
12. Mehta J, Kamdar V, Dumesic D. Phenotypic expression of polycystic ovary syndrome in South Asian women. Obstet Gynecol Surv. 2013; 68:228-34.
13. Prell T, Ringer TM, Wullenkord K, Garrison P, Gunkel A, Stubendorff B, et al. Assessment of pulmonary function in amyotrophic lateral sclerosis: when can polygraphy help evaluate the need for non-invasive ventilation? J Neurol Neurosurg Psychiatry. 2016; 87:1022-6.
14.Zolfagharzadeh M, Pirouzi M, Asoodeh A, Saberi MR, Chamani J. A comparison investigation of DNP-binding effects to HSA and HTF by spectroscopic and molecular modeling techniques? J Biomol Struct Dyn. 2014; 32:1936-1952.
15. Jackson CE, Rosenfeld J, Moore DH, Bryan WW, Barohn RJ, Wrench M, et al. A preliminary evaluation of a prospective study of pulmonary function studies and symptoms of hypoventilation in ALS/MND patients. J Neurol Sci. 2001; 191:75-8.
16. Radunovic A, Annane D, Rafiq MK, Brassington R, Mustfa N. Mechanical ventilation for amyotrophic lateral sclerosis/motor neuron disease. Cochrane Database Syst Rev. 2017; 10:CD004427.
17. Javad Mousavi SA, Zamani B, Shahabi Shahmiri S, Rohani M, Shahidi GA, Mostafapour E, et al. Pulmonary function tests in patients with amyotrophic lateral sclerosis and the association between these tests and survival. Iran J Neurol. 2014; 13:131-7.
18. Chandrasoma B, Balfe D, Naik T, Elsayegh A, Lewis M, Mosenifar Z. Pulmonary function in patients with amyotrophic lateral sclerosis at disease onset. Monaldi Arch Chest Dis. 2012; 77:129-33.
19. Sanei H, Asoodeh A, Hamedakbari-Tusi S, Chamani J. Multi-spectroscopic investigations of aspirin and colchicine interactions with human hemoglobin: binary and ternary systems. J Solution Chem. 2011; 40:1905-31.
20. Perez T. Amyotrophic lateral sclerosis (ALS): evaluation of respiratory function. Rev Neurol (Paris). 2006; 162:4S188-94.
21. Traxinger K, Kelly C, Johnson BA, Lyles RH, Glass JD. Prognosis and epidemiology of amyotrophic lateral sclerosis. Neurol Clin Pract. 2013; 3:313-20.