Association Between Rectus Abdominis Denervation and Ventilation Dysfunction in Patients with Amyotrophic Lateral Sclerosis

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Abstract

Background: Spontaneous potentials in electromyography (EMG) of paraspinal muscles are associated with diaphragm denervation and, therefore, poor respiratory function in amyotrophic lateral sclerosis (ALS) is understandable. EMG changes in the rectus abdominis (RA) display an effect similar to those in paraspinal muscles with respect to the function of lower motor neurons in the thoracic spinal cord. The RA denervation was examined to determine its association with ventilation dysfunction in ALS.

Methods: We collected the clinical data of 128 patients with sporadic ALS in Department of Neurology of Peking University Third Hospital from 2009 to 2013. EMG, Revised ALS Functional Rating Scale (ALSFRS-R) and forced vital capacity (FVC) were performed in all patients and the differences in the EMG changes in RA between those with and without FVC ≥ 80% were analysed.

Results: The mean FVC value was 83.4% ± 17.1% (range: 45%–131%) of the predicted value. A total of 79 patients displayed FVC ≥ 80%, and 49 patients displayed FVC < 80%. Compared with the patients displaying a normal FVC (60/79, 75.9%), spontaneous activity in RA was significantly different among those patients displaying an FVC < 80% (47/49, 95.9%). In addition, spontaneous potentials in RA were more frequently detected in patients exhibiting dyspnea (32/33, 97.0%) than in patients without dyspnea (75/95, 78.9%).

Conclusion: Spontaneous potentials in RA are associated with ventilation dysfunction and dyspnea in ALS patients.

Key words: Denervation; Dyspnea; Forced Vital Capacity; Rectus Abdominis; Ventilation Dysfunction

INTRODUCTION

Neurogenic changes based on electromyography (EMG) of the rectus abdominis (RA) muscles are regarded as evidence of lesions in lower motor neurons (LMNs) of the thoracic spinal cord in amyotrophic lateral sclerosis (ALS).[1,2] In previous reports, fibrillation (fib) potentials and positive sharp waves (psw) in C6 and T5 paraspinal muscles were associated with diaphragm denervation and, therefore, poor respiratory function in ALS is understandable.[3,4] EMG changes in RA display an effect similar to those in paraspinal muscles with respect to the function of LMNs in the thoracic spinal cord.[1] Compared with those neurons innervating the distal muscles of limbs, LMNs innervating axial muscles, such as the diaphragm and the paraspinal and RA muscles, were situated more medially in the anterior horn.[4,5] These characteristics suggested that neurogenic changes in RA should be associated with respiration dysfunction in ALS in a manner being similar to neurogenic changes in the diaphragm and the paraspinal muscles. RA denervation was examined to determine its association with ventilation dysfunction in ALS.

METHODS

Patients

We collected clinical data from 128 patients with sporadic ALS from 2009 to 2013. All patients received detailed...
neurological, neuroimaging, neurophysiological, and hematological investigations, including Revised ALS Functional Rating Scale (ALSFRS-R) and forced vital capacity (FVC) assessments.

According to the revised El Escorial criteria, 52 patients were diagnosed with definite ALS and the remaining with probable ALS. ALSFRS-R, FVC, and EMG were simultaneously assessed. FVC values were expressed as percentages of the predicted values. FVC values <80% were considered as abnormal FVC, representing ventilation dysfunction. The Ethical Committee of Peking University Third Hospital approved the present study.

**Electrophysiological investigation**

EMG recordings were obtained from the bulbar, limb, and thoracic muscles including but not limited to the sternocleidomastoid, first interosseus dorsalis, RA, and tibialis anterior muscles of all 128 patients using a concentric needle electrode according to standard settings (Keypoint; Medtronic, Skovlunde, Denmark). At least one more muscle innervated by different roots and peripheral nerves besides first interosseus dorsalis and tibialis anterior muscles was examined for both cervical and lumbosacral spinal cord regions, such as extensor digitorum communis, biceps brachii, or triangular muscles in upper limbs and gastrocnemius, quadriceps femoris, or biceps femoris muscles in lower limbs. Care was taken to ensure complete relaxation when spontaneous activity (fibrillations and positive sharp waves; fib-psw) was investigated. In each muscle, we searched for spontaneous activity at two sites in each of four different insertions. We carefully observed the EMG recordings for spontaneous activity, which was determined to be pathological only when the waves were identified at >2 sites within the same muscle. Fib-psw was considered as present if observed in reproducible trains after at least 300 ms following needle insertion. The motor unit action potential (MUP) configuration was assessed during moderate voluntary activity. A minimum of 20 MUPS were measured in each muscle. The recruitment patterns of each motor unit were evaluated during maximal voluntary effort. When at least two muscles innervated by different roots and peripheral nerves showed neurogenic damages in upper and lower limbs, the changes were regarded as EMG signs of LMN damages in the cervical and lumbosacral spinal cord regions, respectively.

EMG of RA was investigated above the umbilicus while the subjects lay in a comfortable supine position. RA contraction was detected as bulging between the tendinous intersections of the subjects. The needle was inserted approximately 1 cm lateral to the midline at the second or third belly bilaterally. Spontaneous activity in RA, including superficial and deep muscle layers, was examined according to methods mentioned above. Then, subjects were instructed to maximally elevate the upper body. An interference pattern was evaluated during this exercise to measure the maximal voluntary contraction of RA. Given that moderate voluntary activity of RA was difficult to control, only spontaneous activity and the recruitment pattern of RA were examined.

The differences in the EMG changes in RA between patients with and without FVC ≥80% were analyzed. In total, 33 patients exhibited an ALSFRS-R respiratory subset score of <12. Diseases related to the cardiovascular system and lungs were excluded. The relationship between fib-psw of RA and dyspnea was also evaluated.

**Statistical analysis**

Data were analyzed using SPSS 13.0 software for Windows (SPSS Inc., Chicago, IL, USA). Quantitative results were expressed as mean ± standard deviation (SD). The independent t-test, the paired t-test, and the Chi-square test were used. A value of $P < 0.05$ was considered statistically significant. The sensitivity, specificity, and positive and negative predictive values of the results were calculated.

**Results**

**Clinical characteristics**

A total of 128 ALS patients experienced a mean onset age of 51.6 ± 10.9 years (range: 24–80 years), exhibited a mean disease duration of 16.6 ± 12.6 months from the initial symptom (range: 3–81 months), and included 79 males and 49 females. The disease was characterized by bulbar onset in 17 patients, upper limb onset in 73 patients, and lower limb onset in 38 patients [Table 1]. The mean FVC value was 83.4% ±17.1% (range: 45%–131%) of the predicted value, and the mean ALSFRS-R score was 40.0 ± 5.8 (range: 15–47). A total of 79 patients displayed FVC ≥80% (mean ALSFRS-R score of 41.6 ± 4.6), and 49 patients displayed FVC <80% (mean ALSFRS-R score of 37.5 ± 6.7). No significant differences in onset age, disease duration, gender, or onset site were noted between the two FVC groups. The ALSFRS-R score of FVC ≥80% group significantly differed from that of FVC <80% group ($P < 0.001$).

**Electromyography**

Fib-psw of RA was detected in 107 patients (107/128, 84.0%), including 60 patients in FVC ≥80% group and 47 patients in FVC <80% group [Table 1]. Compared with patients displaying a normal FVC value (60/79, 75.9%), fib-psw in RA significantly differed in patients displaying FVC <80% (47/49, 95.9%) ($P = 0.003$). Fib-psw in RA showed high sensitivity and negative predictive value for FVC <80%, which were 95.9% and 90.5%, respectively. Reduced recruitment pattern of RA was found in 118 cases (118/128, 92.2%), including 71 (71/79, 89.9%) in FVC ≥80% group and 47 (47/49, 95.9%) in the other group. No significant differences were noted in frequency of reduced recruitment pattern of RA between the two groups ($P > 0.05$). There was no relation between FVC and fib-psw in the first interosseus dorsalis or tibialis anterior muscles [Table 1]. All 128 ALS patients were separated into two groups based on ALSFRS-R respiratory subset scores. In total, 33 patients exhibited dyspnea (ALSFRS-R respiratory subset score <12),...
and 95 patients did not exhibit dyspnea (ALSFRS-R respiratory subset score = 12). Fib-psw of RA was detected in 32 patients exhibiting dyspnea (32/33, 97.0%) and 75 patients not (75/95, 78.9%). Comparison of these two groups revealed statistically significant differences in the spontaneous activity of RA (P = 0.016) [Table 2].

**DISCUSSION**

In patients with ALS, dyspnea is a common symptom, and respiratory failure is a typical cause of death.[9] Neuropathological examinations might play an important role in determining the cause of dyspnea. de Carvalho et al.[3] reported that fib-psw in the C6 and T5 paraspinal muscles were associated with a lower FVC value and diaphragm denervation in ALS. RA is an important respiratory muscle and displays some characteristics that are similar to paraspinal muscles. First, both are axial muscles; RA lies within the anterior abdominal wall adjacent to the anterior median line, and the paraspinal muscles are adjacent to the posterior median line.[3] Thus, RA and paraspinal muscles are the flexor and extensor muscles of the spine, respectively. Second, RA plays a role in exhalation, and the paraspinal muscles are also considered as accessory muscles of ventilation.[3] Third, both RA and lower paraspinal muscles are innervated by nerves from the lower thoracic spinal cord. Fourth, as axial muscles, LMNs that regulate RA and paraspinal muscles are distributed medially along the anterior horn in a manner similar to the innervation of the diaphragm.[10] Finally, EMG changes in both RA and paraspinal muscles indicate lesions of LMNs within the thoracic region of the spinal cord in ALS.[10] These mentioned above indicate the possibility of a biological susceptibility of diaphragmatic, paraspinal and RA neurons, and their consequent concurrent involvement in ALS. Focal and regional susceptibilities were found in ALS by clinical and pathological studies.[10-12] The focal susceptibility of LMNs might be helpful in understanding the pathogenesis and progression in ALS. Therefore, we hypothesized that neurogenic changes in RA are associated with ventilation dysfunction in ALS.

We observed that spontaneous potentials in RA were associated with a lower FVC value and dyspnea in ALS patients. The sensitivity and negative predictive value of fib-psw in RA were high for finding a low FVC. The results indicated that the diaphragm and RA were concomitantly involved in ALS.

Compared with the diaphragm and the intercostal and paraspinal muscles, RA displays several advantages for EMG examination. RA is a relatively safe and convenient muscle for EMG recording. In addition, it is easy for subjects to perform voluntary muscle movements. Most importantly, patients must be in a lateral decubitus or prone position before respiratory symptoms emerge. Initial respiratory muscle involvement can be detected via EMG. In this study, we observed that the percentage of ALS patients displaying fib-psw in the RA was considerably greater in patients exhibiting a lower FVC value or dyspnea than patients exhibiting a higher FVC value or no dyspnea, respectively. Given its safety and convenience, EMG of RA represents a good method to evaluate the involvement of respiratory muscles in early stage ALS, aside from lesions in the LMNs of the thoracic spinal cord.

There were some limitations in this study. EMG of the diaphragm or paraspinal muscles was not performed in this study because of risks or patients’ intolerance. The

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**Table 1: Clinical characteristics and fib-psw in RA of 128 patients with ALS**

| FVC     | n  | Onset age (years) | Gender, n (male:female) | Duration (months) | Bulbar onset | Upper limb onset | Lower limb onset | ALSFRS-R score | Fib-psw in the FID | Fib-psw in the TA | Fib-psw in the RA |
|---------|----|-------------------|-------------------------|-------------------|--------------|------------------|-----------------|-----------------|--------------------|--------------------|------------------|
| ≥80%    | 79 | 50.5 ± 10.9       | 49:30                   | 15.1 ± 10.2       | 14           | 41               | 24              | 41.6 ± 4.6       | 68                 | 71                 | 60                |
| <80%    | 49 | 53.3 ± 10.6       | 30:19                   | 19.0 ± 15.6       | 3            | 32               | 14              | 37.5 ± 6.7*      | 45                 | 46                 | 47*               |

*P value for contrast of variates between patients with FVC ≥80% or not; P < 0.05, as compared with patients with FVC ≥80%. Values are presented as n or mean ± SD. Fib-psw: Fibrillations and positive sharp waves; RA: Rectus abdominis; ALS: Amyotrophic lateral sclerosis; FVC: Forced vital capacity; ALSFRS-R: Revised ALS Functional Rating Scale; FID: First interosseus dorsalis; TA: Tibialis anterior; --: Not applicable; SD: Standard deviation.

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**Table 2: Dyspnea and fib-psw of the RA in 128 patients with ALS**

| ALSFRS-R score (respiration subset) | n  | Fib-psw in the RA |
|-------------------------------------|----|-------------------|
| 12                                 | 95 | 75                |
| <12                                | 33 | 32*               |

*P value for contrast of fib-psw in the RA between patients with an ALSFRS-R respiratory subset score of 12 or not; P < 0.05, as compared with patients with an ALSFRS-R respiratory subset score of 12. Fib-psw: Fibrillations and positive sharp waves; RA: Rectus abdominis; ALS: Amyotrophic lateral sclerosis; ALSFRS-R: Revised ALS Functional Rating Scale; --: Not applicable.
The influence of denervation of RA on ventilation was not directly compared with that of the diaphragm or paraspinal muscles in view of the diaphragm being the most important respiratory muscle. Moreover, it was difficult to perform EMG of RA in some ALS patients who were unable to lie flat or might have gastrostomy or be obese. These technical factors should be noted and improved.

In conclusion, diaphragm and RA are concomitantly involved and spontaneous potentials in RA are associated with ventilation dysfunction and dyspnoea in ALS patients. EMG of RA may be a relatively safe and simple method to evaluate the involvement of respiratory muscles in ALS. Respiratory function assessments, such as FVC, should be performed when fib-psw of RA are detected in ALS patients with dyspnea or not.

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Conflicts of interest
There are no conflicts of interest.

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