Utility of Rectus Abdominis Ultrasound as a Respiratory Function Test for Amyotrophic Lateral Sclerosis

Rina Ando, Yuki Yamanishi, Satoshi Tada, Noriyuki Miyaue,
Mohammed Emamussalehin Choudhury, and Masahiro Nagai

BACKGROUND: Amyotrophic lateral sclerosis (ALS) causes deterioration of respiratory function. Muscle weakness of the orbicularis oris interferes with the accurate assessment of respiratory function using spirometry. Reduced forced vital capacity (FVC) is an indicator that helps determine the appropriate timing to provide noninvasive ventilation (NIV) for the survival of ALS patients. We employed ultrasonography to evaluate changes in respiratory function by measuring the thickness of the rectus abdominis (RA) muscle as a possible alternative to spirometry. METHODS: Sixteen subjects with ALS were included in this study. The thickness of RA muscles was measured using ultrasonography, and respiratory fluctuations, such as vital capacity (VC), FVC, FEV_1, percentage of predicted VC (%VC), percentage of predicted FVC (%FVC), percentage of predicted FEV_1 (%FEV_1), and FEV_1/FVC, were evaluated using spirometry. RESULTS: Sixteen subjects underwent assessment by ultrasonography. A positive correlation was observed between the percent change in RA muscle thickness evaluated from maximal expiration to maximal inspiration and %VC ($P = .001$), %FVC ($P = .001$), FEV_1 ($P = .009$), and %FEV_1 ($P = .02$). CONCLUSIONS: RA ultrasonography was useful for predicting a reduction in VC in subjects with ALS and may help determine the best timing for introducing NIV. *Key words: amyotrophic lateral sclerosis; ultrasonography; spirometry; respiratory function tests; ventilation; prognosis.* [Respir Care 2022;67(5):520–525. © 2022 Daedalus Enterprises]

Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease of the upper and lower motor neurons resulting in bulbar paralysis (dysarthria and dysphagia), muscle weakness, atrophy, and spasticity.[1] Moreover, it causes atrophy of the respiratory muscles leading to the deterioration of respiratory function. Therefore, periodic evaluation of respiratory function is crucial for the prognostication of patients with ALS. Indeed, these patients are tested clinically using spirometry, and occasionally using arterial blood gas analysis, to evaluate respiratory function and the degree of respiratory distress. However, there are limitations of using spirometry to assess respiratory function in patients with ALS exhibiting bulbar paralysis due to the weakness of the orbicularis oris muscle that may hinder the creation of a seal around the equipment's mouthpiece.[2,3] In a retrospective study, some subjects with ALS exhibited forced vital capacity (FVC) below 75% even in the absence of dyspnea.[4] Therefore, we utilize arterial blood gas analysis to assess the respiratory function of patients with ALS with bulbar paralysis and check for an increase in P_{aCO_2}. However, arterial blood gas analysis requires the drawing of arterial blood, which can be difficult and painful. Therefore, other alternatives should be explored for the evaluation of respiratory function in patients with ALS.

To stabilize respiratory function, maintain proper ventilation, and improve survivability in patients with ALS, noninvasive ventilation (NIV) or invasive ventilation is commonly required. A clinical report showed an improvement in the quality of life and survival of patients with ALS

Drs Ando, Yamanishi, Tada, Miyaue, and Nagai are affiliated with Department of Neurology and Clinical Pharmacology, Ehime University Graduate School of Medicine, Ehime, Japan. Dr Choudhury is affiliated with Department of Neurology and Clinical Pharmacology, Ehime University Graduate School of Medicine, Ehime, Japan.

Correspondence: Rina Ando MD PhD, Department of Neurology and Clinical Pharmacology, Ehime University Graduate School of Medicine, Tohon Ehime, 791–0295, Japan. E-mail: ando.rina.cn@ehime-u.ac.jp.

when using NIV,[5] whereas another described NIV as an established long-term treatment modality for ALS.[4] Reduction of FVC to 50% of predicted or less is considered an indication for introducing NIV in patients with ALS to promote their survival.[4,6]

There is growing evidence pointing to the use of ultrasonography to evaluate the muscles of patients with ALS; for example, bulbar muscle ultrasound could assess upper motor neuron involvement in the bulbar region of ALS patients.[7] Ultrasonography is a noninvasive procedure that can be performed at the bedside along with other clinical and surgical interventions. Ultrasonography is used to assess muscular fasciculations and confirm limb muscular thickness.[8-11] In addition, several reports have revealed the correlation between diaphragmatic thickness and respiratory function of subjects with ALS.[2,12,13] However, for inexperienced clinicians, identifying and measuring the thickness of a diaphragm by ultrasonography is difficult.

During regular medical examinations of patients with ALS, we detected the fasciculation of the tongue, limb, and paraspinal muscles using ultrasonography. Additionally, we detected fasciculations of the rectus abdominis (RA) muscles along the lower thoracic nerves (Th 5–12) because the RA muscles are superficially located and easily identifiable for observation and analysis. Furthermore, we observed the movement of the RA muscles in effortless abdominal breathing and its absence during resting breathing. Although the RA is not involved directly in breathing at rest, it extends during inspiration and contracts with other auxiliary respiratory muscles during expiration in abdominal breathing. Thus, we postulated that if there was an association between the changes in RA muscles during abdominal breathing and the spirometry findings reflective of respiratory function the changes in RA muscles could be an alternative respiratory function test.

In this study, ultrasonography was performed to evaluate changes in the respiratory function of patients with ALS by measuring the changes in the thickness of the RA muscles.

Methods

In total, 16 subjects diagnosed with ALS according to the Awaji criteria in the neurological department of Ehime University Hospital from April 2014–October 2020 were enrolled in this study (Table 1). These patients were chosen after excluding those who could not undergo spirometry or abdominal breathing due to cognitive decline and those who could not appropriately undergo spirometry due to severe bulbar palsy. Eleven men and 5 women underwent assessment by ultrasonography, none of whom had severe bulbar palsy, thus allowing spirometry assessments. Additionally, none of the subjects had dementia or lung disorders. This study was approved by the clinical research ethics committee of Ehime University Hospital, and consent was obtained from all subjects.

The thickness of the RA muscle was evaluated with subjects in the supine position by one of our investigators who was trained in ultrasonography. The Sonosite MicroMaxx ultrasound system (FUJIFILM Sonosite, Bothell, Washington) and the GE LOGIQ V5 ultrasound system (GE Healthcare, Madison, Wisconsin) with linear probes (5–13 MHz and 6–12 MHz, respectively) were used in our study. The probe was placed under the xiphoid process, and the RA muscles were identified on both sides of the white line (midline structure of the aponeurosis). We measured the thickness of both RA muscles at their widest point (central area). Measurements were made at maximum inspiration (full inspiration during abdominal breathing), maximum expiration (full exhalation during abdominal breathing), and resting breathing (Fig. 1). The percent change in RA muscle thickness was calculated as the thickness during maximal expiration minus the thickness during maximal inspiration divided by the thickness during maximal inspiration.

The respiratory function of the subjects was measured in a sitting position using the same spirometer (DISCOM-21 FXIII, Chest, Tokyo, Japan) by physiological examining technicians. We used the spirometer to measure the vital capacity (VC), FVC, FEV_1, percentage of predicted VC (%VC), percentage of predicted FVC (%FVC), percentage of predicted FEV_1 (%FEV_1), and the FEV_1/FVC.

QUICK LOOK

Current knowledge

Patients with amyotrophic lateral sclerosis (ALS) experience decreased respiratory function as the disease progresses and require monitoring to evaluate respiratory distress. Spirometry cannot always be efficiently performed in patients with bulbar paralysis. There is a correlation between diaphragmatic thickness and respiratory function; however, identification of the diaphragm through ultrasonography is challenging.

What this paper contributes to our knowledge

The rectus abdominis (RA) muscle is a superficially located muscle involved in abdominal breathing. The percent change in RA thickness is positively correlated with vital capacity (VC), forced vital capacity (FVC), percentage of predicted VC, %FVC, FEV_1, and percentage of predicted FEV_1. Subjects with ALS exhibiting reduced percent change in RA muscle thickness had reduced respiratory function. The percent change in RA muscle thickness can be used as an indicator of respiratory function.

Table 1.: Demographic and Clinical Characteristics of Patients

No	Age, y	Sex	Duration of Disease, y	Onset symptom	Manual Muscle Test					Orbicularis Oris Muscle	Dysarthria	Results of Spirometry						
					Neck flexors	Deltoid	Iliopsoas	Carpal extensor	Anterior tibialis			VC, L	FVC, L	FEV$_1$, L	%VC	%FVC	%FEV$_1$	FEV$_1$/FVC
1	64	M	3.0	Muscle weakness of left arm	5	3	5	3	5	Normal	–	3.24	3.17	2.49	93.9	91.9	92.2	78.5
2	72	M	6.0	Muscle weakness of both legs	5	5	1	5	1	Mild weakness	±	3.81	3.75	2.34	107.0	105.3	81.3	62.4
3	70	M	2.0	Muscle weakness of right leg	4	3	4	4	1	Normal	–	2.38	2.32	1.58	78.5	76.6	81.0	68.1
4	72	M	2.0	Muscle weakness of respiratory	4	5	3	5	1	Normal	–	1.69	1.84	1.74	49.4	53.8	65.9	94.6
5	58	M	2.0	Muscle weakness of left arm	5	1	4	0	4	Normal	±	1.68	1.74	1.44	46.5	49.2	48.6	82.8
6	61	F	2.0	Muscle weakness of left leg	5	5	5	5	1	Normal	–	3.25	3.41	2.73	131.0	137.5	133.2	80.1
7	59	F	2.0	Muscle weakness of left leg	4	5	4	5	3	Normal	–	2.27	2.25	2.06	92.3	91.5	102.0	91.6
8	67	M	1.5	Muscle weakness of trunk	5	4	5	5	5	Normal	–	3.73	3.58	2.70	111.7	107.2	108.0	75.4
9	66	M	1.0	Muscle weakness of both arms	5	2	4	4	5	Normal	–	3.86	3.74	2.84	107.8	104.5	97.6	75.9
10	64	M	3.0	Muscle weakness of left arm	5	3	4	4	5	Normal	±	3.31	3.10	2.40	96.2	90.1	89.9	77.4
11	58	F	2.0	Muscle weakness of right leg	5	2	2	5	0	Normal	–	3.05	3.05	2.50	118.2	118.2	112.6	82.0
12	52	M	3.0	Muscle weakness of right arm	5	2	3	3	0	Normal	–	4.15	4.05	3.44	114.0	111.3	113.5	84.9
13	71	M	3.0	Muscle weakness of right arm	5	5	5	3	3	Normal	±	2.91	2.94	2.25	93.6	94.5	107.7	76.5
14	64	M	3.0	Muscle weakness of right arm	4	5	5	5	5	Normal	±	3.36	3.37	2.78	102.8	103.1	116.3	82.5
15	56	F	7.0	Muscle weakness of neck	3	3	5	5	5	Normal	±	2.46	2.62	2.01	96.9	103.1	93.5	76.7
16	67	F	1.0	Leg cramps	5	4	4	4	5	Mild weakness	+	2.51	2.10	2.09	94.0	83.0	104.0	99.5

This table shows all subjects who participated in this study. Subject 16 had moderate weakness of orbicularis oris muscle; however, she was able to perform spirometry accurately. VC = vital capacity
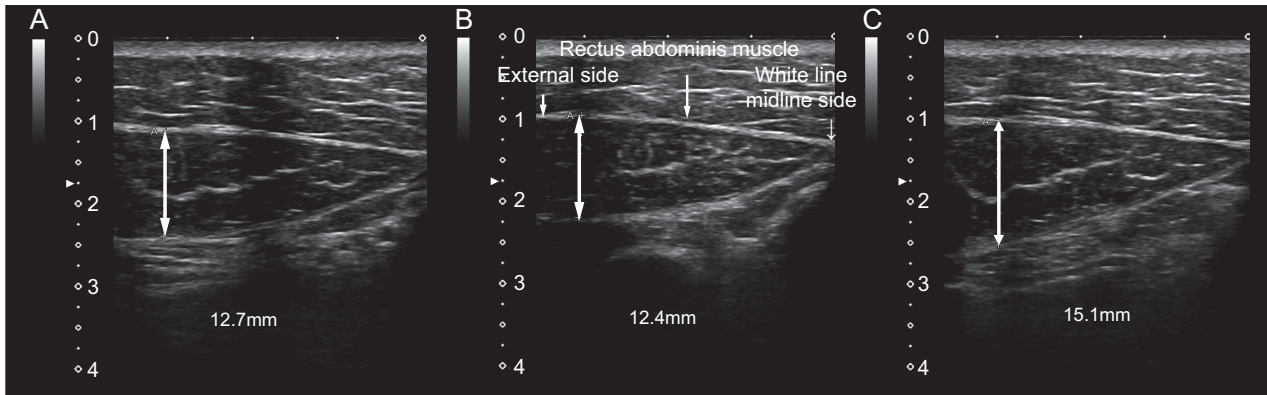
Fig. 1. Normal echo of rectus abdominis muscles (RA) in a healthy subject. The probe is placed under the xiphoid process, and the RA muscles are identified on both sides of the white line. We measured the thickness of both RA muscles at their widest (central part) during A: resting breathing, B: maximal inspiration, and C: maximal expiration.

Statistical analysis was performed using SAS JMP v14.2 software (SAS Institute, Cary, North Carolina). We analyzed the correlation between the percent change in RA muscle thickness and the RA muscle thickness with resting breathing and the results of spirometry using the Pearson correlation analysis. Statistical significance was set at $P < .05$.

Results

All 16 subjects underwent ultrasonographic analysis of the RA muscles and spirometry to evaluate respiratory function. The percent change in RA muscle thickness was positively correlated with the RA muscle thickness at resting breathing and the volume of VC and FVC ($P = .03$, $P = .009$, and $P = .007$, respectively). Moreover, the percent change in RA muscle thickness was positively correlated with %VC ($P = .001$) (Fig. 2A). Additionally, the %FVC, FEV_1, and $\%FEV_1$ showed a positive correlation with the percent change in RA muscle thickness ($P = .001$, $P = .009$, and $P = .02$, respectively) (Fig. 2B, 2C, 2D). However, there was no correlation between the FEV_1/FVC and the percent change in RA muscle thickness.

Discussion

We used ultrasonography to measure the thickness of the RA muscle as an alternative approach to evaluating respiratory function. Our study revealed that the percent change in RA muscle thickness could be used as an indicator of respiratory function.

Several previous studies have used ultrasonography in patients with ALS to confirm diaphragmatic movement and fasciculation. Some reports showed that the echo variations of muscles or fasciculation observed on ultrasound were useful for the diagnosis of ALS.[8-11] The benefits of ultrasonography include convenience, noninvasiveness, and repeatability throughout the disease course. The use of the

RA muscle was preferable in this analysis since it was difficult to detect the fasciculation of paraspinal muscles. Additionally, the RA muscles are innervated by the lower thoracic nerves (Th5–12). Further, we observed the movement of the RA muscles during active breathing but not during resting breathing. Although the diaphragm is the primary muscle involved in abdominal breathing, the RA is equally one of the muscles utilized, the evidence for which is the abdominal distention and deflation during inspiration and expiration, respectively, in abdominal breathing. In this study, we examined the relationship between RA muscles and respiratory function.

Hiwatani et al[12] reported that evaluating diaphragmatic thickness during respiration using ultrasonography is a useful modality to assess the respiratory function of patients with ALS; they observed a correlation between the thickening ratio and the %VC and P_{aCO2}. Several other diaphragm ultrasonography studies have demonstrated its usefulness as a tool to assess respiratory function.[2,3,13-15] Pinto et al[13] reported the correlation between FVC and diaphragm thickness and between the diaphragm–compound muscle action potentials and its thickness during full inspiration. The findings showed that diaphragm thickness correctly reflected respiratory muscle atrophy and motor nerve loss. We attempted to perform diaphragm ultrasonography in our center and found varying results among the expert neurologists and other investigators. The reason for this variation could be the difficulty in identifying the diaphragm. Conversely, the RA muscles are located superficially, making them easily recognizable landmarks and allowing reproducibility among investigators, as reflected by the identical findings among the investigators in this study.

In this study, the percent change in RA muscle thickness from maximal expiration to maximal inspiration was positively correlated with %VC, %FVC, and $\%FEV_1$. The results showed a good probability of predicting %VC, %FVC, and $\%FEV_1$ by measuring the percent change in RA
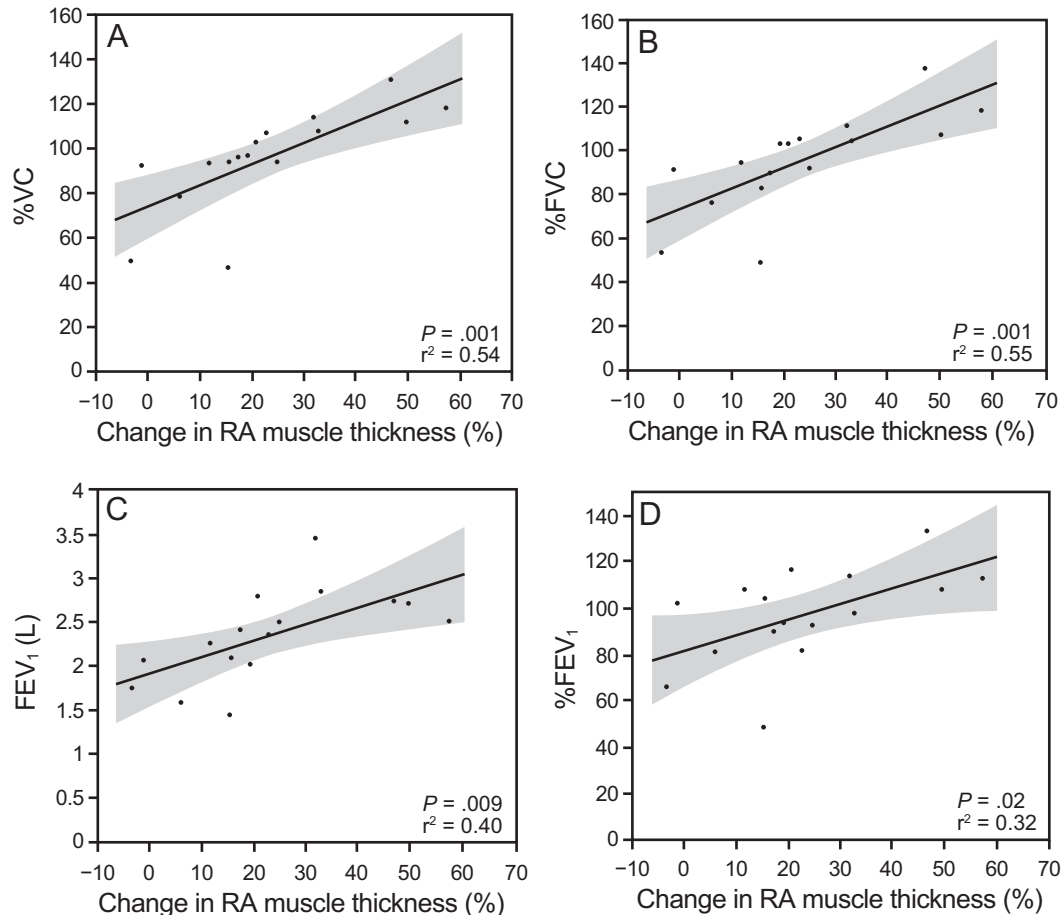
Fig. 2. The relationship between the percent change in rectus abdominis (RA) muscle thickness from maximal expiration to maximal inspiration and results of spirometry. A: The percent change in RA muscle thickness from maximal expiration to maximal inspiration is positively correlated with the percentage of predicted vital capacity (%VC) by the Pearson correlation analysis. B: The percent change in RA muscle thickness from maximal expiration to maximal inspiration is positively correlated with the percentage of predicted FVC (%FVC) by the Pearson correlation analysis. C: The percent change in RA muscle thickness from maximal expiration to maximal inspiration is positively correlated with FEV1 by the Pearson correlation analysis. D: The Pearson correlation analysis reveals a positive correlation between the percent change in RA muscle thickness from maximal expiration to maximal inspiration and the percentage of predicted FEV_1 (%FEV_1). These results show that the percent change in RA muscle thickness can be applied in predicting respiratory function.

muscle thickness from maximal expiration to maximal inspiration in subjects with ALS; thus, ultrasonography can be a good alternative for patients with ALS who cannot undergo spirometry due to bulbar paralysis. In addition to its noninvasiveness, it might make it easier to evaluate respiratory function in patients with difficulty in maintaining a sitting position for spirometry.

In future studies, we plan to analyze the abdominal transverse, external oblique, and internal oblique muscles to assess respiratory function in patients with ALS. Certain accessory muscles, which are located superficially, are used during abdominal breathing. Additionally, we will study the relationship between the thickness of these muscles, respiratory function tests, spirometry, and arterial blood gas analysis results and identify accessible and detectable markers of respiratory function. According to the latest ALS treatment guidelines, the criteria for administering respiratory support include (1) $P_{aCO_2} \geq 45$ mm Hg, (2) arterial oxygen saturation of $\leq 88\%$ during sleep lasting for ≥ 5 min, and (3) %FVC $< 50\%$ or maximum inspiratory pressure (P_{Imax}) < -60 cm H_2O. Furthermore, sniff nasal inspiratory pressure (SNIP) has been suggested to be useful for the early assessment of respiratory dysfunction.[16] Thus, in addition, we will study the relationship between the percent change in RA muscle thickness from maximal expiration to maximal inspiration of ALS patients and P_{aCO_2}, P_{Imax}, and SNIP.

The main limitations of the study included the small sample size, being a single-center study, and the inability to follow subjects over time due to the rapid deterioration of the disease. Furthermore, a device to obtain the P_{Imax} and SNIP was not available. Despite these limitations, we

demonstrated that RA muscle ultrasonography could be a predictive test to evaluate the respiratory function of patients with ALS. Additionally, RA muscle ultrasonography can be applied during follow-up assessment to detect deterioration of respiratory function during disease progression.

Conclusions

In this study, we observed a correlation between the results of RA ultrasonography and tests of respiratory function in subjects with ALS; thus, RA ultrasonography is useful for predicting a reduction in respiratory function of patients with ALS. We concluded that ultrasonography is a noninvasive and convenient tool that can be performed at the bedside, making it useful to assist in the best timing for introducing NIV. This study is the starting point for observations on the usefulness of RA muscle ultrasonography, suggesting that further studies are needed in the future.

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