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Ultrasonography of Diaphragm Can Predict Pulmonary Function in Spinal Cord Injury Patients: A Pilot Case-Control Study

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Background: Ultrasonography of the diaphragm is an under-utilized instrument in cervical spinal cord injury patients. We conducted a pilot study to first compare the difference of diaphragm thickness and the excursion between patients with cervical spinal cord injury and healthy volunteers, and second to correlate diaphragmic ultrasonography and pulmonary function in cervical spinal cord injury patients.

Material/Methods: Thirty patients with C4–C5 cervical spinal cord injury of more than 1 year and thirty healthy volunteers were included in this study. All demographic data were evaluated. All participants underwent diaphragmic ultrasonography evaluation and pulmonary function test. Diaphragm thickness of both sides and diaphragm excursions of the right hemi-diaphragm were obtained at the end of quiet tidal breathing and maximal inspiration. We compared diaphragmatic thickness and excursions, and we analyzed the relationship between diaphragmatic ultrasonography and pulmonary function.

Results: All spinal cord injury patients had restrictive pulmonary dysfunction compared to the control group of healthy volunteers. Diaphragm thickness on both sides was significantly increased in spinal cord injury patients. Diaphragmatic excursion in spinal cord injury patients was increased on the right hemi-diaphragm during tidal breathing. However, the right hemi-diaphragmatic excursion was no difference in both groups during maximal inspiration. Right hemi-diaphragmatic excursion during deep breathing correlated positively with expiratory volume in 1 second ($P<0.01$) and forced vital capacity ($P<0.01$). Right hemi-diaphragm thickness at end of maximum inspiration correlated positively with expiratory volume in 1 second ($P<0.01$) and forced vital capacity ($P<0.01$). Left hemi-diaphragm thickness at end of maximum inspiration correlated positively with expiratory volume in 1 second ($P<0.01$) and forced vital capacity ($P<0.01$).

Conclusions: Diaphragm thickness and motion of the cervical spinal cord injury patients were different from controls. Pulmonary function was impaired in spinal cord injury patients. Ultrasonography of the diaphragm as a non-invasive method that is correlated with pulmonary function.

MeSH Keywords: **Diaphragm • Spinal Cord Injuries • Ultrasonography, Doppler, Color**

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Background

Lesions in the cervical or thoracic segments of the spinal cord impair respiratory function due to complete or partial paralysis of respiratory muscles, including combined restrictive and obstructive ventilatory impairment [1,2]. The diaphragm, as the major respiratory muscle, is innervated by the phrenic nerve. Lesions above C3 lead to diaphragm paralysis, and the patient requires mechanical ventilation to sustain respiratory function. Patients with lesions between C3–C5 may require respiratory assistance in the acute phase, and some of these patients may become ventilator-independent in the chronic phase of their spinal cord injury. In lesions below the C5 segment, the diaphragm and sternocleidomastoid muscles may operate normally, but inspiratory muscles (mainly intercostal muscles) are paralyzed. These factors can lead to a decrease in chest compliance, which may affect diaphragm function and cause diaphragm fatigue. Accurate assessment of diaphragmatic function is important for effective clinical management in cervical spinal cord injury (SCI) patients.

With the advantage of being non-invasive and non-ionizing, ultrasonography is a highly sensitive tool and widely applied to assess diaphragmatic functions [3,4]. Several neuromuscular ultrasound techniques have been utilized to evaluate the diaphragm, including B-mode, M-mode, and measurements of changes in diaphragm thickness [5]. The M-mode technique shows highly inter-operator reliability and reproducibility [6]. But ultrasonography of the diaphragm is an under-utilized instrument in patients with cervical SCI. In a previous study that used diaphragm ultrasounds in patients with cervical SCI, the researchers found that the process of ultrasound evaluation was well tolerated by cervical SCI patients, and diaphragm movement was not fully associated with the level of injury and the American Spinal Injury Association classification [7]. Thus, in this study, we sought to explore the differences in diaphragm thickness and excursions between SCI patients and healthy volunteers, then correlate diaphragmatic ultrasonography with pulmonary function in cervical SCI patients.

Material and Methods

Materials

This study was conducted at the Department of Spinal and Neural Functional Reconstruction of China Rehabilitation Research Center (CRRC) for adults between March 2017 and October 2017. Ethical clearance was provided through the Center of Human Research Ethics Committee (NO.2017-015-1). This study was registered (NO.ChiCTR-ROC-17010973). Patients were included if they: 1) were between 18 and 60 years of age; 2) suffered from motor-complete cervical SCI (neurological level C4–C5; American Spinal Injuries Association Impairment Scale A or B); 3) had no history of mechanical ventilation or ventilation within less than 30 days; 4) had suffered for more than 1 year since the injury. Patients were excluded if: 1) they had abnormal chest structures, which affected diaphragmatic function; 2) had neuromuscular diseases, such as peripheral neuropathy, myopathy, stroke, motor neuron disease; 3) had lung diseases (COPD, etc.) that can affect pulmonary function; and 4) refused to participate in this study. For the healthy control group, participants who were matched on gender and body mass index (BMI), and were recruited using the same exclusion criteria. All the participants signed informed consent.

Ultrasonographic measurement

Ultrasonography was performed by an experienced operator using "Samsung Medison" Ultrasonic Imaging System (type. SONOACE R3). Diaphragm thickness was assessed following procedures previously described [8–10]. A 2-dimensional ultrasound was used to measure the diaphragm thickness at the zone of apposition using a linear array transducer (7.5 MHz). The diaphragm is a s3-layered structure consisting of 2 hyperechoic lines of pleural and peritoneal fascia and hypoechoic muscles between them. The electronic calipers were positioned to measure the thickness of the diaphragm muscle between the inner edges of these membranes. The anterior subcostal view was used to evaluate diaphragm excursion. A lower frequency curvilinear transducer (3.5 MHz) was placed in the anterior subcostal region between the mid-clavicular and anterior axillary lines. The 2-dimensional model was initially used to obtain a clear view of the diaphragm, the M-mode was then used to measure the excursion of the diaphragm. Diaphragm thickness was measured on both sides, in contrast, diaphragm excursions were recorded solely on the right side. Ultrasonographic measurements were performed at the end of quiet tidal breathing and maximal inspiration. The patients were studied in the supine position throughout the procedure. All variables were the average of 3 different breathing cycles.

Pulmonary function assessment

The Jaeger PFT system – MasterScreen™ (CareFusion, Hoechberg, Germany) was used to test pulmonary function of all cervical SCI patients and controls. Values of forced expiratory volume of 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, maximum voluntary ventilation (MVV), and tidal volume (VT) were collected for statistical analysis. Sitting position was chosen to perform this test.

Statistical analysis

Data are shown as the mean ± standard deviation or median (min-max) depending on the distribution. All statistical analysis

Table 1. Demographics of patients with cervical spinal cord injury and control group (mean ± standard deviation).

Demographic	Patients with CSCI (N=30)	Control group (N=30)	*P* value
Age, year	39.6±15.8	44.9±11.0	0.14
Gender			
Male	27	27	1.0
Female	3	3	
Height, meters	1.67±0.08	1.69±0.09	0.37
Weight, kg	64.6±11.2	63.8±12.5	0.81
BMI, kg/m^2	22.8±3.4	23.2±3.7	0.66
Smoking (%)	9 (30%)	8 (26.7%)	0.77
ASIA classification			
A	21	……	……
B	9	……	……
Neurological level (n)			
C4	12	……	……
C5	18	……	……
Time since injury, month	16.4±3.2	……	……

BMI – body mass index.

was conducted by SPSS 20.0 (SPSS Inc., Chicago, IL, USA). The demographic difference between the SCI patients and control participants were assessed using *t*-tests and χ^2 (chi-squared) tests. Diaphragmatic ultrasonography date (thickness and excursion) and pulmonary function were compared using paired *t*-test (normally distributed) or Wilcoxon test (non-normal distributed). The association between diaphragmatic ultrasonography and pulmonary function in SCI patients was explored using spearman correlation analysis. Differences were considered significant if $P<0.05$.

Results

Demographics of patients with cervical SCI and the control group are given in Table 1. There were 30 SCI patients (27 males and 3 females) included (12 SCIs were C4, 18 SCIs were C5; 21 SCIs were ASIA A and 9 SCIs were ASIA B) and mean time after the injury was 16.4±3.2 months. No statistically significant difference was found between healthy controls and cervical SCI patients in gender, age, smoking history, and BMI (see Table 1). Compared to the control group, diaphragm thickness on both sides in the cervical SCI patient group was significantly increased at the end of quiet tidal breathing and maximal inspiration. Diaphragmatic excursion of the cervical SCI patient group was significantly increased during quiet breathing compared to the healthy control group (see Table 2). No significant difference was found in diaphragmatic excursion between the control group and cervical SCI group during deep breathing.

For pulmonary function testing, all the measurements of patients with cervical SCI had worse results than healthy controls (see Table 3). FVC, FEV1, FEV1/FVC, VC, and MVV were significantly decreased in the cervical SCI group. A significant positive correlation was observed between right hemi-diaphragm excursion during deep breathing and FEV1 (rho=0.74, $P<0.01$) and FVC (rho=0.70, $P<0.01$) in cervical SCI patients. A significant positive correlation was observed between right diaphragm thickness at end of maximum inspiration and FEV1 (rho=0.70, $P<0.01$) and FVC (rho=0.71, $P < 0.01$) in cervical SCI patients. A significant positive correlation was observed between left diaphragm thickness at end of maximum inspiration and FEV1 (rho=0.79, $P<0.01$) and FVC (rho=0.80, $P<0.01$) in cervical SCI patients.

Discussion

Ultrasound imaging of the diaphragm is a reliable and reproducible tool for diagnosis of neuromuscular diaphragm dysfunction [11] and widely applied in different conditions [3].

Table 2. Diaphragm muscle thickness (cm) and right diaphragmatic excursions (cm) in patients with cervical spinal cord injury and control group (mean ± standard deviation).

Diaphragm feature	CSCI patients	Control group	*P* value
Right-tidal breathing	0.20±0.03*	0.16±0.04	**<0.001**
Right-max	0.37±0.05*	0.31±0.08	**0.001**
Left-tidal breathing	0.21±0.03*	0.17±0.04	**<0.001**
Left-max	0.38±0.04*	0.32±0.08	**<0.001**
Right TR	1.77±0.21	1.89±0.38	0.181
Left TR	1.83±0.27	1.91±0.57	0.374
Quiet breathing	2.17±0.57*	1.48±0.26	**<0.001**
Deep breathing	4.60±0.83	4.79±1.24	**0.485**

CSCI – cervical spinal cord injury; tidal breathing – diaphragm thickness at the end of tidal breathing; max – diaphragm thickness at maximum inspiration; TR (thickening ratio) – thickness of maximal inspiration/thickness of tidal breathing. * Statistically significant difference from “control group”.

Table 3. Pulmonary function test results in patients with cervical spinal cord injury and control group (mean ± standard deviation).

Pulmonary function	CSCI patients	Control group	*P* value
FVC, (L)	2.1±1.0*	4.7±0.7	**<0.001**
FVC%	43.7±12.3*	102.7±9.4	**<0.001**
FEV1, (L)	1.9±0.9*	3.9±0.6	**<0.001**
FEV1%	48.1±10.5*	104.8±11.1	**<0.001**
FEV1/FVC, %	89.2±3.6*	86.5±5.3	**0.029**
VC, (L)	2.1±1.1*	4.9±0,7	**<0.001**
VC%	48.8±29.1*	103.1±13.6	**<0.001**
MVV, (L)	62.2±28.1*	138.3±17.2	**<0.001**
MVV%	51.3±18.7*	101.4±9.2	**<0.001**

FEV1 – forced expiratory volume in 1 second; FVC – forced vital capacity; FEV1/FVC – the ratio of FEV1 to FVC; VC – vital capacity; MVV – maximum voluntary ventilation; % – values are percentages of the predicted value. * Statistically significant difference from “control group”.

This technique has not been employed as a routine clinical assessment in SCI patients, and there are currently few published studies. Hardy et al. [7] used B mode ultrasound in 3 cervical SCI patients and measured the magnitude and direction of the diaphragm movement during inspiration. They found diaphragm movements were not coherent with the level of injury. After the pressure threshold inspiratory muscle training, West et al. [12] found the diaphragm thickness was significantly increased without pulmonary function tests benefits. Malas et al. [13] compared the thickness of diaphragms in patients with different segments of SCI with healthy volunteers and found that the contractile capacity of the diaphragm was decreased in patients with high-level SCI and the thickness of the diaphragm was greater than healthy controls. In the current study, we found a similar result: diaphragmatic hypertrophy occurred in patients with C4–C5 level cervical SCI. However, our results on the thickness of the diaphragm were lower compared to previous studies by West [12] and Malas [13]. This may have been due to racial differences in patient populations as Asians have lower height and weight than Europeans. In addition, the participants in West et al. study were paralympic athletes, who were likely physically stronger than ordinary persons. There are 2 reasons possible explanations for the differences in diaphragmatic hypertrophy from our study compared to these other studies. First, the level of injury of our patients was C4–C5, so the diaphragm was partially denervated.

After over 1-year (16.4±3.2 months) recovery, the denervation of the diaphragm may be eased. Second, during inspiration, the diaphragm and sternocleidomastoid must compensate for the workload of other paralyzed inspiration muscles (intercostal muscles) and lead to hypertrophy. One study [14] showed that participants with cervical SCI exhibited significantly higher electromyography (EMG) activity than non-injured participants in the inspiratory muscles and the diaphragm region. These findings demonstrated the compensatory recruitment of accessory muscles and overactivity of the diaphragm in cervical SCI patients.

Diaphragm excursion is also seen as a sign of diaphragmatic contractile ability [15,16] and mainly related to the inspiratory volume [17]. In tetraplegia, during spontaneous breathing the lack of activity in the external intercostal muscles causes distortion where the upper anterior rib cage moves inward during inhalation diminishing the extent of rib-cage expansion that the diaphragm can contribute [18]. Our study found that at the end of quiet tidal breathing, right hemi-diaphragm excursion in the SCI group was greater compared to the control participants when compensating for insufficient tidal volume. Meanwhile, right hemi-diaphragm excursion during maximal inspiration was not significantly different between the cervical SCI group and the healthy control group. This is mainly related to the adjacent anatomy of the right hemi-diaphragm, as the liver interferes with diaphragm excursion moving caudally during maximum inspiration.

The correlation between ultrasonography and spirometry volumes has not been explored in cervical SCI patients. In stroke patients, the diaphragmatic motion during deep breathing positively correlated with FVC and FEV1 [19]. Houston et al., suggested that the supine position could achieve better correlation between the inspired volume and hemi-diaphragmatic motion [17]. After cervical SCI, the decrease of chest wall compliance and denervation of respiratory muscles affects the pulmonary functions. In cases with complete-motor lesions, values of FVC have been reported to be near 100% of the predicted value in low paraplegia but less than 50% in high tetraplegia [20]. In our study, SCI patients presented with a pulmonary restriction on FVC, FEV1, VC, and MVV. We found a significant positive correlation between right hemi-diaphragm excursion during deep breathing by ultrasound and spirometric volumes (FEV1: rho=0.74, $P<0.01$; FVC: rho=0.71, $P<0.01$). FVC and FEV1 testing requires the patient to finish a maximum inhalation through deep breathing. During this process, the diaphragm performs its highest contraction capacity, thus, a significant correlation between diaphragm excursion and inspiratory volumes is obtained. Diaphragm thickness at the end of maximum inspiration of both sides has a significant positive correlation with FVC and FEV1. This indicates that hypertrophy of the diaphragm might have a beneficial effect on the respiratory function tests.

Our study had some limitations. The participants were selected by strict criteria, which may limit the ability of our results to apply to other SCI patients with other levels and severities of injury. In addition, this study only assessed the right hemi-diaphragm excursions because the visualization of the left hemi-diaphragm was less accessible. However, the findings in this study have vital functional and clinical significance. It revealed the usefulness of evaluating diaphragmatic thickness and motion via ultrasonography. Ultrasonography of the diaphragm as an imaging technique with the advantages of a non-invasive, non-ionizing method. It is available to directly assess diaphragmatic function, and can be applied to estimate pulmonary function in SCI patients for correlation between sonographic and spirometric parameters. Ultrasonography of the diaphragm provides an option to evaluate the pulmonary function for patients who cannot finish a pulmonary function test. Further research should aim to first explore the application of ultrasonography of the diaphragm in SCI patients with other levels and severities of injuries. Ultrasonography can also be used to evaluate the longitudinal change of diaphragm and respiratory function.

Conclusions

We found that patients with C4–C5 segment SCI had significant impairment in pulmonary function compared to healthy controls. In these patients, diaphragm thickness and motion are different from healthy controls. Ultrasonography can be applied to evaluate the diaphragm function. Diaphragm ultrasonography and pulmonary function are correlated. In the future, we will explore the application of diaphragm ultrasonography in SCI patients and monitor diaphragm function after interventions.

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Conflict of Interests

None.

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