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ORIGINAL ARTICLE

Effects of diaphragm thickness on rehabilitation outcomes in post-ICU patients with spinal cord and brain injury

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Abstract

Background Intensive care unit (ICU) complications affect outcomes but it remains unknown if the diaphragm thickness affects rehabilitation outcomes after ICU. We conducted a pilot study to evaluate the effect of diaphragm thickness on rehabilitation outcomes of post-ICU patients with spinal cord injury (SCI) and traumatic brain injury (TBI) and to evaluate factors that may be associated with diaphragm atrophy.

Materials and methods Fifty-one patients (26 SCI, 25 TBI) who admitted to the rehabilitation clinic from the ICU included in this study. All demographic data were recorded. All participants underwent diaphragmatic ultrasonography evaluation before and after 12 weeks of neurologic rehabilitation program. The diaphragm thickness and outcome parameters were compared in all patient groups and in each patient subgroups. Evaluation parameters of patients before and after treatment were compared in patient subgroups.

Results Diaphragm atrophy was found in 14 patients (64%) in TBI group and 12 patients (46%) in SCI group. The diaphragm thickness negatively correlated with the ICU length of stay and positively correlated with the before/after rehabilitation functional scores and the change in functional independence measure scores ($p < 0.05$). According to the regression analysis; the change in functional independence measure scores was found to be affected by the diaphragm thickness ($p < 0.05$).

Conclusions The diaphragm thickness may be an effective factor on the rehabilitation process.

Keywords Diaphragm · Ultrasound · Rehabilitation · Intensive care

Introduction

The diaphragm is well known as the principal muscle of respiration and contributes to the mechanical stabilization of the trunk. Contraction of the diaphragm increases intra-abdominal pressure, working synergistically with the pelvic floor and abdominal muscles to increase trunk stability [1]. In addition to this, during aerobic exercise, which requires endurance, patients readily report fatigue. This may lead to difficulty in ensuring consistent rehabilitation treatment, thereby reducing the patient's ability to perform daily activities and decreasing his/her chances of making a functionally sufficient recovery and leading an independent life.[2].

Patients in intensive care unit (ICU) are often exposed to prolonged immobilization, which can play an important role in neuromuscular complications. The combination of prolonged mechanical ventilator (MV) and the effects of immobility causes significant changes to muscle fibers, reducing both respiratory and peripheral muscle strength [3]. Diaphragmatic thickness has been shown to reduce by 6% or 7.5% per day in mechanically ventilated patients [4], and ultrasound imaging of the diaphragm is a reliable and reproducible tool for diagnosis of neuromuscular diaphragm dysfunction and widely applied in different conditions [5].

Spinal cord injury (SCI) is a common cause of chronic respiratory failure and the severity of diaphragm paresis is an important determinant of long-term respiratory problems. Respiratory muscle weakness, restrictive respiratory insufficiency and consequently atelectasis, and pneumonia are commonly seen clinical problems in SCI patients.

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Especially, SCI at or above the level of the C3-4–5 phrenic motor neurons causes both inspiratory and expiratory muscle paralysis, causing tracheostomy cannulation and mechanical ventilation [6].

Mechanical ventilation is also frequently required in the management of traumatic brain injury (TBI) and respiratory failure can be multi etiological (coma, aspiration pneumonia, chest trauma, neurogenic pulmonary edema, transfusion-related acute lung injury) [7].

Mechanical ventilator/injury/ICU (critical illness polyneuropathy)-related diaphragm atrophy in may influence functional recovery during rehabilitation process, but it remains understudied. This study aimed to evaluate the effect of diaphragm thickness on rehabilitation outcomes of post-ICU patients with spinal cord injury (SCI) and traumatic brain injury (TBI), and to evaluate factors that may be associated with diaphragm atrophy.

Materials and methods

Study setting

Twenty-eight SCI and 28 TBI patients who had been admitted from the ICU to our rehabilitation clinic for neurologic rehabilitation were enrolled in this study between January 2016 and January 2019. Patients were included if they (1) were > 18 years of age, (2) have not participated in any rehabilitation program before, (3) not treated in any clinic other than intensive care unit, and (4) had SCI at or below C6 (to exclude phrenic motor neuron injury) neurological injury level in the SCI patient group. Patients were excluded if they (1) had chest trauma or operation, which affected diaphragmatic function; (2) had neuromuscular diseases, such as central or peripheral neuropathy, myopathy; (3) had lung diseases (COPD, bronchiectasis, etc.) that can affect pulmonary function; (4) smoking and use of alcohol; (5) had disease duration was < 1 month and > 1 year; and (6) had metabolic diseases, such as diabetes mellitus and hypo–hyperthyroidism [8, 9].

Electrophysiological evaluation was performed to rule out critical disease neuropathy/myopathy and neuromyopathy in all patients. Five patients (2 SCI, 3 TBI) were diagnosed as critical illness neuropathy and excluded from the study. The study was continued with 51 patients (26 SCI and 25 TBI).

Subjects were informed about the study and their written consent was obtained at the beginning of the study. The approval of the Ethical Board of the hospital was obtained, and the study was conducted in accordance with the principles of the Helsinki Declaration.

Demographic characteristics

Demographic features of the patients including age, gender, and educational status were recorded.

Disease characteristics

Etiology, presence of additional trauma, length of stay in ICU (days), presence and duration of tracheostomy, mechanical ventilation and feeding tube, and Glasgow Coma Scale (GCS) level (during admission to rehabilitation) were recorded.

Functional disability was assessed with the Functional Independence Measure (FIM). FIM analyzes the motor and cognitive function of disability. There are 18 items in the FIM, related to self-care, sphincter control, transfer, movement, communication, and social perception. Each item is scored between one and seven points [10].

Injury severity was classified according to the American Spinal Injury Association Impairment Scale (ASIA).

Disability rating scale (DRS) and Rancho Los Amigos (RLA) scale were used to define cognitive and behavioral patterns for TBI patients. DRS is an observer-rated instrument designed to measure general functional disability in individuals with TBI. The DRS is an 8-item scale that assesses four domains, including level of consciousness, cognitive functioning related to self-care, level of dependence, and occupational ability. Total score is the sum of all 8 items. Scores range from 0 to 30, with higher scores representing a greater level of disability [11].

Rancho Los Amigos (RLAS) is a comprehensive behavioral rating scale developed specifically to monitor the stages of recovery in the adult TBI population. The RLAS evaluates key features of consciousness and cognitive functioning, such as level of awareness of the environment, response to stimuli, ability to follow command, confusion, attention, and the appropriateness of verbalization and motor actions. The RLAS consists of eight hierarchical levels, with level one representing no response and level eight representing purposeful and appropriate cognitive function.[12].

Musculoskeletal ultrasound

All measurements were performed in supine with the head in a neutral position without using a pillow. Real-time imaging diaphragm of cross-sectional thickness at the end of inspiration was performed by ultrasound device (GE Logiq P5, General electric, Korea) and 7–12 MHz linear array transducer, by physical medicine and rehabilitation specialist. The transducer was placed on the line and special care was taken to avoid excessive pressure. This scanning was repeated 3 times to reduce the measurement errors and average of three measurements was taken.

Diaphragm thickness was measured ultrasonographically, using a standardized technique at the zone of apposition on the mid-axillary line [13]. In previous study, it proved difficult to consistently visualize the left hemidiaphragm, so measurements of left hemidiaphragm thickness were not performed in this study [14].

Study protocol

Ultrasonographic evaluation was performed for all subjects with blinded specialist. Also, subjects were assessed other outcome parameters by other blinded specialist. All patients had received traditional neurologic rehabilitation program for 12 weeks. After 12 weeks, all evaluations were repeated.

Comparisons

Evaluation parameters of patients before and after treatment were compared in patient subgroups. The diaphragm thickness and outcome parameters were correlated in all patient groups and in each patient subgroup. The effects of diaphragm thickness on outcome parameters and treatment changes were compared.

Statistical analysis

Statistical Package for the Social Sciences (SPSS 22.0 for Windows) software package was used in the analysis of the data. In descriptive statistics, the data were expressed as mean and standard deviation (SD) for continuous variables and as frequencies and percentages (%) for nominal variables. Normality was evaluated with Kolmogorov–Smirnov test. For statistical analysis of differences between the groups, Mann–Whitney *U* test was used, and differences in within group were evaluated using Wilcoxon test. Pearson's correlation coefficients were calculated to assess the univariate relationship between the diaphragm and related factors in patients. For significantly correlation, regression analysis was performed by taking the normal thickness of the diaphragm as the dependent variable. Values of $p < 0.05$ were considered statistically significant.

Results

Fifty-one patients (12 males, 39 females) with a mean age of 37.51 ± 14.15 years were evaluated. The mean length of stay in ICU was 49.65 ± 43.90 days. There were 26 patients (51%) in SCI group and 25 patients (49%) in TBI group. The clinical and demographical features of the patients are summarized in (Table 1).

Tracheostomy (TBI: 88.13 ± 106.71, SCI: 3.01 ± 11.34) and mechanical ventilator (TBI: 33.10 ± 43.69, SCI: 7.37 ± 24.12) durations were significantly different among the two groups. ($p = 0.011$, $p = 0.0037$). The mean pre-treatment FIM was 59.26 ± 25.00 in the all groups, and the mean FIM after treatment was 64.78 ± 27.23. The change of mean FIM was 5.51 ± 11.23 and the change was significant ($p = 0.003$).

There were eight patients (30.8%) in ASIA A, ten patients (38.5%) in ASIA C, seven patients (26.9%) in ASIA D, and one patient (3.8%) in ASIA B. (6 C6; 2 C7,T1,T2 and T6; 4 T12, L1 and L2 levels). The differences in functional disability scores before and after treatment were significant (pre-treatment FIM mean 68.43 ± 17.54, post-treatment FIM mean 72.68 ± 18.61, changing FIM mean 4.25 ± 3.80, $p = 0.037$).

The pre/post-treatment values of the outcome scales (DRS, RLAS, FIM) of TBI patients and the results of the change with treatment were compared, and the changes in all parameters were significant before and after the treatment ($p < 0.05$).

Diaphragmatic atrophy was present in 51% ($n = 26$) of all patients. According to subgroups, diaphragmatic atrophy was found in 14 patients in TBI ($n = 64$) group and 12 (46.2%) patients in SCI group.

Correlation analysis of diaphragm thickness and outcome parameters are shown in (Tables 2, 3, 4). According to this, when patients were evaluated both as subgroups and as a total study group, it was found that the diaphragm thickness correlated negatively with the length of ICU stay, and positively correlated with the before/after rehabilitation FIM scores and change in FIM scores ($p < 0.05$).

In the TBI group, the diaphragm thickness was also correlated with the before/after rehabilitation DRS values (both $p = 0.008$), but had no effect on DRS change ($p = 0.455$) (Table 5).

According to the regression analysis, it was found that the diaphragm thickness was an effective factor on the rehabilitation process and diaphragm thickness increases as the length of ICU stay was shortened. Also, FIM changes before and after rehabilitation were found to be affected by the diaphragm thickness ($p < 0.05$).

Discussion

The present study is the first study investigating the effect of diaphragmatic atrophy on rehabilitation outcomes in post-ICU patients diagnosed with SCI and TBI. Our results showed that the diaphragm thickness was an effective factor on the rehabilitation process and the level of

Table 1 Demographic ve disease characteristics of subjects

	All subject ($n=51$)	SCI group ($n=26$)	TBI group ($n=25$)
Age (years) mean (SD)	37.51 (14.25)	37.06 (15.91)	37.83 (13.26)
Gender *n* (%)			
Female	39 (76.5)	18 (69.2)	21 (84)
Male	12 (23.5)	8 (30.8)	4 (16)
Education *n* (%)			
Illiterate	1 (1.9)	0	1 (4)
Literate	5 (9.8)	3 (11.5)	2 (8)
5 years	10 (19.6)	5 (19.3)	5 (20)
8 years	16 (31.4)	11 (42.3)	5 (20)
11 years	19 (37.3)	7 (26.9)	12 (48)
More than 11 years	0	0	0
Etiology *n* (%)			
In-car traffic accident	18 (35.3)	1 (3.8)	17 (68)
Road traffic accidents	19 (37.3)	13 (50)	6 (24)
Falls	14 (27.4)	12 (46.2)	2 (8)
Diagnosis *n* (%)			
SCI	26 (51)	26 (100)	0
TBI	25 (49)	0	25 (100)
Presence of additional trauma *n* (%)			
Limb fracture	7 (13.7)	4 (15.4)	3 (12)
Internal organ injury	3 (5.9)	1 (3.8)	2 (8)
Mean length of ICU stay (SD)	49.65 (43.90)	25.31 (29.48)	66.50 (61.38)
Tracheostomy *n* (%)	19 (37.3)	3 (11.5)	16 (64)
Mechanical ventilator *n* (%)	25 (49)	5 (19.3)	20 (80)
Feeding tube *n* (%)	12 (23.5)	0	12 (48)
GCS (before rehabilitation) mean (SD)	13.56 (3.10)	13.75 (3.87)	13.66 (2.37)
Diaphragm thickness (mm) mean (SD)	2.43 (1.19)	2.45 (1.15)	2.42 (1.02)
Diaphragm atrophy *n* (%)	26 (51)	12 (46.2)	14 (64)

SD standard deviation; *SCI* spinal cord injury; *TBI* traumatic brain injury; *ICU* intensive care unit, *GCS* Glasgow coma scale

Table 2 Correlation analysis of diaphragm thickness and outcome parameters in the all study group

	LOS ICU r/p	Tracheostomy r/p	MV r/p	Feeding tube r/p	GCS r/p	FIM (pre-treatment) r/p	FIM (post-treatment) r/p	FIM (change) r/p
Diaphragm thickness	−0.529/0.001	0.046/0.775	0.131/0.414	0.177/0.269	0.230/0.148	0.505/0.010	0.472/0.011	0.339/0.030

r correlation *LOS* length of stay; *ICU* intensive care unit; *GCS* glasgow coma scale; *MV* mechanical ventilator; *FIM* functional independence measure

Table 3 Correlation analysis of diaphragm thickness and outcome parameters in SCI group

	LOS ICU r/p	Tracheostomy r/p	MV r/p	Feeding tube r/p	FIM (pre-treatment) r/p	ASIA (pre-treatment) r/p	Motor level (pre-treatment) r/p	FIM (post-treatment) r/p	FIM (change) r/p
Diaphragm thickness	−0.745/0.001	0.285/0.287	0.352/0.181	0.070/0.798	0.373/0.055	0.258/0.335	0.145/0.591	0.390/0.056	0.188/0.045

r correlation *LOS* length of stay; *ICU* intensive care unit; *MV* mechanical ventilator; *FIM* functional independence measure; *ASIA* American spinal injury association impairment

Table 4 Correlation analysis of diaphragm thickness and outcome parameters in TBI group

	LOS ICU r/p	Tracheostomy r/p	MV r/p	Feeding tube r/p	GCS pre-treatment r/p	FIM pre-treatment r/p	DRS pre-treatment r/p	RLA pre-treatment r/p	FIM post-treatment r/p	DRS post-treatment r/p	RLA post-treatment r/p	FIM (change) r/p	DRS (change) r/p	RLA (change) r/p
Diaphragm thickness	−0.584/0.002	−0.385/ 0.057	0.173/ 0.407	0.271/0.191	0.358/0.079	0.592/0.002	−0.519/0.008	0.056/0.789	0.529/0.007	−0.517/0.008	0.014/0.947	0.396/0.027	−0.157/0.455	0.177/0.397

r correlation *LOS* length of stay; *ICU* intensive care unit; *MV* mechanical ventilator; *GCS* glasgow coma scale; *FIM* functional independence measure; *DRS* disability rating scale; *RLAS* Rancho Los Amigos Scale

functional independence was affected by the thickness of the diaphragm.

The diaphragm is the major muscle of inspiration, and its function is critical for optimal respiration. Diaphragmatic failure has long been recognized as a major contributor to death in a variety of systemic neuromuscular disorders. It has been reported that mortality and morbidity increase in the presence of diaphragmatic dysfunction due to critical illness neuro/myopathy, especially in patients in ICU. In these patients, diaphragm weakness is thought to develop from disuse secondary to ventilator-induced diaphragm inactivity and as a consequence of the effects of systemic inflammation, including sepsis.

In our study, although there was 46.2% diaphragmatic atrophy in patients with SCI, there was no significant relationship between diaphragm thickness and mechanical ventilation and tracheostomy duration. First, as the patients with SCI above C6 were excluded from the study, the lower MV and tracheostomy rates and shorter ICU length of stay may explain these results. Second, expiratory muscle paralysis affecting abdominal abutment of the diaphragm movements during the inspiration may be a cause of reduced diaphragm function.

Zhu and colleagues find diaphragmatic hypertrophy in patients with low-level cervical SCI. In patients with low-level cervical SCI, the diaphragm thickness of both the left and the right side is statistically thicker than able-bodied participants. However, in this study, they have included patients with disease duration of less than 1 year [15].

Malas et al. found that although patients with high-level SCI decreased contractile capacity of the diaphragm, they had thicker diaphragm muscles than controls. This might have been due to the compensatory effect of the diaphragm (performing its maximum contraction capacity and increasing frequency of inspiration) against its partial/total denervation and denervation of other respiratory muscles, respectively. In that study, the time after the injury has not been reported. Likely, compensatory mechanisms in the diaphragm may have occurred in patients with C2-C4 level SCI after many years. Malas et al. compared the thickness of diaphragms in SCI patients with lower level (C6 and below) similar to our study group with healthy volunteers and found that the thickness of the diaphragm was similarly to healthy controls [16]. The reason of the diaphragm atrophy in our SCI group may be as a result of stress response that occurs with the increase of catabolism in traumatic events. Our study group consisted of patients admitted directly from the ICU to the rehabilitation service, and the mean time after trauma was 25 days. Furthermore, supporting this suggestion, diaphragm atrophy was more prominent in TBI patient group than SCI group.

In this study, diaphragmatic atrophy was found in 64% of TBI patients. In the literature, there were no studies evaluating

Table 5 Regression analysis results

	RC	SE	OR (95% CI)	*P* value
LOS ICU	− 0.368	0.033	− 0.081 (− 0.148 to − 0.015)	0.018
FIM (pre-treatment)	0.405	0.007	0.008 (0.014–0.002)	0.019
FIM (post-treatment)	0.512	0.002	0.009 (0.014–0.004)	0.017
FIM (change)	0.339	0.007	0.015 (0.002–0.028)	0.027

RC regression coefficients; *SE* standard error; *OR* odds ratio; *CI* confidence interval; Length of stay; *ICU* intensive care unit

diaphragm thickness in TBI patients. However, in a study by Johnson et al., they had detected diaphragmatic atrophy in half of the patients in the pediatric intensive care unit and they suggested that the presence of TBI increases the severity of diaphragm and muscle atrophy [17]. TBI often results in a hypermetabolic state with negative nitrogen balance, which may contribute to exaggerated muscle breakdown [18]. In animal studies, TBI-associated muscle wasting occurs regardless of nutritional status, suggesting that brain injury may initiate specific signaling cascades that alter muscle function [19].

The most important result of our study is that whether patients were evaluated as a separate groups or as a whole study group, the diaphragm thickness was found to be positively correlated with the functional independence scores before/after rehabilitation and the change in these measurements. There are no studies in the literature evaluating the effect of diaphragm thickness on rehabilitation outcome.

Study limitations

Our study had some limitations. The small sample size and participant diversity may explain that they do not show some significant differences between subgroups. Likewise, the number of patients in different groups was small to assess any kind of correlation between diaphragm thickness and functional outcome. The small sample size also limited the number of factors to be evaluated in the regression modeling. Also, there are high incidences of female patients in our studied group. The reason for this may be due to exclusion criteria. We excluded alcohol consumption and smoking from study, because alcohol and cigarettes can affect the thickness of the diaphragm with neurotoxic and structural damage effects [8, 9]. Unfortunately, the use of these substances is 30 times higher in men than in women [20].We believe that future studies with a larger scale and homogeneous distribution will make our results more understandable.

Conclusions

The diaphragm thickness may be an effective factor on the rehabilitation process of SCI and TBI patients even when there is no neurological damage directly affecting the diaphragm after trauma. Further studies with larger sample sizes are required to support our results.

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Compliance with ethical standards

Conflict of interests The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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