



FUNCTIONAL STATE OF THE DIAPHRAGM IN PATIENTS WITH CERVICAL SPINAL CORD INJURY AT THE STAGES OF RESPIRATORY SUPPORT

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Objective. To analyze the role of the functional state of the diaphragm in patients with cervical spinal cord injury at the stages of respiratory support and to substantiate additional criteria for their readiness to transfer to spontaneous breathing.

Material and Methods. The state of the diaphragm was assessed by ultrasound in 24 patients with spinal cord injury. The excursion of the diaphragm during quiet breathing, the excursion and thickness of the diaphragm during forced breathing, and the change in forced expiratory volume from the moment of admission till the end of mechanical ventilation were analyzed.

Results. On the first day, on the background of mechanical ventilation, there was a significant decrease in the excursion and thickness of the diaphragm during forced breathing ($p = 0.002$; $p = 0.008$) which persisted up to 3 days ($p < 0.001$; $p < 0.001$); by the fifth day of mechanical ventilation, the indicators increased to the initial levels ($p = 0.112$; $p = 0.433$); and by the 10th day they exceeded the initial values ($p < 0.001$). When comparing the excursion and thickness of the diaphragm during the transfer of patients to spontaneous breathing with the data on their admission, a significant difference was obtained ($p < 0.001$; $p < 0.001$). The dynamics of forced expiratory volume indicators was similar to those of diaphragm excursion during forced breathing.

Conclusion. A peculiarity of the functional state of the diaphragm in patients with cervical spinal cord injury in the acute period was a significant decrease in diaphragm excursion and the development of ventilator-induced diaphragm dysfunction (VIDD) associated with mechanical ventilation in replacement modes. The tactics of early tracheostomy and the use of auxiliary ventilation modes determined the absence of progression of VIDD during prolonged mechanical ventilation. The presence of a strong correlation between the diaphragm excursion during forced breathing and the forced expiratory volume allows concluding that these indicators can be additional objective criteria for the readiness of patients with cervical SC injury to transfer to spontaneous breathing, since they reflect not only the functional state of the diaphragm, but also the state of the lung tissue.

Key Words: spinal cord injury, respiratory failure, diaphragm dysfunction, mechanical ventilation, diaphragm ultrasound, weaning from mechanical ventilation.

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Acute respiratory failure associated with the cervical spinal cord injury is due to paralysis of respiratory muscles and dysfunction of diaphragm that provides the negative inspiratory pressure required for lung ventilation. Depending on the level of spinal cord injury, diaphragm paralysis or paresis develops [1]. A sharp change in the breathing mechanics determines the need for invasive mechanical ventilation [1, 2]. Patients with spinal cord injury have some of the highest mechanical ventilation dependences across the total patient cohort in intensive care units [2, 3].

In 2021, a meta-analysis covering 39 studies with 14,637 clinical cases in total was published [2]. According to this analysis, 90 % of patients with complete functional injury to the cervical spinal

cord needed mechanical ventilation that lasted on average 30.9 days. Previously, we obtained quite comparable results: 92 % of patients with the ASIA A spinal cord injury needed long-term mechanical ventilation [4].

However, using mechanical ventilation in the replacement mode excepted active diaphragm involvement in the act of breathing. This may lead to muscle atrophy processes in diaphragm. Added lung complications in this background increases diaphragm weakness and mechanical ventilation duration. Life-long dependence on respiratory therapy persisted in 15 % of patients with cervical spinal cord injury [2].

Stopping prolonged mechanical ventilation is one of the most difficult tasks

in intensive care. It becomes even more difficult in patients with cervical spinal cord injury due to persistent generalized muscular weakness [3]. When a patient is transferred to spontaneous breathing unreasonably early, the requirement to re-transfer to mechanical ventilation emerges in 20 % of cases against inefficient respiratory function. This re-transfer is associated both with an increase in the duration of stay in intensive care units and the total duration of hospital stay, and with an increase in hospital mortality [5, 6]. In order to solve the problem of most accurately determining the patient's readiness to be transferred to spontaneous breathing, in addition to the generally accepted indications for termination of mechanical ventila-

tion, an assessment of the functional state of the diaphragm with ultrasound is used [7]. In this case, diaphragm excursion and diaphragm thickening index are the main studied features. According to the literature [8], in the general population of patients on long-term mechanical ventilation, the sensitivity of the technique, when transferring to spontaneous breathing, to the excursion and the thickening index is 0.786 and 0.893, and the specificity is 0.711 and 0.796, respectively.

Despite the great interest in ultrasound assessment of the functional state of the diaphragm against the background of prolonged mechanical ventilation in the general population of patients, however, the issue remains poorly understood in relation to patients with a cervical spinal cord injury.

As a study hypothesis, it was assumed that it is possible to reduce the percentage of re-transferred patients to mechanical ventilation when the values of diaphragm excursion during forced breathing (DEFB) and diaphragm thickness during forced breathing (DTFB) while transferring patients with a spinal cord injury to spontaneous breathing, reach or exceed the initial ones, together with the generally accepted criteria for readiness to stop mechanical ventilation,

The objective is to analyze the role of the functional state of the diaphragm in patients with cervical spinal cord injuries at the stages of respiratory support and substantiate additional criteria for the readiness to transfer to spontaneous breathing.

Material and Methods

The prospective study included 24 patients with cervical spinal cord injuries who received high-tech medical care in 2019–2021. The inclusion criteria were: the severity of spinal cord injury types A and B according to ASIA; mechanical ventilation demand for over 24 hours. The exclusion criteria: the severity of spinal cord injury types C and D according to ASIA. Severity of spinal cord injuries was assessed according to the classification of the American Spinal

Injury Association and the International Medical Society of Paraplegia [9].

According to urgent indications, all patients in the acute injury period underwent decompression and stabilization surgery. Upon completing the surgical stage, the patients were transferred to the ICU for extended mechanical ventilation. The approach to intensive care measures according to the protocol adopted in the clinic was the same in all patients and included a set of therapeutic interventions aimed at correcting the existing organ dysfunctions. The parameters of respiratory support were selected according to the concept of protective mechanical ventilation. When choosing a mechanical ventilation mode, preference was given to the pressure control modes with the possibility of spontaneous breathing in a patient (BiPAP, CPAP, PS).

The study analyzed age, gender, duration of mechanical ventilation, length of stay in the ICU, total duration of hospital stay, dynamics of the main indicators of the functional state of the diaphragm: diaphragm excursion during quiet breathing (DEQB), DEFB, DTFB. The control points of the study: admission of patients to an admission unit, the 1st, 3rd, 5th, 7th, 10th, 15th, 20th, 25th days of observation, termination of mechanical ventilation.

The functional state of the diaphragm was assessed with a GE-LOGIQe portable ultrasound device (USA). The study was performed with patients in the recumbent position, a sectoral sensor was used, that was placed along the mid-clavicular line in the hypochondrium, the liver served as a sample frame. The direction of the sensor is maximally perpendicular to the dome of the diaphragm. After correct diaphragm visualization in the B-mode (image quality setting), switch to the M-mode (study of anatomical structures in a sweep along the time axis) was made to display the diaphragm movement along the selected line. The diaphragm on the monitor of the ultrasound device was visualized as a hyperechoic line. DTFB was measured along the outer edges at the height of forced inspiration. DEFB was measured along

the outer cranial edge of the diaphragm from the point of diaphragm rest to the peak point of forced inspiration. DEQB was measured along the cranial outer edge from the point of rest to the point of maximum excursion height at quiet breathing.

Diaphragm examination was performed during spontaneous breathing at the time of the patient admission to the hospital. Postoperative monitoring was carried out when consciousness was restored and the patient was transferred to spontaneous breathing for the duration of the study. It made possible to neutralize the effect of the mechanical ventilation device.

Due to the existing inhomogeneities in the diaphragm ultrasound technique and in order to minimize possible errors in the results obtained, the diaphragm was examined by 2 specialists with strict adherence to the described technology. In addition, we considered it necessary to determine the reference values of the studied indicators for the applied technology in 30 healthy volunteers.

The study complies with the ethical standards of the WMA Declaration of Helsinki “Ethical Principles for Medical Research Involving Human Subjects” and the Order of the Ministry of Health of the Russian Federation No. 200n as of April 1, 2016 “On Approval of Rules for Good Clinical practice”. The studies were approved by the facility’s Biomedical Ethics Committee. All patient data are depersonalized.

Statistical calculations were carried out using the RStudio program in the R language (version 3.6.1).

Continuous indicators were tested for compliance with the normal distribution law using the Shapiro-Wilk test. Due to the small number of continuous indicators that satisfy the applicability condition for the parametric criteria, at different time points in patients, the comparison was carried out by the nonparametric Wilcoxon test, and in the groups of sick and healthy patients, the nonparametric Mann-Whitney U-test was used. Pairwise associations of continuous indicators were studied by calculating the Spearman’s rank correlation

coefficients with the calculation of the achieved level of p significance.

For descriptive statistics of continuous data, the median [first quartile; third quartile] was calculated; binary and categorical data are presented as «number of patients (percentage of the total number of patients in the group)».

Statistical hypotheses were tested at a critical significance level of 0.05, i.e., the difference was considered statistically significant at the achieved level of $p < 0.05$.

Results

Most of the patients included in the study were men – 22 (91.6 %). The mean age of the patients was 38.67 ± 15.03 years. Out of them 18 (75 %) patients had ASIA A severity level of spinal cord injury, and 6 (25 %) – ASIA B.

The analyzed indicators of the functional state of the diaphragm at admission compared with the reference values are presented in the Table.

When comparing the DEQB values, there was no statistically significant difference with the reference values, while the DEFB values turned out to be significantly lower. The DTFB values even slightly exceeded the reference values. In our opinion, it was the result of the diaphragm reaction to compensate the loss of the function of the auxiliary respiratory muscles (intercostal and pectoral muscles, muscles of the abdominal wall) by means of a greater contraction.

An analysis of the values of the functional state of the diaphragm in dynamics showed that on the 1st day of postoperative follow-up with mechanical ventilation there was a significant decrease in DEFB and DTFB in comparison with the data obtained at patient admission ($p = 0.002$; $p = 0.008$). This condition persisted on the 3rd day of mechanical ventilation ($p < 0.001$; $p < 0.001$). The dynamics of the presented values indicates the development of ventilator-induced diaphragm dysfunction (VIDD) associated with respiratory support in replacement ventilation modes against the background of medicated sedation in order to synchronize patients with the mechanical ventilation device. On the 1st–3rd

days, patients underwent tracheostomy that made it possible to stop medicated sedation and use softer mechanical ventilation modes with the possibility of patient's spontaneous inspiration. On the 5th day of respiratory support, the values of DEFB and DTFB increased to the initial level ($p = 0.112$; $p = 0.433$), and by the 10th day they even exceeded the initial values ($p < 0.001$). Then this trend continued until making a decision to stop mechanical ventilation. A statistically significant difference was obtained ($p < 0.001$; $p < 0.001$), when comparing DTFB and DEFB at the time of transferring patients to spontaneous breathing with the data on admission to the hospital. An analysis of the DEQB dynamics showed statistically significant differences with values on admission only at the time of mechanical ventilation termination ($p = 0.002$; Fig. 1).

Values of forced expiratory volume showed dynamics similar to those of DEFB (Fig. 2). The forced expiratory volume decreased to the maximum on the 3rd day of mechanical ventilation ($p < 0.001$), followed by recovery to the level of the initial values on the 5th day ($p = 0.341$). On the 10th day of mechanical ventilation while transferring patients to spontaneous breathing, the forced expiratory volume values significantly exceeded the initial values ($p < 0.001$; $p < 0.001$).

The Spearman's rank correlation coefficient between forced expiratory volume and DEFB was calculated, showing positive relationships at all stages of the study. Strong correlation was detected on the 5th, 7th, 25th days ($r = 0.87$; $p < 0.001$, $r = 0.72$; $p < 0.001$, $r = 0.94$; $p = 0.005$). Average correlation was detected on the 1st, 3rd, 15th days of follow-up and when transferring a patient to spontaneous breathing ($r = 0.52$, $p < 0.009$; $r = 0.67$, $p < 0.001$; $r = 0.62$, $p = 0.033$; $r = 0.65$, $p = 0.001$).

When the generally accepted criteria for the patient readiness to be transferred to spontaneous breathing were achieved and when the current values of diaphragm mobility and thickness reached or exceeded the level of preoperative values, mechanical ventilation

was stopped. A re-transfer to mechanical ventilation was required for 1 (4.1 %) patient.

The total mechanical ventilation duration was 19.79 ± 14.40 days. The number of days spent in the ICU and total hospital stay were 34.25 ± 16.51 and 50.21 ± 20.53 days, respectively.

Discussion

The main generally accepted criteria in intensive care for stopping mechanical ventilation are the aborting the acute phase of the underlying disease and its complications, stabilization the hemodynamics and the neurological status, absence of inflammatory changes in the lungs, and an adequate cough impulse. For patients with spinal cord injury, these criteria did not demonstrate high efficacy. When analyzing the literature, we have not found any studies or clearly defined clinical recommendations on the criteria for stopping mechanical ventilation in the studied patient population. At the same time, it is possible to single out the most frequently recommended parameters: vital lung capacity over 10 ml/kg, respiratory rate 12–20 per minute, minute ventilation less than 10 l/min, PaO_2 more than 80 mm Hg, and PaCO_2 less than 45 mm Hg. [10].

According to a meta-analysis data [5] that included six studies with a total of 387 patients with acute cervical spinal cord injury, the average frequency of unsuccessful attempts to transfer patients to spontaneous breathing after prolonged mechanical ventilation is 20–25 %, and in some studies – 60 %. Such high rates of unsuccessful attempts to transfer patients with spinal cord injury to spontaneous breathing are due to the specifics of the pathogenesis of respiratory failure, particularly, the diaphragm often remains the only respiratory muscle that provides almost 75 % of pulmonary ventilation in this category of patients. Preserving its functional status is one of the main aims when determining a mechanical ventilation tactics [3, 10].

The study showed that already after 24 hours of mechanical ventilation, ven-

Table

Functional state of diaphragm in patients on admission (n = 24)

| Measured indicators | On admission MED – (IQR) | Reference values MED – (IQR) | Wilcoxon <i>t</i> -test (p level) |
|---|--------------------------|------------------------------|-----------------------------------|
| Diaphragm excursion during quiet breathing, sm | 2.23 [1.87; 2.4] | 1.95 [1.78; 2.28] | 0.428 |
| Diaphragm excursion during forced breathing, sm | 4.70 [4.18; 5.15] | 7.40 [6.45; 8.12] | <0.001* |
| Diaphragm thickness during forced breathing, sm | 0.55 [0.51; 0.57] | 0.50 [0.47; 0.53] | 0.005* |

MED – Median; IQR – InterQuartile Range; * statistically significant differences.

tilator-induced diaphragm dysfunction was registered with ultrasound. On the 3rd day of follow-up, it became maximally pronounced. The obtained results correspond to the literature data that also indicate development of ventilator-induced diaphragm dysfunction after 24 hours of mechanical ventilation [11–14]. A distinctive feature of the obtained data is the regression of ventilator-induced diaphragm dysfunction already on the 5th day of postoperative follow-up. This result was achieved, in our opinion, due to performing an early tracheostomy followed by the rejection of medicated sedation and the use of mechanical ventilation modes that do not suppress the patient's spontaneous inspirations.

The obtained statistically significant differences in the analyzed values at the stages of observation suggest that the DEFB and DTFB values are the markers of compensatory mechanisms development for an existing respiratory failure that indicate the correct choice of tactics for applying auxiliary mechanical ventilation modes and can be successfully used as additional criteria in determining the patient's readiness for spontaneous breathing. Several earlier published works confirm the development of similar compensatory mechanisms in case of respiratory failure in patients with a complicated cervical spinal cord injury [15, 16].

According to the literature [16, 17], it is known that spirometric indicators are significantly reduced in the analyzed patient population. Forced expiratory volume that showed a quite strong correlation with DEFB in our study, can be a tool for assessing the state of the respiratory system, reflecting not only the func-

tional state of the diaphragm, but also the state of the lung tissue.

The efficacy of assessing the functional state of the diaphragm with ultrasound in patients with cervical spinal cord injury in the study is evidenced by a small number of unsuccessful cases of weaning patients from mechanical ventilation.

The primary benefit of the study is that we determined the reference values for indicators of the functional state of the diaphragm with a specific ultrasound technique and assessed the functional state of the diaphragm in dynamics – from the moment of admission to the hospital to the transfer of the patient to spontaneous breathing. There are, however, some limitations. First, a small number of clinical observations that is due to

the low incidence of spinal cord injuries with the ASIA A and B severity levels. Second, we did not take into account the effect of gender differences, since only two female patients were included in the study, and the absolute majority was formed by male patients. Third, only the functional state of the right dome of the diaphragm was assessed, although other researchers also face this limitation due to the lack of an adequate sample frame for ultrasound of the left diaphragm dome. These limitations most likely affected the diagnostic accuracy of the study and, therefore, this fact highlights the need for further research, including randomized studies, in order to apply the obtained generalizations to all patients with cervical spinal cord injuries.

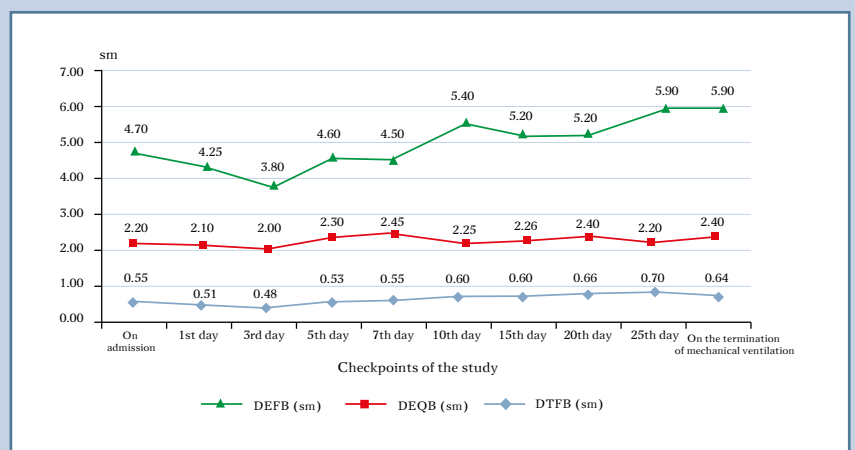
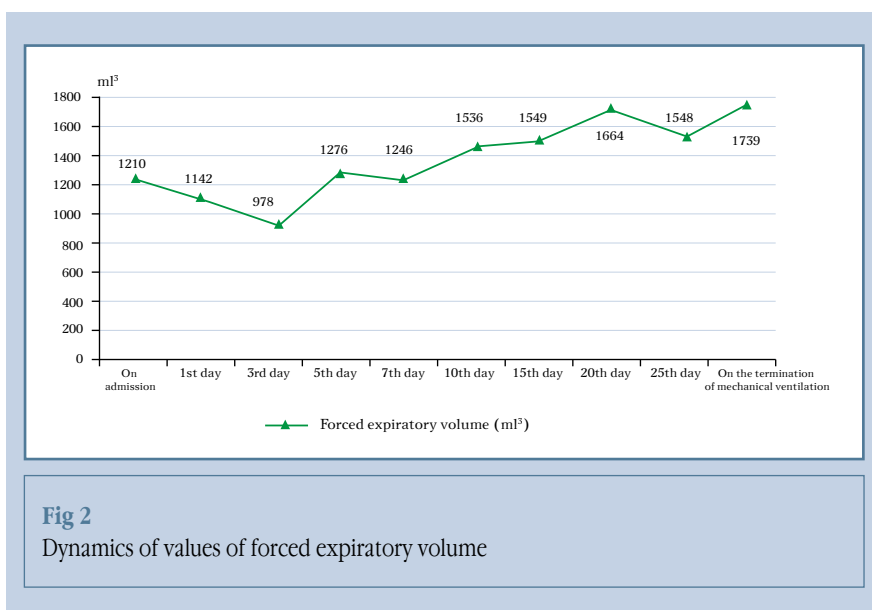


Fig 1

Dynamics of diaphragm excursion and thickness in patients with cervical spinal cord injury: DEFB – diaphragm excursion during forced breathing; DEQB – diaphragm excursion during quiet breathing; DTFB – diaphragm thickness during forced breathing



Conclusion

The main feature of the functional state of the diaphragm in patients with a cervical spinal cord injury in the acute peri-

od was a significant decrease in DEFB and the development of a ventilator-induced diaphragm dysfunction associated with mechanical ventilation in replacement modes against the

background of medicated sedation. The tactics of early tracheostomy and the use of auxiliary ventilation modes ensured the absence of progression of ventilator-induced diaphragm dysfunction during prolonged mechanical ventilation.

When the generally accepted criteria for the readiness of patients to transfer to spontaneous breathing and the current DEFB and DTFB values are not lower than the level of preoperative values, mechanical ventilation can be stopped.

A strong correlation between DEFB and forced expiratory volume allows us to conclude that these values can be objective additional criteria for the readiness of patients with a cervical spinal cord injury to spontaneous breathing, reflecting not only the functional state of the diaphragm, but also a lung tissue condition.

The study had no sponsors. The authors declare that they have no conflict of interest.

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