https://doi.org/10.15360/1813-9779-2022-5-24-31

Respiratory Mechanics and Gas Exchange in Acute Respiratory Distress Syndrome Associated with COVID-19

Ravshan A. Ibadov[1,2], Djurabay M. Sabirov[3], Sardor Kh. Ibragimov[1]*, Bakhodir B. Burkhonov[1,2], Raufbek R. Ibadov[1,2]

[1] Republican Specialized Scientific and Practical Medical Center for Surgery named after academician V.Vakhidov
10 Kichik Halka Yuli Str., Chilanzar district, 100115 Tashkent, Republic of Uzbekistan
[2] Republican Specialized Infectious Diseases Hospital Zangiota-1
Katartal settlement, Zangiata district, 111800 Tashkent region, Republic of Uzbekistan
[3] Center for the development of professional qualification of medical workers
51 Parkent str., Mirzo Ulugbek district, 100007 Tashkent, Republic of Uzbekistan

Механика дыхания и газообмен при остром респираторном дистресс-синдроме, ассоциированном с COVID-19

Р. А. Ибадов[1,2], Д. М. Сабиров[3], С. Х. Ибрагимов[1]*, Б. Б. Бурхонов[1,2], Р. Р. Ибадов[1,2]

[1] Республиканский специализированный научно-практический медицинский центр хирургии им. акад. В. Вахидова,
Узбекистан, 100115, г. Ташкент, р-н Чиланзар, ул. Кичик халка йули, д. 10
[2] Республиканская специализированная инфекционная больница Зангиота-1,
Узбекистан, 111800, Ташкентская область, Зангиатинский р-н, поселок Катартал
[3] Центр развития профессиональной квалификации медицинских работников,
Узбекистан, 100007, г. Ташкент, р-н Мирзо Улугбек, ул. Паркентская, д. 51

For citation: *Ravshan A. Ibadov, Djurabay M. Sabirov, Sardor Kh. Ibragimov, Bakhodir B. Burkhonov, Raufbek R. Ibadov.* Respiratory Mechanics and Gas Exchange in Acute Respiratory Distress Syndrome Associated with COVID-19. *Obshchaya Reanimatologiya* = *General Reanimatology.* 2022; 18 (5): 24–31. https://doi.org/10.15360/1813-9779-2022-5-24-31 [In Russ. and Engl.]

Summary

Aim. To compare respiratory mechanics and gas exchange in patients with acute respiratory distress syndrome (ARDS) with and without COVID-19.

Material and methods. We examined 96 patients, who were divided into two groups. The main group included 48 patients with COVID-19-associated ARDS. The control group included 48 patients with ARDS not associated with COVID-19. Most characteristic patients were selected for the following baseline parameters: age, sex, SAPS II score, disease severity, plateau pressure (Pplateau), oxygenation index (PaO_2/FiO_2), and arterial-alveolar oxygen gradient ($A\text{-}aO_2$). Respiratory mechanics and gas exchange parameters assessed immediately after ARDS diagnosis and on days 1, 3 and 7 of treatment included arterial oxygen (PaO_2) and carbon dioxide ($PaCO_2$) pressure, tidal volume (Vt), respiratory rate (RR), respiratory minute volume (RMV), positive end expiratory pressure (PEEP), and $P_{plateau}$.

Results. Patients in the main group had higher Vt (9.7 vs. 5.1 ml/kg, $P<0.001$), RR (38 vs. 30 min^{-1}, $P<0.001$), and RMV (27.7 vs. 10.5 l/min, $P<0.001$). Control group patients showed hypercapnia ($PaCO_2$ 43 vs. 38 mmHg, $P<0.001$), lower respiratory compliance (30 vs. 48 ml/cm H_2O, $P<0.001$) and ventilation ratio (VR) (1.5 vs. 2.0, $P<0.01$). Lower PEEP values were required for patients in the main group. However, despite the higher rate of tracheal intubation in the control group (50% vs 16.7%) in the initial period of intensive care, the proportion of patients receiving invasive lung ventilation was significantly higher in the main group (33.3% vs.14.6%) by day 7.

Conclusion. The initial phase (the first 7 days) of ARDS associated with COVID-19 is characterized by higher values of Vt, RR and RMV, as well as lung compliance vs «typical» ARDS with almost identical PaO_2/FiO_2 values.

Keywords: COVID-19; ARDS; respiratory support; respiratory mechanics

Conflict of interest. The authors declare no conflict of interest.

Read the full-text English version at www.reanimatology.ru

Correspondence to:

Sardor Kh. Ibragimov
E-mail: dr.sardor.ibragimov@gmail.com

Адрес для корреспонденции:

Сардор Хамдамович Ибрагимов
E-mail: dr.sardor.ibragimov@gmail.com

Introduction

The pandemic new coronavirus infection COVID-19 has led to a dramatic increase in the incidence of acute respiratory distress syndrome (ARDS) worldwide [1, 2]. As experience in the management of patients with COVID-19-associated ARDS accumulates, efforts are being made to develop its classification, according to the mechanical changes of the respiratory system, in order to optimize algorithms of respiratory therapy [3, 4]. To date, viral pneumonia was shown to be accompanied by a variety of clinical manifestations and disorders of respiratory mechanics with the underlying interaction between such major factors as viral load, patient reactivity, baseline physiological reserve and comorbidity as well as the patient's adaptive capacity for hypoxemia and the time from the onset of the disease to the beginning of intensive care [5–7].

Despite disease-specific differences in the pathogenesis of ARDS, most authors suggest using similar methods of respiratory support for its control. These include lung ventilation with low tidal volume (Vt) (4–8 ml/kg) and maintenance of plateau pressure below 30 cm H_2O. Individualized use of high levels of positive end-expiratory pressure (PEEP), 12–16-hour ventilation in the prone position, muscle relaxants, and recruitment maneuvers are recommended for patients with COVID-19 on mechanical lung ventilation (MLV) [8–10]. Recently, the personalized respiratory support with pulmonary protection has become the basis of ARDS treatment and was shown to reduce mortality. The ventilation strategy is also discussed in the context of recent debates about phenotypic heterogeneity in patients with COVID-19-related ARDS [2, 5, 11, 12]. Although early reports suggested that COVID-19-associated ARDS has mostly unique features, new data indicate that the respiratory mechanics of patients with or without COVID-19-associated ARDS are broadly similar [3, 6, 13, 14].

Large variations in mortality in different medical centers indicate that respiratory support can contribute significantly to the outcome of COVID-19-associated ARDS [15, 16]. The understanding of respiratory mechanics in COVID-19 pneumonia and the feasibility of involving the unstable alveoli in gas exchange can provide a background for adjustment of respiratory settings. While solid evidence supporting the paradigm change in ventilation control is still lacking, an individualized approach with respect to respiratory biomechanics of each patient has been proposed [4, 7, 15, 17].

The aim of the study was to compare parameters of respiratory mechanics and gas exchange in patients with acute respiratory distress syndrome (ARDS) associated with COVID-19 and not related to COVID-19.

Material and Methods

Forty-eight adult patients with COVID-19-associated ARDS hospitalized in the Republican Infectious Hospital Zangiota-1 (Tashkent, Uzbekistan) during the period July 1 to August 27, 2021 were included in the prospective study and comprised the first (main) group. SARS-CoV-2 was identified by reverse transcriptase-polymerase chain reaction of nasal swabs. The SARS severity was assessed by oxygenation index (RaO_2/FiO_2) according to Berlin definitions [14].

The second group (control) consisted of 48 adult patients with ARDS not related to COVID-19, hospitalized in the Vakhidov Republican Research and Medical Center of Surgery (Tashkent, Uzbekistan) from January 2017 to August 2021.

Inclusion criteria for patients in the study were age older than 18 years and diagnosis of ARDS (according to Berlin definitions).

Patients who underwent tracheal intubation immediately upon admission to the ICU were not included in the study.

The patients were selected according to the principle of initial characteristics representativity according to the following criteria: age, sex, SAPS II score, disease severity, plateau pressure (Pplateau), oxygenation index (RaO_2/FiO_2), and alveolar-arterial oxygen gradient ($A\text{-}aO_2$).

Invasive lung ventilation with sedation was started in the volume control mode with Vt of 6–8 ml/kg of predicted body weight and respiratory rate (RR) up to 35 min^{-1} (adjusted according to arterial blood pH). Oxygen fraction (FiO_2) was set to achieve an arterial blood oxygen saturation greater than 93%.

The PEEP parameters were set by the attending physician according to gas exchange and hemodynamic tolerance values with an upper limit of Pplateau of 28 cm H_2O.

During the first 12 hours of the patients' stay in ICU we analyzed the ventilator settings in the non-invasive ventilation mode (CPAP), including the patient's supine position. Respiratory mechanics and possibility of lung recruitment were assessed.

Initial measurements were made immediately after ARDS diagnosis with the patient being on non-invasive ventilation. The following parameters were measured from 6 to 12 am on days 1,3, and 7 of treatment: PaO_2, FiO_2, $PaCO_2$, Vt, RR, MV, PEEP, and Pplateau (with a breath hold of 0.2 to 0.3 s).

Alveolar-arterial oxygen gradient was estimated using the formula: $A\text{-}aO_2 = [(AP–PH_2O) \times FiO_2) – (PaCO_2/RQ)] – PaO_2$ (mm Hg),

Where AP is the atmospheric pressure, PH_2O, the partial pressure of water vapor, and RQ, the respiratory coefficient. AP, PH_2O, and RQ were considered to be 760 mmHg, 47 mmHg, and 0.8, respectively.

Table 1. Baseline parameters of non-invasive lung ventilation in the studied groups.

Parameters	Values in groups		*P-value*
	Main, *n*=48	Control, *n*=48	
Age, years (min–max)	53 (31–72)	56 (38–71)	0.216
SAPS II, points (min–max)	47 (37–58)	48 (37–59)	0.465
Sex (F/M), *n*	37/11	35/13	0.281
Moderate ARDS, *n* (%)	33 (68.8%)	35 (72.9%)	—
Severe ARDS, *n* (%)	15 (31.2%)	13 (27.1%)	—
Vt, ml/kg (min–max)	9.7 (6.1–14.2)	5.1 (3.9–6.9)	<0.001
RR, min^{-1} (min–max)	38 (25–45)	30 (25–35)	<0.001
MV, l/min (min–max)	27.7 (12–38)	10.5 (9.3–11.8)	<0.001
$PaCO_2$, mmHg (min–max)	38 (34–43)	43 (37–49)	<0.001
PEEP, cmH_2O (min–max)	10 (8–14)	8 (7–12)	0.072
Plateau pressure, cmH_2O (min–max)	24 (20–27)	25 (22–28)	0.655
CRS, ml/cmH_2O (min–max)	48 (28–70)	30 (23–40)	<0.001
PaO_2/FiO_2, mmHg (min–max)	128 (67–163)	136 (80–167)	0.105
A-aO_2 gradient, mmHg (min–max)	347 (242–514)	351 (271–485)	0.554
VR (min–max)	2.0 (1.6–2.6)	1.5 (1.3–2.0)	<0.001

Note. SAPS II — Simplified Acute Physiology Score; F — females; M — males; ARDS — acute respiratory distress syndrome; V_t — tidal volume; MV — minute volume; $PaCO_2$ — partial pressure of CO_2 in arterial blood; PEEP — positive expiratory end pressure; CRS — compliance of respiratory system; PaO_2/FiO_2 — oxygenation index; A-aO_2 gradient — alveolar-arterial oxygen gradient; VR — ventilation ratio.

Compliance of respiratory system (CRS) was calculated as the ratio of Vt to the difference between Pplateau and established PEEP.

Ventilation ratio (VR) was calculated as the ratio of [MV (ml/min) × $PaCO_2$ (mm Hg)] to [patient weight (kg) × 100 × 37.5].

PaO_2/FiO_2, A-aO_2 gradient, CRS, and VR were calculated on days 1, 3, and 7.

The study materials were analyzed using parametric and nonparametric statistical analysis methods, using STATISTICA 13.3 software (StatSoft Inc.). Accumulation, correction, and synthesis of the initial data as well as the visualization of the results were performed in Microsoft Office Excel 2019 electronic spreadsheets.

The normality of quantitative variable distribution was assessed using the Shapiro–Wilk test. All parameters had a normal distribution. The data were combined into variation series, where arithmetic mean values and standard deviations were calculated. Student's t-test was calculated to compare the mean values. The differences were considered significant at $P<0.05$.

Results

Initially, 164 patients with COVID-19-associated ARDS and 62 patients with non-COVID-19-associated ARDS were included in the study. During statistical analysis and comparison of patients baseline characteristics (age, sex, SAPS II score, disease severity, plateau pressure ($P_{plateau}$), RaO_2/FiO_2 and A-aO_2), 48 patients with COVID-19-associated ARDS were matched against the same number of patients with non-COVID-19-associated ARDS. The main baseline characteristics and ventilator parameters in the groups are shown in Table 1.

Patients with COVID-19-associated ARDS had higher tidal volumes (9.7 versus 5.1 mL/kg, $P<0.001$), respiratory rate (38 versus 30 min^{-1}, $P<0.001$), minute ventilation (27.7 versus 10.5 L/min, $P<0.001$), compliance of respiratory system (48 versus 30 ml/cm H_2O, $P<0.001$), and ventilation ratio (2.0 versus 1.5, $P<0.001$). Hypercapnia was more common in the control group patients ($PaCO_2$ 38 vs. 43 mmHg, $P<0.001$).

Ventilation parameters in patients of both groups on days 1, 3, and 7 of treatment are shown in Table 2. Within the first 24 hours from the study start, 8 (16.7%) patients in the study group were intubated, as were 24 (50%) patients in the control group. On day 3, 6 (12.5%) patients in the main group were intubated, and by day 7, another 2 (4.2%) did so, thus the percentage of intubation in the main group ($P<0.001$) was 33.3% (16 out of 48) within a week, whereas in the control group 3 (6.25%) patients were switched to noninvasive CPAP support on day 3. Only 12.5% (6 out of 48) patients in the study group were completely weaned off noninvasive ventilation, while in the control group this parameter was 20.8% (10 out of 48), with 3 of them (6.25%) were transferred to spontaneous respiration on day 3 of the study, and 17 out of 48 (35.4%) patients were extubated ($P<0.001$). Thus, 14.6% (7 of 48) of patients in the control group remained on invasive lung ventilation on day 7.

Indications for tracheal intubation included hypoxemia ($SpO_2<92\%$), RR over 30 per min, impaired consciousness, and, additionally, increased visible chest excursions and chest X-ray abnormalities. In 3 cases, invasive ventilation in group 1 patients was started due to circulatory failure with the underlying acute myocardial infarction, and in 2 cases it was due to septic shock.

The Vt and MV were almost equal in both groups throughout the study. Respiratory rate

Table 2. Parameters of invasive ventilation in the studied groups.

Parameter	Values in groups					
	Day 1		Day 3		Day 7	
	Main	Control	Main	Control	Main	Control
Spontaneous breathing, *n* (%)	—	—	—	3 (6.25%)	6 (12.5%)	10 (20.8%)
	—		*P*<0.001		*P*<0.001	
Non-invasive ventilation, *n* (%)	40 (83.3%)	24 (50%)	34 (70.8%)	21 (43.75%)	26 (54.2%)	14 (29.2%)
	P<0.001		*P*<0.001		*P*<0.001	
Intubated, *n* (%)	8 (16.7%)	24 (50%)	14 (29.2%)	21 (43.75%)	16 (33.3%)	7 (14.6%)
	P<0.001		*P*<0.001		*P*<0.001	
Extubated, *n* (%)	—	—	—	3 (6.25%)	—	17 (35.4%)
	—		*P*<0.001		*P*<0.001	
V_t, ml/kg	6.1 (5.9–6.8)	6.0 (6.0–6.0)	6.1 (5.9–6.9)	6.0 (6.0–6.1)	6.4 (5.9–7.4)	6.0 (6.0–6.8)
	0.0321		0.210		0.758	
RR, min^{-1}	32 (24–40)	26 (18–35)	28 (25–33)	29 (24–33)	31 (26–35)	26 (20–32)
	P<0.001		*P*=0.884		*P*=0.007	
MV, l/min	11.9 (9.8–13.0)	10.9 (9.3–1.6)	11.5 (10.3–14.2)	11.6 (10–13.2)	12.3 (10.4–14.6)	12.5 (10.4–14.0)
	P=0.059		*P*=0.553		*P*=0.954	
PEEP, см H_2O	8 (6–12)	14 (8–16)	10 (6–12)	10 (7–16)	12 (6–16)	7 (5–14)
	0.004		0.489		<0.001	
P_{lateau} pressure, cm H_2O	24 (21–28)	32 (22–36)	25 (21–28)	26 (20–28)	27 (23–28)	23 (19–28)
	0.007		0.784		0.016	
FiO_2, %	75 (50–100)	60 (50–70)	70 (50–100)	55 (40–70)	60 (40–100)	50 (40–60)
	P=0.021		*P*=0.026		*P*=0.079	

Note. For quantitative parameters, minimal and maximal values are shown. V_t — tidal volume; RR — respiratory rate; MV — minute volume; PEEP — positive expiratory end pressure; FiO_2 — oxygen fraction in the oxygen-air mixture.

among patients on noninvasive ventilation was different between 2 groups: in the main one it was 32 (from 24 to 40), while in the controls it was 26 (from 18 to 35) (*P*<0.001). On day 3 of treatment, the values were equal, and on day 7 increased again in the main group (31 vs 26, respectively, *P*=0.007).

During day 1, the PEEP values were adjusted in the range between 6 and 12 cm H_2O with a mean of 8 cm H_2O in patients from the main group. They were higher in the control group patients due to their specific response to recruitment maneuvers. Further, due to the initiation of invasive lung ventilation with sedation and myoplegia in most patients and adjustment to higher PEEP values, these values demonstrated no differences between the groups (*P*=0.489), but their range (from 7 to 16 cm H_2O) was wider in the control group than in the main one (from 6 to 12 cm H_2O). With progressing COVID-19 pneumonia and decreasing of ventilated lung tissue volume, PEEP values were to be increased and became higher in the study group (12 [6–16] cm H_2O) than in the control one (7 [5–14] cm H_2O) (*P*<0,001).

The PaO_2/FiO_2 values were different between patient groups as early as on day 1 of the study, reaching 170.8 mm Hg in the control group versus 153.5 mm Hg in the main group (*P*<0.001), as they were on day 3 (217.91±68.26 versus 175.0±73.45 mm Hg, *P*<0.001), and on day 7 (268.54±65.23 versus 240.0±63.94 mm Hg) (Fig., *a*).

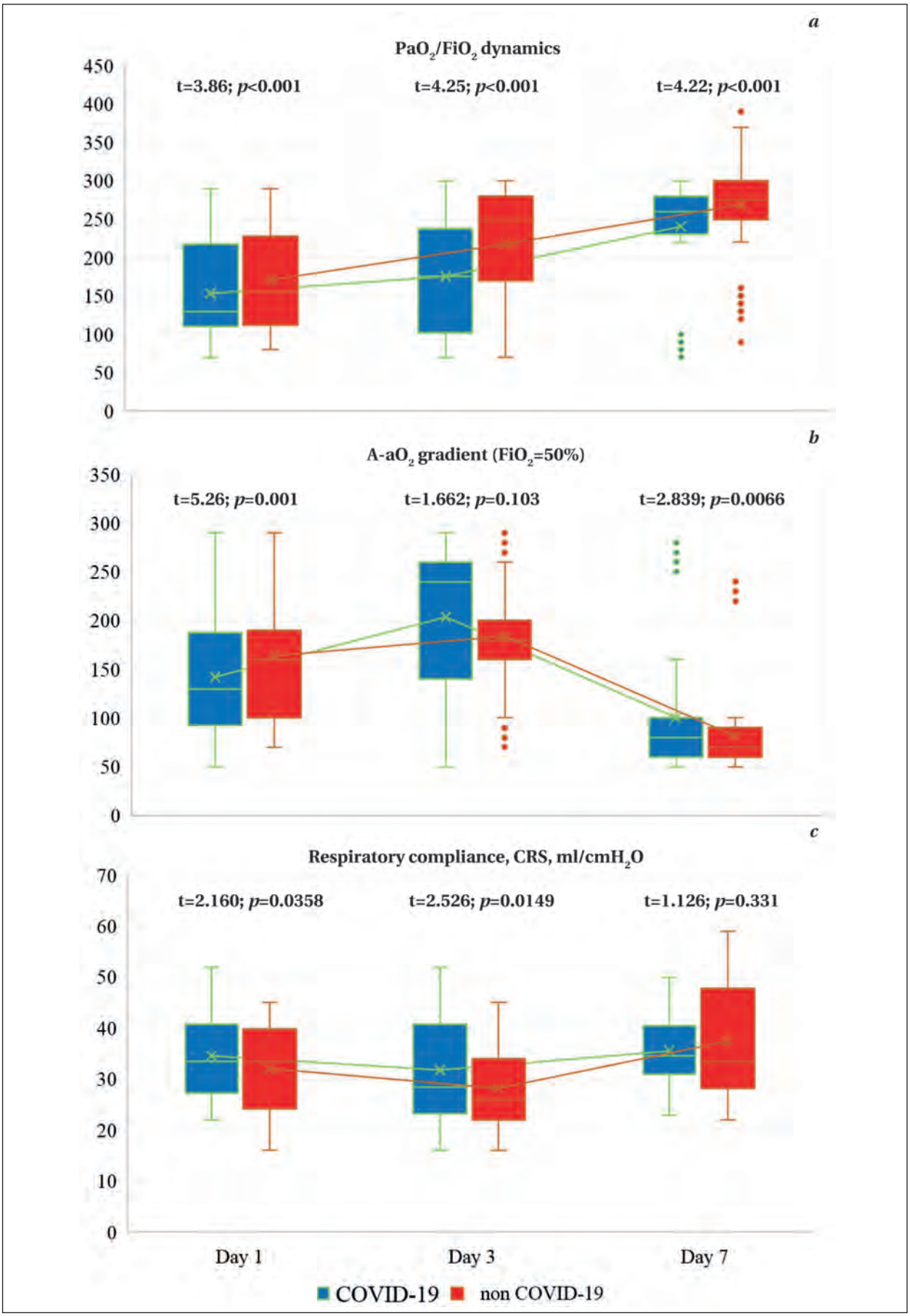
The Figure (*a*) shows that during respiratory therapy there was an increase in PaO_2/FiO_2 both in the control group (from 170.8 to 268.54±65.23 mmHg) and in the main group (from 153.5 to 240.0±63.94 mm Hg), i. e. the parameter was higher on day 3 than on day 1 of the study.

The alveolar-arterial gradient values in the main group were lower on the first day of mechanical lung ventilation than in the control group (142.0±65.75 versus 163.75±68.31) (*P*<0.001), (Fig., *b*). On the third day of mechanical ventilation, this parameter increased in both groups with no significant differences, and on the 7th day, it dropped in both groups, which was probably due to a decrease in the oxygen fraction used, being higher in the main group than in the control one (100.417±62.09 and 81.875±41.95, respectively, *P*=0.0066).

CRS values in the main group were higher than those in the controls on both the 1st and 3rd days of mechanical ventilation (34.521±8.53 versus 32.000±8.61 (*P*=0.0358) and 31.83±10.32 versus 28.125±8.01 (*P*=0.0149), respectively) (Fig., *c*). On day 7, the differences were absent.

Ventilation rate (VR) values were higher in patients in the main group than in the control one on days 1 and 3, but also did not differ between the groups on day 7 of treatment. A decrease in RR during CPAP support could be associated with an increase in Vt and cause higher VR in patients with COVID-19 on the first day of noninvasive lung support.

COVID-19-associated ARDS was initially characterized by higher values of Vt, MV, RR and CRS than non-COVID-19-associated ARDS. Later, during respiratory therapy, patients with COVID-19-associated ARDS, due to higher CRS, required lower



Changes in the studied parameters in the groups of patients.
Notes. PaO_2/FiO_2 – oxygenation index (*a*); A-aO_2 — alveolar-arterial oxygen gradient (*b*); CRS — compliance of respiratory system.

PEEP settings than those with non-COVID-19-associated ARDS, while V_t and MV were almost identical.

It should be emphasized that patients with ARDS associated with COVID-19 required tracheal intubation less frequently at the initial stage of treatment, but on day 7, the proportion of patients receiving invasive ventilation in the study group was higher than in the control group, and no extubation was observed in the main group.

Discussion

Our observations show that the initial (1–5 days) characteristics of COVID-19-associated ARDS change over time and approach those of «typical» ARDS.

L.Gattinoni et al. suggested that relatively high CRS correlating with low PaO_2/FiO_2 can identify a separate subgroup of patients with ARDS associated with COVID-19 requiring a specific algorithm of respiratory support [3, 15]. In contrast, other authors argue that this pattern of respiratory mechanics is just a clinical phenotype which is also seen in patients with ARDS of other etiologies and is determined by severity and stage of the disease [16, 18, 19].

According to the study by O. Voennov et al., two types of clinical hypoxia phenotypes depending on SpO_2 level and dyspnea severity can be distinguished among COVID-19 patients. The first type is characterized by a decrease in saturation down to 93% and an increase in RR up to 25 per minute, and does not require lung ventilation. The second phenotype with RR over 25 and SpO_2 under 93% can associate with arterial hypoxemia and tissue hypoxia with acidosis and requires mechanical ventilation [20].

The H-/L-phenotyping system suggested by L. Gattinoni et al. in patients with ARDS associated with COVID-19 was not confirmed in the studies of LDJ Bos et al. who concluded that lung compliance itself does not correlate with the extent of affected lung tissue, and most patients can be classified neither to H-, nor to L-subphenotype, but have mixed characteristics. Patients were often found to have extensive pulmonary damage and diffuse changes on chest CT, which could indicate potentially recruitable lung tissue. CRS was similar to that in other cohorts of patients with COVID-19 and with non-COVID-19-related ARDS [15, 21–23].

Different pulmonary compliance with initially equal values of blood oxygenation were observed in patients with and without COVID-19, both at baseline and on days 1 and 3 of respiratory support. These differences decreased as the disease progressed, with hypoxemia becoming more severe in patients in the main group, indicating its «discordance» with the lung compliance. The V_t reduction is known to be beneficial mainly in patients with low CRS, therefore, individual adjustment of respiratory support taking with respect to disease severity, airway pressure and lung compliance parameters, and in a continuous mode rather than based on the initial values, is necessary [16, 17, 24, 25].

Our results also argue in favor of systematic assessment of respiratory mechanics and personalization of ventilator settings in patients with COVID-19-associated ARDS.

Previously published studies evaluating COVID-19-associated ARDS respiratory mechanics have shown inconsistent results. For example, pulmonary compliance has been shown to decrease with lung injury volume greater than 50%, as in ARDS of other etiology, but the possibility of alveolar recruitment still exists [8, 9, 15, 16]. The results of our study show that even with more than 50% lung damage, CRS can be both high and low, with respiratory mechanics studied in the early disease, i. e., up to 10 days from onset of the first symptoms of respiratory failure. Patients with varying severity of pneumonia, extent of lung damage, and moderate to severe ARDS were evaluated.

Significantly higher CRS measured on day 1 in patients with COVID-19 compared to those without COVID-19 is consistent with previous reports [18].

The evidence of greater pulmonary compliance during the first day of mechanical ventilation in patients with ARDS and COVID-19 compared to patients without COVID-19 is also in line with earlier findings [18].

High parameters of PEEP can cause excessive alveolar distention and increased physiological dead space, indirectly affecting VR and CRS. Thus, Yaroshetskiy A. I. et al. observed low potential of lung recruitment and response to PEEP increase in COVID-19 patients, and PEEP over 10 cm H_2O after 7 days resulted in lung overextension in most patients on mechanical ventilation [26].

Therefore, the identified patterns of respiratory mechanics to a greater extent reflect the differences in ventilator management than in pathophysiology of ARDS of various etiologies. In addition, the progression of any disease leading to tracheal intubation can neutralize the specific characteristics of respiratory biomechanics (including situations with practically identical initial PaO_2/FiO_2). The patients in the main group had more significant decrease of arterial blood oxygenation than those in the control group, which confirms the «discordance» between hypoxemia and lung compliance, and suggests that V_t reduction is mainly beneficial for patients with low CRS and good response to low PEEP.

Conclusion

We conclude that the management of patients with COVID-19-associated ARDS should be based on individual changes in disease severity, airway pressure, and lung compliance values.

References

1. *World Health Organization*. Clinical management of COVID-19 — living guidance. 25 January 2021. WHO/2019-nCoV/clinical/2021.2. Available at: Living guidance for clinical management of COVID-19 (who.int).
2. *Ge H., Pan Q., Zhou Y/, Xu P., Zhang L., Zhang J., Yi J., Yang C., Zhou Y., Liu L., Zhang Z.* Lung mechanics of mechanically ventilated patients with COVID-19: analytics with high-granularity ventilator waveform data. *Front Med (Lausanne)*. 2020; 7: 541. DOI: 10.3389/fmed.2020.00541. PMID: 32974375.
3. *Gattinoni L., Chiumello D., Rossi S.* COVID-19 pneumonia: ARDS or not? *Crit Care*. 2020; 24 (1): 154. DOI: 10.1186/s13054-020-02880-z. PMID: 32299472.
4. *Navas-Blanco J.R., Dudaryk R.* Management of respiratory distress syndrome due to COVID-19 infection. *BMC Anesthesiol*. 2020; 20 (1): 177. DOI: 10.1186/s12871-020-01095-7. PMID: 32689937.
5. *Yang X., Yu Y., Xu J., Shu H., Xia J., Liu H., Wu Y., Zhang L., Yu Z., Fang M., Yu T., Wang Y., Pan S., Zou X., Yuan S., Shang Y.* Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020; 8 (5): 475–481. DOI: 10.1016/S2213-2600 (20)30079-5. PMID: 32105632.
6. *Alhazzani W., Møller M.H., Arabi Y.M., Loeb M., Gong M.N., Fan E., Oczkowski S., Levy M.M., Derde L., Dzierba A., Du B., Aboodi M., Wunsch H., Cecconi M., Koh Y., Chertow D.S., Maitland K., Alshamsi F., Belley-Cote E., Greco M., Laundy M., Morgan J.S., Kesecioglu J., McGeer A., Mermel L., Mammen M.J., Alexander P.E., Arrington A., Centofanti J.E., Citerio G., Baw B., Memish Z.A., Hammond N, Hayden F.G., Evans L., Rhodes A.* Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med*. 2020; 46 (5): 854–887. DOI: 10.1007/s00134-020-06022-5. PMID: 32222812.
7. *Matthay M.A., Aldrich J.M., Gotts J.E.* Treatment for severe acute respiratory distress syndrome from COVID-19. *Lancet Respir Med*. 2020; 8 (5): 433–434. DOI: 10.1016/S2213-2600 (20)30127-2. PMID: 32203709.
8. *Ziehr D.R., Alladina J., Petri C.R., Maley J.H., Moskowitz A., Medoff B.D., Hibbert K.A., Thompson B.T., Hardin C.C.* Respiratory pathophysiology of mechanically ventilated patients with COVID-19: a cohort study. *Am J Respir Crit Care Med*. 2020; 201 (12): 1560–1564. DOI: 10.1164/rccm.202004-1163LE. PMID: 32348678.
9. *Lu S., Huang X., Liu R., Lan Y., Lei Y., Zeng F., Tang X., He H.* Comparison of COVID-19 induced respiratory failure and typical ARDS: similarities and differences. *Front Med (Lausanne)*. 2022; 9: 829771. DOI: 10.3389/fmed.2022.829771. PMID: 35712114/.
10. *Li X., Ma X.* Acute respiratory failure in COVID-19: is it «typical» ARDS? *Crit Care*. 2020; 24 (1): 198. DOI: 10.1186/s13054-020-02911-9. PMID: 32375845.
11. *Gattinoni L., Chiumello D., Caironi P., Busana M., Romitti F., Brazzi L., Camporota L.* COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Med*. 2020; 46 (6): 1099–1102. DOI: 10.1007/s00134-020-06033-2. PMID: 32291463.
12. *Lucchini A., Giani M., Isgrò S., Rona R., Foti G.* The «helmet bundle» in COVID-19 patients undergoing non invasive ventilation. *Intensive Crit Care Nurs*. 2020; 58: 102859. DOI: 10.1016/j.iccn.2020.102859. PMID: 32249028.
13. *Bösmüller H., Matter M., Fend F., Tzankov A.* The pulmonary pathology of COVID-19. *Virchows Arch*. 2021; 478 (1): 137–150. DOI: 10.1007/ s00428-021-03053-1. PMID: 33604758.
14. *Ranieri V.M., Rubenfeld G.D., Thompson B.T., Ferguson N.D., Caldwell E., Fan E., Camporota L., Slutsky A.S., ARDS Definition Task Force.* Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012; 307 (23): 2526–2533. DOI: 10.1001/jama.2012.5669. PMID: 22797452.
15. *Gattinoni L., Coppola S., Cressoni M., Busana M., Rossi S., Chiumello D.* COVID-19 does not lead to a «typical» acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2020; 201 (10): 1299–1300. DOI: 10.1164/rccm.202003-0817LE. PMID: 32228035.
16. *Goligher E.C., Ranieri V.M., Slutsky A.S.* Is severe COVID-19 pneumonia a typical or atypical form of ARDS? And does it matter? *Intensive Care Med*. 2021; 47 (1): 83-85. DOI: 10.1007/s00134-020-06320-y. PMID: 33237346.
17. *Goligher E.C., Costa E.L.V., Yarnell C.J., Brochard L.J., Stewart T.E., Tomlinson G., Brower R.G., Slutsky A.S., Amato M.P.B.* Effect of lowering Vt on mortality in acute respiratory distress syndrome varies with respiratory system elastance. *Am J Respir Crit Care Med*. 2021; 203 (11): 1378–1385. DOI: 10.1164/rccm.202009-3536OC. PMID: 33439781.
18. *Chen L., Del Sorbo L., Grieco D.L., Junhasavasdikul D., Rittayamai N., Soliman I., Sklar M.C., Rauseo M., Ferguson N.D., Fan E., Richard J.C.M., Brochard L.* Potential for lung recruitment estimated by the recruitment-to-inflation ratio in acute respiratory distress syndrome. A clinical trial. *Am J Respir Crit Care Med*. 2020; 201 (2): 178–187. DOI: 10.1164/rccm.201902-0334OC. PMID: 31577153.
19. *Panwar R., Madotto F., Laffey J.G., van Haren F.M.P.* Compliance phenotypes in early acute respiratory distress syndrome before the COVID-19 pandemic. *Am J Respir Crit Care Med*. 2020; 202 (9): 1244–1252. DOI: 10.1164/rccm.202005-2046OC. PMID: 32805143.
20. *Военнов О.В., Турентинов А.В., Мокров К.В., Зубеев П.С., Абрамов С.А.* Клинические варианты гипоксии у пациентов с COVID-19. *Общая реаниматология*. 2021; 17 (2): 16–26. DOI: 10.15360/1813-9779-2021-2-16-26. [*Voennov O.V., Turentinov A.V., Mokrov K.V., Zubeev P.S., Abramov S.A.* Clinical phenotypes of hypoxia in patients with COVID-19. *General Reanimatology//Obshchaya reanimatologya*. 2021. (in Russ.). DOI: 10.15360/1813-9779-2021-2-16-26. Corpus ID: 235505057].
21. *Bos L.D.J., Paulus F., Vlaar A.P.J., Beenen L.F.M., Schultz M.J.* Subphenotyping acute respiratory distress syndrome in patients with COVID-19: consequences for ventilator management. *Ann Am Thorac Soc*. 2020; 17 (9): 1161–1163. DOI: 10.1513/AnnalsATS.202004-376RL. PMID: 32396457.
22. *Bhatraju P.K., Ghassemieh B.J., Nichols M., Kim R., Jerome K.R, Nalla A.K., Greninger A.L., Pipavath S., Wurfel M.M., Evans L., Kritek P.A., West T.E., Luks A.,*

Gerbino A., Dale C.R., Goldman J.D., O'Mahony S., Mikacenic C. Covid-19 in critically ill patients in the Seattle region - case series. *N Engl J Med*. 2020; 382 (21): 2012–2022. DOI: 10.1056/NEJMoa2004500. PMID: 32227758.

23. *Tan W., Xu D-Y., Xu M-J., Wang Z-F., Dai B., Li L.L., Zhao H-W., Wang W., Kang J.* The efficacy and tolerance of prone positioning in non-intubation patients with acute hypoxemic respiratory failure and ARDS: a meta-analysis. *Ther Adv Respir Dis*. 2021; 15: 17534666211009407. DOI: 10.1177/17534666211009407. PMID: 33888007.
24. *Alqahtani J.S., Mendes R.G., Aldhahir A., Rowley D., Al Ahmari M.D., Ntoumenopoulos G., Alghamdi S.M., Sreedharan J.K., Aldabayan Y.S., Oyelade T., Alrajeh A., Olivieri C., AlQuaimi M, Sullivan J., Almeshari M.A., Esquinas A.* Global current practices of ventilatory support management in COVID-19 patients: an international survey. *J Multidiscip Healthc*. 2020; 13: 1635–1648. DOI: 10.2147/JMDH. S279031. PMID: 33239884.
25. *Coppo A., Bellani G., Winterton D., Di Pierro M., Soria A., Faverio P., Cairo M., Mori S., Messinesi G., Contro E., Bonfanti P., Benini A., Valsecchi M.G., Antolin L., Fot G.* Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. *Lancet Respir Med*. 2020; 8 (8): 765–774. DOI: 10.1016/S2213-2600 (20)30268-X. PMID: 32569585.
26. *Yaroshetskiy, A.I., Avdeev, S.N., Politov, M.E. Nogtev P.V., Beresneva V.G., Sorokin u.D., Konanykhin V.D., Krasnoshchekova A.P., Merzhoeva Z.M., Tsareva N.A., Trushenko N.V., Mandel I.A., Yavorovskiy A.G.* Potential for the lung recruitment and the risk of lung overdistension during 21 days of mechanical ventilation in patients with COVID-19 after noninvasive ventilation failure: the COVID-VENT observational trial. *BMC Anesthesiol*. 2022; 22 (1): 59. DOI: 10.1186/s12871-022-01600-0. PMID: 35246024.

Received 20.05.2022
Online First 29.09.2022