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Clinical characteristics and outcomes of patients with COVID-19–associated acute respiratory distress syndrome

Ravshan Alievich IBADOV, Sardor Khamdamovich IBRAGIMOV, Hilola Pulatovna ALIMOVA, Bakhodir Bakhromjonovich BURKHONOV, Raufbek Ravshanovich IBADOV

State Institution "Republican Specialized Scientific and Practical Medical Center for Surgery named after academician V.Vakhidov", Uzbekistan
State Institution "Republican Specialized Infectious Diseases Hospital Zangiota No. 1" , Uzbekistan
Corresponding author's Email: dr.sardor.ibragimov@gmail.com

ABSTRACT

Aim. The aim was to analyze the results of intensive care for COVID-19 associated acute respiratory distress syndrome (ARDS) using optimized tactical aspects of respiratory support. Methods. In this prospective study, the comparison group included 436 consecutive patients admitted to the ICU of "A-block Zangiota-1" in the period from January 1, 2021 to June 30, 2021 (taking into account the representativeness of the main group), whose the therapeutic and tactical aspects of management were based on the first own experience with results analysis across organizational and therapeutic approaches. The main group included 288 patients admitted from July 1, 2021 to October 1, 2021, whose therapeutic and tactical aspects of management were developed on the basis of a fundamental revision of the differential diagnosis, pathomorphological classification and respiratory mechanics of COVID-19 associated ARDS, as well as taking into account the influence of risk factors for the severe course of the disease and various methods and technologies of respiratory support. Accordingly, adapted and optimized respiratory therapy standards have been applied in main group. Results. The frequency of intubations and transfers to mechanical ventilation had no statistical difference between the groups (p=0.362). In the main group, cases of tracheostomy (73.8%) were significantly (p<0.001) more than the comparison group (14.5%). In the comparison group, the proportion of patients with severe ARDS decreased from 29.6% to 23.8% (p=0.067), and in the main group from 31.0% to 17.0% (p<0.001). The average duration of treatment of patients in the ICU was 22 (from 7 to 32) days in the comparison group and 17 (from 9 to 27) days in the main group (p<0.05). The frequency of deaths in COVID-19 associated ARDS was 11.1% in the main group, which was significantly lower (p=0.036) than the comparison group (16.7%). Among patients on invasive mechanical ventilation (intubation and tracheostomy), the mortality rate was 96.0% in the comparison group and 76.2% in the main group of patients (p = 0.003). Conclusion. Providing respiratory support for COVID-19 associated ARDS, taking into account the individual characteristics of respiratory mechanics, can improve the results of treatment of patients with an increase in the oxygenation index, a decrease in the proportion of cases of severe ARDS, and reduce the mortality rate and the length of stay of patients in the ICU.

Original Article

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INTRODUCTION

According to the World Health Organization, "most patients with severe manifestations of COVID-19 pneumonia require respiratory support in the form of non-invasive and/or mechanical ventilation (MV), and usually meet the criteria for acute respiratory distress syndrome (ARDS)" [1, 2, 3]. In this connection, the concept of COVID-19 associated ARDS is increasingly common in the literature. Knowledge of the mechanics of breathing in COVID-19 pneumonia and the potential for involvement of unaffected areas of the lung can provide valuable information for adjusting the settings of various ventilator modes [2, 4, 5]. According to the literature, COVID-19 pneumonia is a specific disease and is characterized by severe hypoxemia, with preserved normal, significantly high or reduced compliance of the respiratory system, and/or severe dyspnea, deep hypocapnic or normo/hypercapnic syndrome [3, 6, 7].

Today, specialists in respiratory mechanics from all over the world are interested in the issues of managing the modes and parameters of ventilators in ARDS, and more and more scientific publications talk about a personalized approach to respiratory therapy in intensive care patients with COVID-19 [5, 8, 9].

Given the various associations of respiratory mechanics, severity of hypoxemia, and the possibility of lung involvement in patients with COVID-19 associated ARDS, there is a need for a more detailed study and systematic assessment of existing knowledge with the development and implementation of evidence-based protocols and recommendations for respiratory therapy of COVID-19 pneumonia [3, 7, 10].

The aim of this study was to analyze the results of respiratory therapy in COVID-19 associated ARDS.

MATERIALS AND METHODS

In the present study, the comparison group included 436 consecutive patients admitted to the intensive care unit "A-block Zangiota-1" in the period from January 1, 2021 to June 30, 2021 (taking into account the representativeness of the main group), therapeutic and tactical aspects of management were based on the first personal experience with an analysis of the results of organizational and therapeutic approaches. The main group included 288 patients admitted from July 1, 2021 to October 1, 2021, whose therapeutic and tactical aspects of management were developed on the basis of a fundamental revision of the differential diagnosis, pathomorphological classification and respiratory mechanics of COVID-19 associated ARDS, as well as taking into account the influence of risk factors for the severe course of the disease and various methods and technologies of respiratory support. Accordingly, adapted and optimized respiratory therapy standards have been applied in this group.

The distribution of patients by sex in the study groups showed that there were no intergroup differences in this indicator. Females predominated in each of the compared groups - 84.9% and 78.5% in the comparison group and the main group, respectively. In terms of age, both in the comparison group and in the main group, the largest number of patients was in the age group of 20-44 years, in the comparison group - 48.6% and in the main group - 52.4%, respectively. When distributing patients according to the severity of the condition at the time of admission, it was noted that in the comparison group, cases with severe COVID-19 pneumonia prevailed (59.8%; 261 out of 436), while in the main group, severe and extremely severe cases were diagnosed with almost equal ratio (50.7% and 49.3%). When distributing patients according to the volume of lung damage, it was noted that up to 50% of lung tissue damage was diagnosed in 35.1% (153 out of 436) of patients from the comparison group and in 29.5% (85 out of 288) from the main group; more than 50% - in 64.9% (283 out of 436) from the comparison group and in 70.5% (203 out of 288) - from the main group.

Ethical approval

The review board and ethics committee of RSPMCS named after acad. V.Vakhidov approved the study protocol and informed consents were taken from all the participants.

RESULTS AND DISCUSSION

The frequency of intubations and transfers to mechanical ventilation was 17.4% (76 out of 436) in the comparison group and 14.6% (42 out of 288) in the main group ($\chi 2=1.03$; $p=0.362$). Table 1 shows that most intubations in the main group were performed in the first 4 days from the start of respiratory support: 21.4% (9 of 42) of cases on days 1-2 and 38.1% (16 of 42) on days 3-4 day, in contrast to the comparison group, where a significant proportion of cases of tracheal intubation occurred on days 7-8 (28.9%; 22 of 76) and after 9 or more days (25.0%; 19 of 76) ($p=0.004$). It should also be noted that in the main group of patients, cases of tracheostomy (73.8%; 31 of 42 intubated) were statistically significantly ($\chi 2=38.9$; $p<0.001$) more than in the comparison group (14.5%; 11 of 76) (Table 2).

A comparative analysis of the dynamics of changes in RR on the background of non-invasive ventilation (NIV) showed that the average rate was reduced from 41 to 16 per min-1 in the main group of patients and from 38 to 20 min-1 in the comparison group ($t=2.41$; $p<0, 05$). Also, as can be seen from Figure 2, during the studied 10 days, the intergroup difference in mean RR was statistically significant.

As noted above, when constructing schemes and protocols for the use of various ventilation modes, it is necessary to focus on achieving target tidal volume (Vt) indicators, which is ensured by individually setting control pressure levels (Psupp, PEEP and Pinsp, Phigh and Plow). In this comparative study, in the main group

of patients, the mean Vt on NIV was reduced from 9.5 ml/kg to 5.1 ml/kg in the first 24 hours and subsequently was statistically significantly lower and within normal values (t=2.62 ; p<0.05), which ensured compliance with the recommendations for protective lung ventilation (Figure 3).

Changes in the PaO2/FiO2 oxygenation index against the background of NIV were indicative. Statistically significant higher rates were noted in the main group of patients already on the 1st day (176 vs. 153 mm Hg in the comparison group, t=2.34; p<0.05), and positive dynamics of PaO2/FiO2 within 10 days (Figure 4). Against the background of ongoing intensive and respiratory therapy in the comparison group, the proportion of patients with severe ARDS decreased from 29.6% (129 out of 436) to 23.8% (104 out of 436) ($\chi2$ = 3.37; p = 0.067), and in the main group from 31.0% (89 of 288) to 17.0% (49 of 288) ($\chi2$=14.99; p<0.001), with a statistically significant intergroup difference, $\chi2$=4.96; p=0.026 (Figure 5). The average duration of treatment of patients in the ICU (Table 3) was 22 (from 7 to 32) days in the comparison group and 17 (from 9 to 27) days in the main group (p<0.05). The frequency of deaths in COVID-19 associated ARDS was 11.1% (32 out of 288) in the main group, which was significantly lower ($\chi2$=4.44; p=0.036) than in the control group (16.7%; 73 out of 436). Among patients on invasive mechanical ventilation (intubation and tracheostomy), the mortality rate was 96.0% (73 out of 76) in the comparison group and 76.2% (32 out of 42) in the main group of patients ($\chi2$=8.95; p=0.003) (Figure 6).

Ejaz et al. [11] reported a high mortality rate in COVID-19 related acute respiratory distress syndrome (ARDS). The severity and the likelihood of developing ARDS and related adverse outcomes are linked with different factors including age more than 60 years, male sex, obesity, hypertension, diabetes mellitus, previous lung disease, and specific parameters such as low lymphocyte count and high D-dimer levels [12-15].

The recent studies are also reported a high proportion of patients with severe ARDS with a varied mortality with ARDS severity. For example, Zhou et al. [16] reported a high mortality rate of 97% in Wuhan during the pandemic period from December to January 2020, while the mortality rate in patients requiring intermittent mandatory ventilation was 81% [5] and among mechanically ventilated patients, a 97% mortality rate was reported by Wang et al. [17], a 42.7% was reported by King et al. [18], a lower rate of 37.5% was reported by Auld et al. [20] and a significantly lower mortality rate of 13% was reported by Søvik et al. [21]; however, only 25% of patients in the cohort had severe ARDS [21]. Grasselli et al. [12] reported a 61.27% mortality rate among patients with definite reported outcomes, while the mortality among invasively ventilated patients in the UK was reported as 56.8% [22].

In our study the mortality rate among patients on invasive mechanical ventilation (intubation and tracheostomy), was 76.2% in the main group of patients which was significantly (p = 0.003) lower than the comparison group with 96.0% mortality rate. Hence, although there are different factors affecting the results of treatment; however, providing respiratory support for COVID-19 related ARDS help to improve the results of treatment of patients with an increase in the oxygenation index, a decrease in the proportion of cases of severe ARDS, and reduce the mortality rate and the length of stay of patients in the ICU.

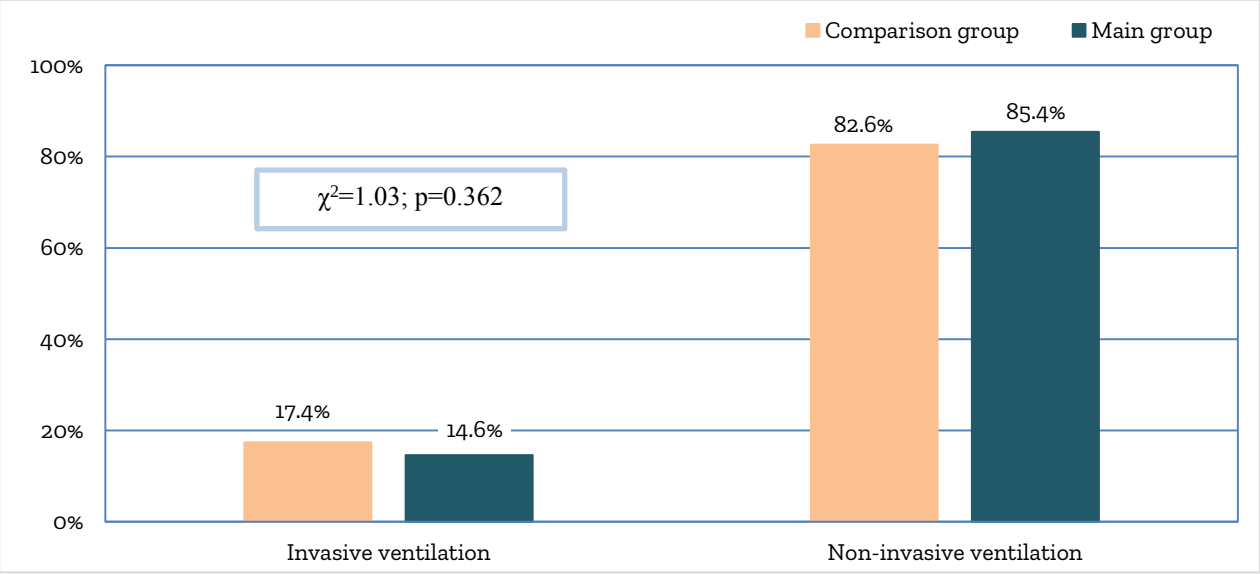

Figure 1. Respiratory therapy regimens for COVID-19 associated ARDS

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Table 1. Number of patients transferred to invasive ventilation with COVID-19 associated ARDS

Day of intubation	Comparison group		Main group		*P-value*	
	n	%	n	%		
1-2 day	6	7,9%	9	21,4%	0.035	0.004
3-4 day	18	23,7%	16	38,1%	0.098	
5-6 day	11	14,5%	8	19,0%	0.518	
7-8 day	22	28,9%	6	14,3%	0.118	
After 9 and more days	19	25,0%	3	7,2%	0.033	
Total	76	100%	42	100%	0.362	

Table 2. Frequency of tracheostomy in study groups

Day of tracheostomy	Comparison group		Main group	
	n	%	n	%
1-2 days post-intubation	0	0,0%	0	0,0%
3-4 days post-intubation	3	3,9%	13	31,0%
5-6 days post-intubation	4	5,3%	10	23,8%
7-8 days post-intubation	4	5,3%	7	16,7%
After 9 and more days post-intubation	0	0,0%	1	2,4%
Total tracheostomies	11/76	14,5%	31/42	73,8%
	χ^2=38.99; p<0.001			

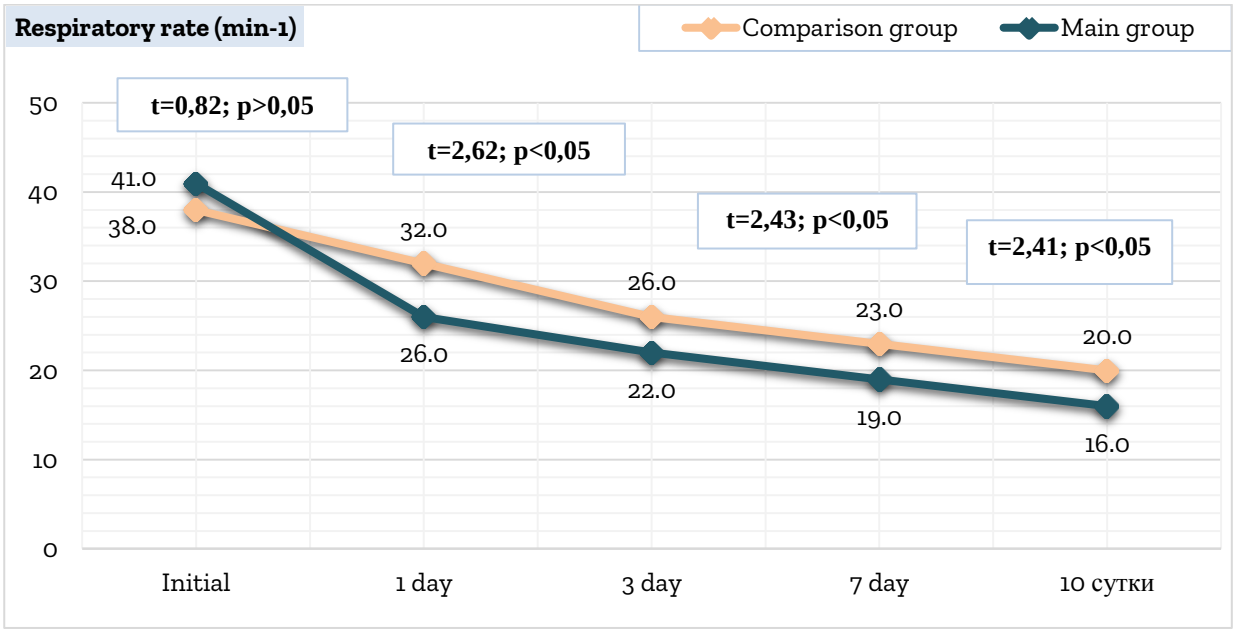

Figure. 2. Comparative dynamics of the rate of respiratory rate (min-1) against the background of NIV

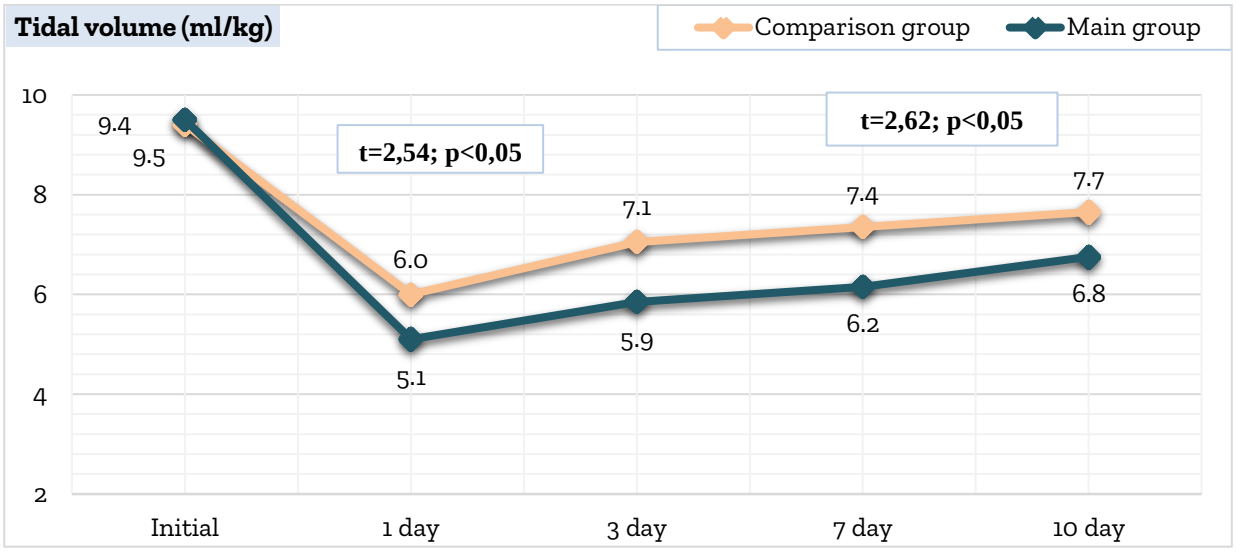

Figure 3. Comparative dynamics of Vt (ml/kg) against the background of NIV

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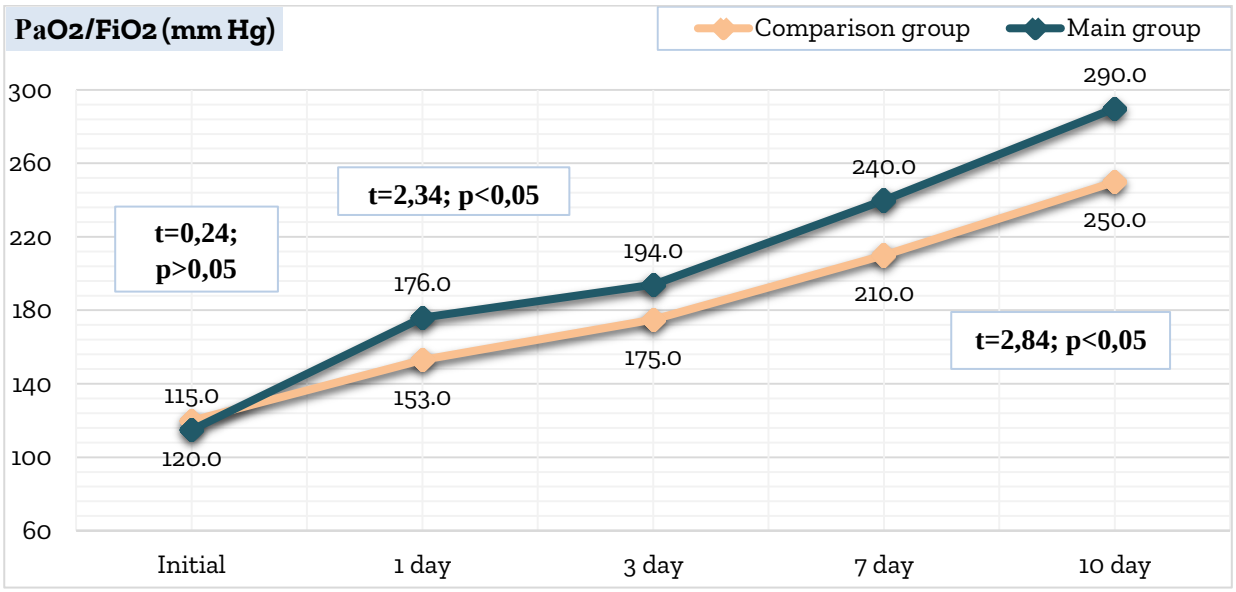

Figure 4. Comparative dynamics of the PaO_2/FiO_2 oxygenation index (mm Hg) against the background of NIV

Table 3. Average duration of treatment in the ICU (days)

Severity of ARDS	Comparison group	Main group	Statistical difference	
Moderate ARDS	16 (12-24)	12 (9-19)	t=3,29	p<0,05
Severe ARDS	24 (18-32)	20 (14-27)	t=2,33	p<0,05
Average	22 (7-32)	17 (9-27)	t=3,14	p<0,05

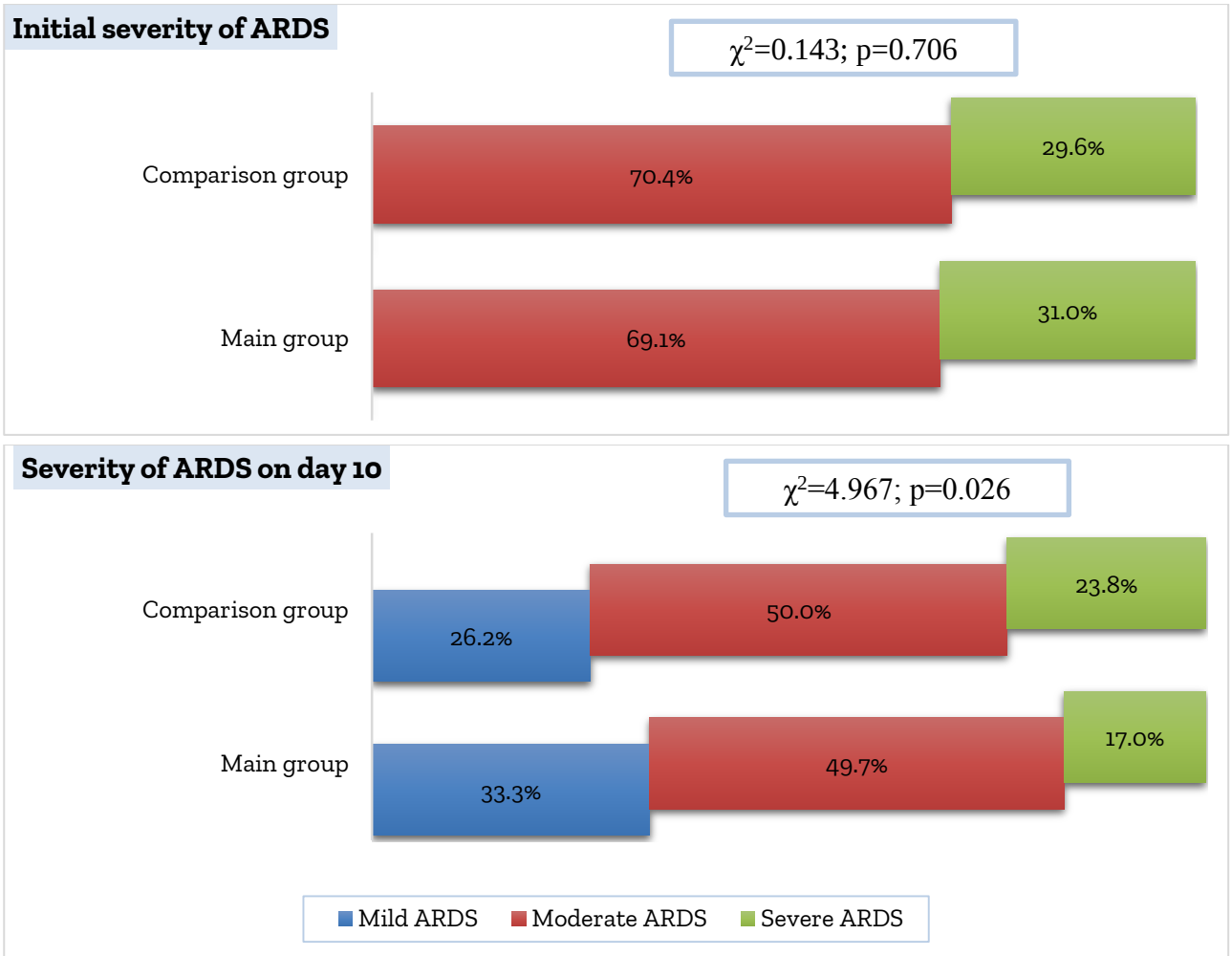

Figure 5. Dynamics of the distribution of cases of COVID-19 associated ARDS by severity against the background of the respiratory therapy tactics undertaken

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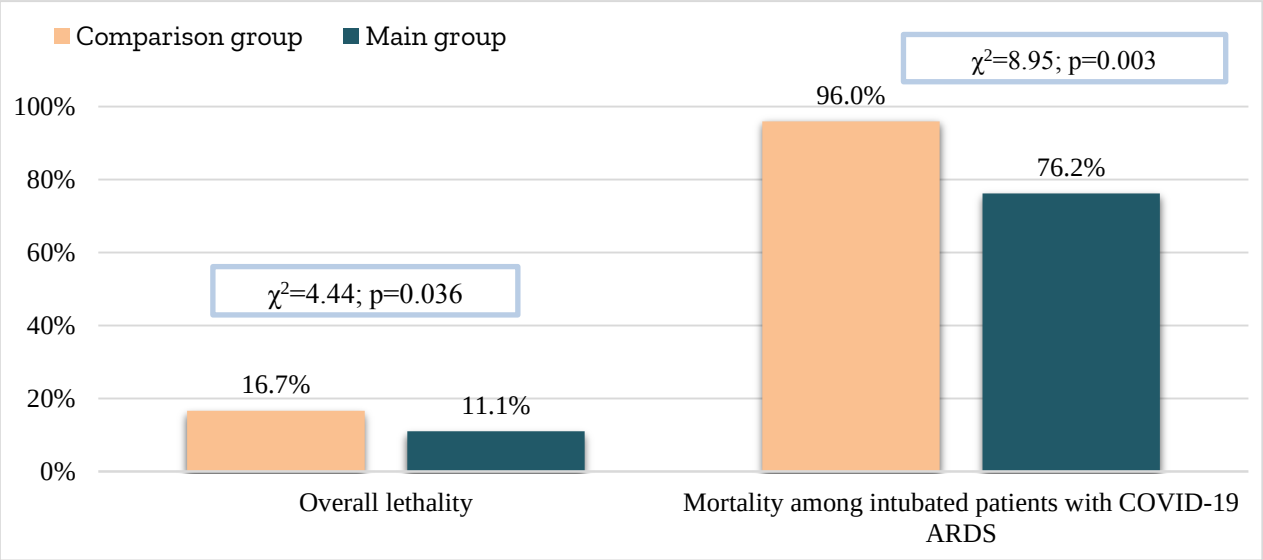

Figure 6. Mortality rates in COVID-19 associated ARDS

CONCLUSION

The proposed schemes and algorithms of respiratory support for COVID-19 associated ARDS, based on the features of the histopathological pattern of lung damage and respiratory mechanics identified during the studies, can improve the results of treatment of patients with COVID-19 associated ARDS with an increase in the oxygenation index, a decrease in the proportion of cases of severe ARDS, to reduce the mortality rate and the length of stay of patients in the ICU. When constructing schemes and protocols for the use of various ventilation modes, it is necessary to focus on achieving the target indicators of Vt, which is ensured by individually setting control pressure levels (Psupp, PEEP and Pinsp, Phigh and Plow).

DECLARATIONS

Acknowledgements

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Authors' contribution

All authors contributed equally to this work.

Competing interests

The authors declare that they have no competing interests.

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