

Providing Care for Developing Respiratory Failure During Mass Admission of Patients with COVID-19

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Summary

The COVID-19 pandemic has posed an unprecedented challenge to healthcare systems around the world. The mass influx of patients with severe hypoxemic respiratory failure, often progressing to acute respiratory distress syndrome (ARDS), has led to an acute shortage of beds in intensive care units (ICUs).

The aim of the study was to evaluate the effectiveness of an organizational model for the care of patients with severe COVID-19 pneumonia, including the creation of intensive observation wards (IOWs) for non-invasive respiratory support outside the ICU, and to develop a prognostic model for the risk of transferring patients to invasive mechanical ventilation (IMV) or non-invasive mechanical ventilation (NIMV).

Materials and methods. A retrospective observational study was conducted at the V. P. Demikhov city clinical hospital of the Voronovskoye Moscow clinical center for infectious diseases from January to December 2021. We analyzed data from 950 patients with confirmed COVID-19 and hypoxemic respiratory failure who started high-flow oxygen therapy (HFOT) in the IOW. The demographic structure, premorbid background, clinical and laboratory parameters, and respiratory and anti-inflammatory therapy regimens (glucocorticoids — GCS: dexamethasone or methylprednisolone, and/or monoclonal antibodies — MAbs) were studied. For 573 patients transferred from the IOW to the ICU, we assessed outcomes and risk factors for the need for NIMV/IMV using binary logistic regression.

Results. Of the 950 patients who started HFOT in the IOW, 573 (60.3%) were transferred to the ICU for escalation of respiratory support. The mortality rate in the ICU group was 25.7% (147 of 573 patients hospitalized in the ICU). When comparing GCS regimens with or without MAbs, the mortality rate in patients receiving methylprednisolone in any treatment regimen was lower than in patients receiving dexamethasone: 14.1% vs. 25.8% (with MAbs, $P < 0.001$) and 15.3% vs. 37.4% (GCS only, $P < 0.001$). According to the logistic regression model, predictors of increased risk for the need for NIMV/IMV were: older age (OR > 1.014 for each year [1.024; 1.058], presence of diabetes mellitus (OR > 1.530 [1.038; 2.2123]), and a higher NEWS score upon transfer to the ICU (OR > 1.342 for each score [1.153; 1.562]). The use of methylprednisolone compared to dexamethasone was associated with a reduced risk of requiring NIMV/IMV (OR = 0.346 [0.238; 0.503]).

Conclusion. The organization of IOW for the implementation of HFOT according to a strict protocol made it possible to provide assistance to a large number of patients in conditions of ICU resource shortages. The use of methylprednisolone was associated with lower mortality in the ICU compared to dexamethasone. The developed prognostic model may be useful for stratifying the risks of escalating respiratory support methods and making timely decisions to transfer patients to non-invasive/invasive mechanical ventilation.

Keywords: acute respiratory failure; COVID-19; high-flow oxygen therapy; glucocorticoids; methylprednisolone; dexamethasone; prognostic model of risks of escalation of respiratory support; intensive care wards.

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

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Introduction

Humanity is constantly faced with epidemics and pandemics that claim thousands of lives. The effectiveness of medical and health care advances that made it possible to «tame» 19th century pathogens such as cholera led epidemiologists, medical historians, and other experts to believe that developed countries had managed to eradicate infectious diseases once and for all in the 20th and 21st centuries. As virologist Sir Frank Macfarlane (Mac) Burnet stated in 1951, «the eradication of infectious diseases has become a significant factor in the social structure». «To write about infectious diseases», he added in 1962, «is to stir up the long forgotten».

The COVID-19 pandemic caused by the SARS-CoV-2 virus has radically changed the landscape of modern medicine, posing unprecedented challenges for healthcare systems around the world [1, 2]. One of the most serious problems has been the massive influx of patients with severe lung damage, rapidly developing hypoxemic respiratory failure, and acute respiratory distress syndrome (ARDS) [3, 4].

Medical facilities around the world have faced enormous pressure on resources, especially in intensive care units (ICUs). A critical shortage of resuscitation beds, ventilators, and qualified personnel has necessitated an urgent reorganization of medical care and a search for new approaches to the management of patients with severe respiratory failure [5–7].

In response to these challenges, many hospitals adopted a strategy of creating intermediate levels of care — so-called intensive observation wards (IOWs) or respiratory support units — based in infectious disease or therapeutic departments. The main task of such units was to provide care to patients receiving ongoing pathogenetic therapy and standard low-flow oxygen therapy (LFOT) for respiratory disorders that do not meet the criteria for immediate transfer to mechanical ventilation but require escalation of respiratory support methods and closer monitoring of vital signs. The key method of respiratory support in IOW was high-flow nasal oxygen therapy (HFOT), which allows the delivery of heated and humidified oxygen-air flow at high speed and with a controlled oxygen fraction (FiO₂) [8, 9].

The effectiveness of this organizational model largely depended on a clear respiratory support protocol regulating both the indications for starting HFOT and the criteria for its effectiveness and the need for timely escalation of therapy — transferring the patient to the ICU for noninvasive mechanical ventilation (NIMV), invasive mechanical ventilation (IMV), or, in refractory cases, extracorporeal membrane oxygenation (ECMO) [10, 11].

Alongside respiratory support, the cornerstone of treatment for severe COVID-19 has been the suppression of the hyperinflammatory response (cytokine storm), which plays a key role in the devel-

opment of ARDS and multiple organ failure. The main method of pathogenetic therapy was the administration of glucocorticoids (GCs), the effectiveness of which has been demonstrated in large international studies such as RECOVERY [12]. However, the optimal regimens, dosages, and choice of specific GCs drug (e. g., dexamethasone or methylprednisolone) remained a subject of debate and required study in real-world clinical practice [12, 13]. According to the temporary methodological recommendations and local protocols in force, various GCs regimens were used, including the use of dexamethasone or methylprednisolone [14–17]. In addition, interleukin inhibitors (monoclonal antibodies — MAb) were used in some patients with signs of severe systemic inflammation [18–21].

In the context of mass admissions and limited ICU resources, assessing the effectiveness of the approaches used and early identification of patients at high risk of adverse outcomes or in need of escalated respiratory support became paramount. The development of prognostic models based on available clinical and laboratory data helps in risk stratification and optimization of patient routing [22–26].

The aim of the study is to evaluate the effectiveness of an organizational model for the care of patients with severe COVID-19 pneumonia, including the creation of (IOWs) for non-invasive respiratory support outside the ICU, and to develop a prognostic model for the risk of transferring patients to invasive mechanical ventilation (IMV) or non-invasive mechanical ventilation (NIMV).

Materials and Methods

A retrospective observational cohort study was conducted at the V. P. Demikhov city clinical hospital of the Voronovskoye Moscow clinical center for infectious diseases. The electronic medical records of patients admitted for treatment from January 1 to December 31, 2021, were analyzed.

Patients. During the specified period, 17,761 patients diagnosed with COVID-19 were hospitalized. 15,521 patients were sent to infectious disease wards, and 2,240 were sent directly to the intensive care unit (ICU), bypassing the emergency room. Of the total number of patients hospitalized in infectious disease wards, 3,053 (19.7%) were transferred to the ICU at various stages of treatment due to negative dynamics in their condition for various reasons.

Of the 15,521 patients, 950 (6.1%) were transferred to the IOWs of infectious disease departments for high-flow oxygen therapy (HFOT). As respiratory failure progressed, patients were transferred to the ICU for non-invasive mechanical ventilation (NIMV), invasive ventilation (IMV), or extracorporeal membrane oxygenation (ECMO).

The criteria for inclusion of patients in the study were: laboratory-confirmed diagnosis of

COVID-19; stay in the IOW/transfer to the ICU; age over 18 years; specific lung damage according to computed tomography (CT) data; presence of symptoms of hypoxemic respiratory failure requiring respiratory support with low-flow oxygen therapy (LFOT) or HFOT/NIMV.

Exclusion criteria: admission to the ICU by-passing the infectious diseases department; pregnancy of various stages; mental illnesses of various etiologies; transfer to the ICU for reasons not related to progressive lung tissue damage; acute surgical diseases.

The patient selection scheme for the study is presented in Fig. 1.

Therapy. Patient examination, diagnosis of the underlying disease, its complications, concomitant diseases, and assessment of the severity of the patients' condition were carried out in accordance with the Temporary methodological recommendations (TMR) «Prevention, diagnosis, and treatment of the novel Coronavirus Infection (COVID-19)» versions 8 to 9, relevant at the time of the study.

Respiratory support was provided using a standard Bobrov system for oxygen therapy with a flow rate of 1–15 L/min (LFOT). High-flow oxygen therapy (HFOT) was used in patients with acute hypoxemic respiratory failure to deliver a humidified and warmed breathing mixture at a flow rate of 15–50 L/min and an oxygen fraction in the breathing mixture of 30 to 60% (AIRVO™ 2 Humidification System, New Zealand). Prone positioning (patient breathing in the prone position) was used for up to 16 hours per day as a second standard position. The third mandatory component was incentive spirometry using a Portex (Smiths Medical) Coach 2 exercise spirometer with a one-way valve and a volume of 4,000 ml, which was performed every 2 hours according to the standard method recommended by the manufacturer.

High-flow oxygen therapy was performed with the following parameters: oxygen flow in the air mixture 15–50 L/min, oxygen fraction in the respiratory mixture 40–60%. To assess the effectiveness of the therapy, the patient's clinical status (complaints, shortness of breath during exercise, respiratory rate) was monitored every 2 hours; SpO₂ while breathing atmospheric air — once a day; the goal of oxygen therapy was SpO₂ 90–96%. The indication for transfer to the intensive care unit was the presence of one of the following criteria: SpO₂ during oxygen therapy < 92%, RR > 26 per minute, with maximum HFOT parameters of more than 50 L/min and FiO₂ > 60%, impaired consciousness (depression, agitation), hypotension (decrease in systolic blood pressure below 90 mm Hg).

Anti-inflammatory therapy was carried out with glucocorticoids alone or in combination with monoclonal antibodies. The first-line drugs for anti-inflammatory therapy in hospitalized patients with

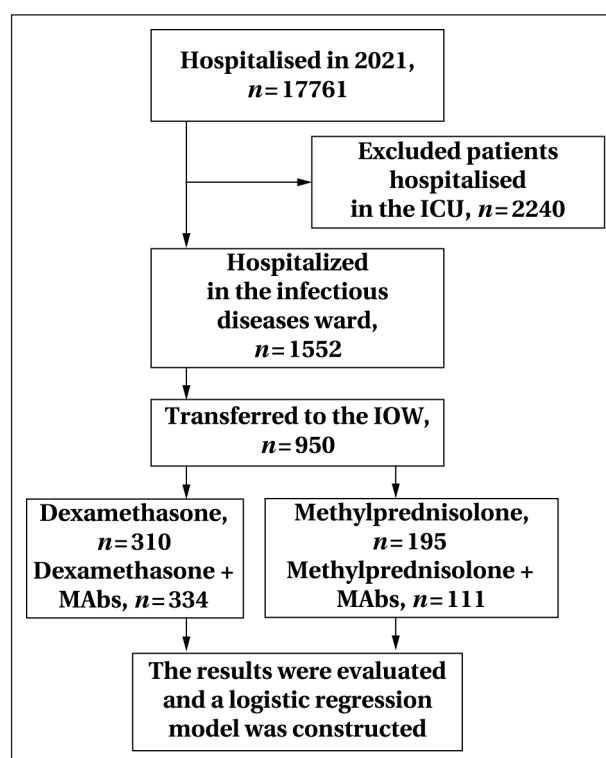


Fig. 1. Scheme of patient selection for analysis and construction of a logistic regression model.

COVID-19 were glucocorticoids (GCs). The indication for the prescription of glucocorticoid hormones outside intensive care units was the development of signs of severe systemic inflammation and/or the progression of macrophage activation syndrome (increase in ferritin, serum C-reactive protein, development of dual/triple cell-line cytopenia). In such cases, one of the glucocorticoid drugs was used in the infectious diseases department:

— methylprednisolone (at a dose of 2 mg/kg/day intravenously, 1 mg/kg over an hour, then 1 mg/kg as a prolonged 24-hour infusion);

or

— dexamethasone (20 mg per day intravenously in two doses for at least 3 days, followed by a gradual dose reduction by 20–25% per dose every 1–2 days for 3–4 days, then by 50% every 1–2 days until complete withdrawal).

The indications for the use of monoclonal antibodies (tocilizumab, olucizumab) were: the presence of pathological changes in the lungs corresponding to CT 1–4 or moderate/severe pneumonia according to X-ray examination (infiltration-type diffuse opacities («white lung» symptom), involvement of ≥ 50% of lung tissue) combined with two or more of the following signs:

— SpO₂ ≤ 93%, shortness of breath at rest;

— body temperature > 38°C for 5 days or recurrence of fever on the 5–10th day of illness after a «clear interval»;

- CRP ≥ 9 N or a 3-fold increase in CRP on the 8th–14th day of illness;
- white blood cell count $< 3.0 \times 10^9/L$;
- absolute lymphocyte count $< 1.0 \times 10^9/L$;
- blood ferritin ≥ 250 ng/mL;
- IL-6 > 40 pg/mL.

Tocilizumab was administered at a dose of 4–8 mg/kg intravenously in combination with glucocorticoids (GCs).

If tocilizumab could not be used, an alternative regimen was considered that included the IL-6 receptor inhibitor levilimab 324 mg once (the contents of two pre-filled syringes of 162 mg/0.9 ml were diluted in 100 ml of 0.9% NaCl solution and administered intravenously by drip over 60 min). If the effect was insufficient, the administration was repeated after 12 hours [14, 20].

Statistical data processing was performed using the IBM SPSS Statistics v.27.0 software package. Quantitative data were presented as the arithmetic mean \pm standard deviation ($M \pm SD$) for normally distributed data, and as the median and interquartile range ($Me [Q1; Q3]$) for data with a distribution other than normal. Qualitative data were presented as absolute numbers and percentages ($n, \%$). The normality of the distribution of the studied parameters was assessed using the Shapiro–Wilk test. Quantitative indicators between groups were compared using the Student's t -test or the Mann–Whitney U test, depending on the normality of the distribution of each parameter. Quantitative indicators were equalized using Pearson's χ^2 test or Fisher's exact test. Differences were considered statistically significant at $P < 0.05$. A two-tailed significance level was used.

The binary logistic regression method was used to determine the probability of NIMV/IMV use in patients and the prognosis of fatal outcome. This method calculates the probability of an event occurring depending on the values of independent variables.

Data from 950 patients were used to perform regression analysis.

The parameters taken as probable predictors of the use of NIMV or IMV were: gender (female — 0; male — 1), age (years), obesity (0 — no; 1 — yes), diabetes mellitus (0 — no; 1 — yes), concomitant cardiovascular diseases (0 — no; 1 — yes), NEWS scale score (scores), length of stay on HFOT (number of days), therapy (Dexamethasone — 0; Methylprednisolone — 1).

To construct the regression functions that make up the prognostic model, we used a multivariate analysis based on binary logistic regression with an adjusted OR estimate (taking into account the joint influence of predictors, corr. OR) and its 95% confidence interval. The predictors were introduced into the model stepwise backward (using Wald statistics), which made it possible to select informative predictors and exclude noisy ones.

To assess the quality of the logistic regression model, we used the Hosmer–Lemeshow test and calculated the percentage of total explained variance using the Nagelkerke method. Binary classification was evaluated based on ROC analysis.

The cutoff point for binarization was determined using the Judd criterion.

Descriptive statistics and hypothesis testing methods were used to analyze the data. Mortality was calculated as the percentage of deceased patients relative to the total number of patients in each group. The chi-square (χ^2) test was used to compare mortality between groups, which allowed to assess whether the observed difference in frequencies was statistically significant.

Results

Patient characteristics. In 2021, HFOT was initiated in 950 patients with COVID-19 pneumonia and hypoxemic respiratory failure in the IOW. The characteristics of this cohort are presented in Table 1.

Table 1. Characteristics of patients hospitalized in the IOW, $N = 950$.

Indicators	Indicator values
Gender	
Male	427 (44.9%)
Female	523 (55.1%)
Age, years	63.4 ± 10.8
Premorbid background	
Obesity	302 (31.8%)
Diabetes mellitus	237 (24.9%)
Cardiovascular diseases	731 (76.9%)
Duration of disease, days	6.02 ± 1.6
Degree of lung tissue damage according to chest computed tomography	
CT1 (less than 25%)	457 (48.1%)
CT 2 (25–50%)	393 (41.4%)
CT 3 (50–75%)	96 (10.1%)
CT 4 (> 75%)	4 (0.4%)

Patients mean age was 63.4 years, with a predominance of women (55.1%). The vast majority (76.9%) had concomitant cardiovascular diseases (CVD). Obesity and diabetes mellitus were found in 31.8% and 24.9% of patients, respectively. HFOT was initiated on average on the 6th day of illness. In most patients, the degree of lung damage on CT corresponded to CT 1–2 (89.5%) at baseline.

Transfer to the ICU and outcomes. Despite the therapy provided in the IOW, 573 patients (60.3% of those receiving HFOT in IOW) were transferred to the ICU for escalation of respiratory support using HFOT with a flow rate > 50 L/min, an inspiratory oxygen fraction $> 60\%$, and NIMV/IMV. The characteristics of patients transferred to the ICU are presented in Table 2.

Among patients transferred to the ICU, women were older than men (68.1 vs. 62.2 years), and they were more likely to have obesity (42.1% vs. 30.9%) and CVD (86.8% vs. 81.4%).

Table 2. Characteristics of patients transferred from the IOW to the ICU.

Parameter	Men, N= 269	Women, N= 304	Total, N= 573
Age, years ($M \pm SD$)	62,17 \pm 10,94	68,1 \pm 10,94	65,3 \pm 11,3
Premorbid background			
Obesity, n (%)	83 (30,9)	128 (42,1)	211 (36,8)
DM, n (%)	76 (28,3)	100 (32,9)	176 (30,7)
CVD, n (%)	219 (81,4)	264 (86,8)	483 (84,3)
Duration of illness before transfer to the ICU, days ($M \pm SD$)	6,12 \pm 1,76	5,97 \pm 1,74	6,04 \pm 1,75
Need for NIMV/IMV, n (%)	108 (40,1)	131 (43,1)	239 (41,7)
(NIMV/IMV)	(37/71)	(43/88)	(80/159)
Mortality in the ICU, n (%)	64 (23,8)	83 (27,3)	147 (25,7)

Table 3. Mortality among ICU patients depending on the anti-inflammatory therapy regimen used.

Treatment regimens	Number of patients, n (%)		
	By treatment regimen	Transferred to ICU	With fatal outcome in the ICU
¹ Dexamethasone only	310	175 (56.5)	65 (37.1)
² Methylprednisolone only	195	118 (60.5)	18 (15.3)
$p_{1,2}$		0.368	< 0.001*
³ Dexamethasone + MAb	334	209 (62.6)	54 (25.8)
⁴ Methylprednisolone + MAb	111	71 (63.9)	10 (14.1)
$p_{3,4}$		0.793	< 0.001*

Note. MAb — monoclonal antibodies. p — level of statistical significance calculated using the χ^2 criterion. * — values of $P < 0.001$ indicate a statistically significant reduction in mortality with methylprednisolone therapy, both as monotherapy and in combination with MAbs, compared with similar use of dexamethasone.

Table 4. Prediction of the need for NIMV/IMV in the ICU based on the results of binary logistic regression ($n=573$).

Predictor	Coeff.	Standard error	Wald stat.	p	Exp (B) (corr. OS)	95% CI for OS, boundaries	
						lower	upper
Age	0.040	0.008	22.505	< 0.001	1.041	1.024	1.058
Gender	0.387	0.187	4.304	0.038	1.473	1.022	2.123
Diabetes mellitus	0.426	0.198	4.607	0.032	1.530	1.038	2.257
CVD	0.758	0.336	5.092	0.024	2.134	1.105	4.124
NEWS scale	0.294	0.077	14.422	< 0.001	1.342	1.153	1.562
GCs therapy	-1.061	0.191	31.006	< 0.001	0.346	0.238	0.503
HFOT	0.101	0.016	37.728	< 0.001	1.106	1.024	1.142
Constant	-6.770	0.762	78.927	< 0.001	0.001	—	—

The overall mortality rate in the ICU was 25.7%, with no statistically significant differences between men (23.8%) and women (27.3%).

Use of anti-inflammatory therapy and outcomes in the ICU. All patients in the ICU were prescribed GCs. In 444 (77.5% of those transferred to the ICU, or 46.7% of those receiving HFOT in IOW), MAbs were additionally used in treatment.

Rate of fatal outcomes, depending on the anti-inflammatory treatment regimen used: GCs monotherapy or in combination with MAbs is presented in Table 3.

It was found that when using methylprednisolone (both as monotherapy and in combination with MAbs), mortality among patients transferred to the ICU was statistically significantly lower than when using dexamethasone (15.3% vs. 37.1% for GCs monotherapy, $P=0.0001$; 14.1% vs. 25.8% for GCs+MAb combination, $p=0.046$). The addition of MAb to dexamethasone statistically significantly reduced mortality (37.1% to 25.8%, $p=0.0117$), while with methylprednisolone, the addition of MAb did not result in a statistically significant change in mortality (15.3% vs. 14.1%, $p=0.823$) in this cohort of ICU patients.

Predictive model of the need for NIMV/IMV.

To identify factors associated with the need for NIMV or IMV in patients transferred to the ICU ($n=573$), a binary logistic regression model was constructed. After stepwise selection using backward elimination, the following predictors were included in the final model: age, presence of diabetes mellitus, NEWS score upon transfer to the ICU, and type of GC used (methylprednisolone vs. dexamethasone). The results are presented in Table 4.

The model showed good predictive power. The Hosmer–Lemeshow test was insignificant ($\chi^2=0.309$, $df=8$, $P>0.05$), indicating good model calibration and a fairly accurate description of the actual data. Nagelkerke's pseudo- R^2 was 0.255, meaning that the model explains 25.5% of the variance in the dependent variable. The area under the ROC curve (AUC) was 0.792 (95% CI: 0.758–0.827; $P<0.001$), indicating high discriminatory power of the model (Fig. 2). The optimal cutoff point, determined by the Youden index, was 0.197, which corresponds to a sensitivity of 75.7% (95% CI: 68.8–81.7%) and a specificity of 70.7% (95% CI: 67.3%–73.9%) for predicting the need for NIMV/IMV.

The regression equation is as follows:
 $Z = 0.040 \times \text{Age} + 0.387 \times \text{Gender} + 0.426 \times$
 $\text{Diabetes mellitus} + 0.758 \times \text{CVD} + 0.294 \times$
 $\text{NEWS scale} - 1.061 \times \text{Therapy} + 0.101 \times$
 $\text{HFOT} - 6.770$

According to the model, the predictors of an increased risk of requiring NIMV/IMV were: older age (OR > 1.014 for each year [1.024; 1.058], gender, presence of diabetes mellitus (OR > 1.530 [1.038; 2.2123]), and a higher NEWS score upon transfer to the ICU (OR > 1.342 for each score [1.153; 1.562]). The use of methylprednisolone (compared to dexamethasone) was associated with a reduced risk of requiring NIMV/IMV (OR = 0.346 [0.238; 0.503]). Gender, obesity, CVD, and duration of ICU stay had a lower weight as independent predictors in the final model.

Discussion

We presented our experience in organizing medical care for patients with severe COVID-19 in the context of significant healthcare system overload in 2021. Faced with a shortage of intensive care beds, our hospital implemented a model of stepwise respiratory support, including the active use of HFOT in specially organized IOW outside the ICU.

The data obtained indicate that this strategy made it possible to provide care to a large number of patients (950 people started HFOT in the IOWs), but a significant proportion of them (60.3%) needed to be transferred to the ICU for escalation of respiratory therapy. The high frequency of transfers reflected the severity of COVID-19-associated respiratory failure during the pandemic waves studied and highlights the importance of clear criteria for timely escalation of treatment. However, it can be assumed that without the HFOT stage in the IOW, the burden on the ICU would have been even higher, and some of the patients successfully treated in the IOW (about 40%) could have occupied ICU beds.

The overall mortality rate among patients transferred to the ICU was 25.7%, which is comparable to data from other studies of that period for patients with severe COVID-19 requiring intensive care [15, 16]. Demographic characteristics and the presence of comorbidities (high incidence of CVD, diabetes mellitus, obesity) also correspond to global data on risk factors for severe COVID-19 [17].

One of the key aspects of our study was to evaluate the impact of different GCs regimens on outcomes in the ICU. The results indicate a statistically significant lower mortality rate in patients receiving methylprednisolone at a dose of 1 mg/kg/day (as a bolus and prolonged infusion) compared to patients receiving dexamethasone 20 mg/day. This difference persisted both with GCs monotherapy and in combination with MABs. Moreover, the use of methylprednisolone was associated with a reduced risk of

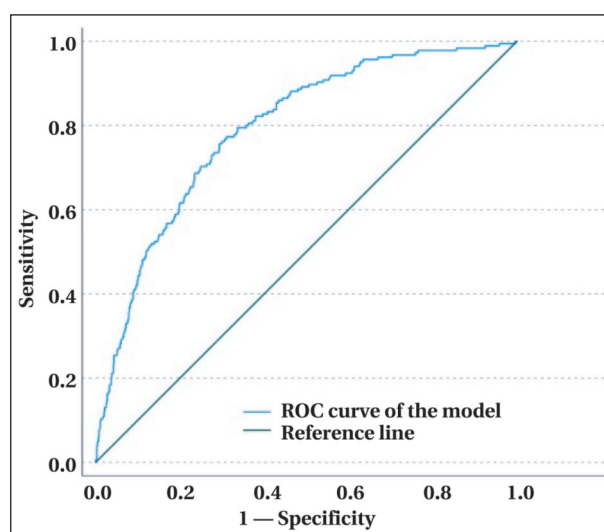


Fig. 2. ROC curve for the predictive model of the need for NIMV/IMV.

requiring NIMV/IMV according to logistic regression data. These results are consistent with data from several other studies suggesting potential advantages of methylprednisolone over dexamethasone in severe COVID-19 ARDS, possibly due to a more pronounced anti-inflammatory effect or better penetration into lung tissue [10, 11, 18]. However, it is important to note the retrospective nature of the analysis, which does not allow us to exclude the influence of unaccounted factors and bias in the choice of therapy. Nevertheless, the data obtained support the hypothesis of the potential advantages of the methylprednisolone regimen used and require further confirmation in prospective studies.

Interestingly, the addition of MABs to GCs was associated with a reduction in mortality only in the dexamethasone group, but not in the methylprednisolone group. This may indicate that when using a more intensive GCs regimen (methylprednisolone 1 mg/kg/day), the additional effect of IL-6 inhibition may be less pronounced or may only be evident in a specific subgroup of patients. This observation also requires further study.

The developed prognostic model for the need for NIMV/IMV in the ICU demonstrated good predictive ability (AUC > 0.792). The identified predictors — age, presence of diabetes mellitus, and severity of condition on the NEWS scale at transfer — are known risk factors for unfavorable COVID-19 outcomes [13, 17]. The inclusion of GCs entity (methylprednisolone as a protective factor) in the model further emphasizes the potential impact of the choice of anti-inflammatory therapy on the course of the disease. This model can be used in clinical practice for the early identification of patients at high risk of requiring invasive respiratory support, allowing for the timely concentration of resources and decisions on treatment intensifi-

Conclusion

cation. However, before widespread implementation, the model requires external validation on other patient cohorts.

Strengths and limitations of the study. The strengths of the study include the analysis of data over a long period (one year) covering various waves of the pandemic, the description of a specific organizational model and treatment protocols, as well as a direct comparison of outcomes for different GCs regimens and the development of a prognostic model. The main limitations are the retrospective design, the possible presence of unaccounted confounding factors, the potential incompleteness of data in electronic records, and the focus of outcome analysis primarily on patients transferred to the ICU (lack of detailed comparison with those who remained in the IOW). Also, the data on the number of patients in various analyses ($n=950$, $N=573$, $N=644+306$) require clear interpretation and coordination.

The organization of IOW for high-flow oxygen therapy is a feasible strategy for managing patients with COVID-19-associated hypoxemic respiratory failure in conditions of a shortage of resuscitation beds, although a significant proportion (about 60%) of patients require escalation of respiratory therapy in the ICU.

The use of methylprednisolone at a dose of 1 mg/kg/day (bolus + prolonged infusion) in patients with severe COVID-19 transferred to the ICU was associated with lower mortality and a lower risk of requiring NIMV/IMV compared with the use of dexamethasone 20 mg/day in the study cohort.

The developed logistic regression model, which includes age, presence of diabetes mellitus, NEWS score, and type of GCS used, has good predictive ability for identifying patients in the ICU at high risk of requiring NIMV/IMV, and may be useful for clinical application after external validation.

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