

Hemoadsorption in Patients with Various Types of Respiratory Support for Severe COVID-19

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Гемосорбция у пациентов с различными видами респираторной поддержки при тяжелом течении COVID-19

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Summary

Study aim. To evaluate the efficacy of hemoadsorption in patients with severe COVID-19 on mechanical lung ventilation (MLV) and noninvasive respiratory support.

Material and methods. We retrospectively analysed longitudinal clinical and laboratory parameters of 49 patients with severe coronavirus infection who were treated in the First Intensive care unit of Grodno University Hospital from September 2020 to November 2021 and underwent hemoadsorption using the Hemo-Proteasorb sorbent. All patients were divided into two groups: Hemo-Proteasorb + MLV (22 patients who underwent hemoadsorption while being on MLV) and Hemo-Proteasorb without MLV (27 patients who had hemoadsorption while receiving the low- and high-flow oxygen therapy or noninvasive lung ventilation).

Results. In the Hemo-Proteasorb + MLV group a decrease in procalcitonin (PCT) (from 0.27 [0.12–2.08] down to 0.14 [0.05–1.77], $P=0.027$), C-reactive protein (CRP) (from 135.4 [10.6–303.0] down to 64.3 [1.2–147.0], $P=0.003$), fibrinogen (from 11.7 [4.9–19.49] to 8.2 [3.7–14.7], $P=0.00004$), and D-dimer (from 1432.0 [443.0–6390.0] to 1087.0 [415.0–3247.0], $P=0.006$) was seen on day 3 after the hemoadsorption session. The Hemo-Proteasorb without MLV group also demonstrated a reduction in the levels of CRP (from 4 [10.6–303.0] to 64.3 [1.2–147.0], $P=0.003$), fibrinogen (from 11.7 [4.9–19.49] to 8.2 [3.7–14.7], $P=0.00004$), D-dimer (from 1432.0 [443.0–6390.0] to 1087.0 [415.0–3247.0], $P=0.006$) on day 3 after the hemoadsorption session. The Hemo-Proteasorb without MLV group also showed a decrease in PCT (from 0.29 [0.14–21.25] to 0.14 [0.04–11.91], $P=0.002$), CRP (from 132.6 [30.7–183.0] to 28.55 [5.3–182.0], $P=0.0002$), fibrinogen (from 10.2 [4.41–15.5] to 6.5 [2.8–11.9], $P=0.00005$), D-dimer (from 1445.0 [365.0–4830.0] to 1049.0 [301.0–3302.0], $P=0.005$), while an increase in SpO_2/FiO_2 (from 238 [88–461] up to 320 [98–471], $P=0.011$) was registered. On days 5–7, positive changes in SpO_2/FiO_2 index (238 [88–461] vs 320 [98–471], $P=0.0020$) were observed in the Hemo-Proteasorb without MLV group, as well as a trend toward further reduction in the levels of CRP (132.6 [30.7–183.0] vs 23.85 [2.2–200.0], $P=0.0001$) and fibrinogen (10.2 [4.41–15.5] to 5.11 [2.3–11.5], $P=0.0017$). The patients were assessed using the NEWS2 score at all the stages of the study. On days 2–3 of the study, a reduction in the mean NEWS2 score was noted in the Hemo-Proteasorb + MLV group (8.0 [4.0–11.0] vs 6.0 [2.0–10.0], $P=0.0002$), whereas on days 5–7 its increase was seen vs stage 2 of the study with its values still lower than those prior to hemoadsorption (8.0 [4.0–11.0] vs 7.0 [2.0–9.0], $P=0.011$). On day 3 of treatment, in the Hemo-Proteasorb without MLV group we observed a decreased mean NEWS2 score (7.0 [3.0–9.0] vs 5.0 [1.0–9.0], $P=0.00002$), on days 5–7, this trend was still present (7.0 [3.0–9.0] vs 3.0 [1.0–8.0], $P=0.00002$).

Conclusion. Hemoadsorption was beneficial for patients with severe COVID-19 during both oxygen therapy and mechanical ventilation due to decreased levels of inflammatory markers, hypercoagulation, and reduced NEWS2 scores.

Keywords: *Sars-CoV-2; COVID-19; cytokine storm; hemoadsorption; Hemo-Proteasorb; mechanical lung ventilation; ventilatory support; noninvasive respiratory support*

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Introduction

The COVID-19, which emerged in December 2019, was a real challenge for researchers and physicians around the world, despite enormous efforts to control the infection was proclaimed pandemic in April 2020 and still was a serious public health threat as of September 2021. The severity of the pandemic is due to the high mortality rate in severe cases. Since patients with severe disease are treated in an intensive care unit and usually have complications such as massive lung injury, respiratory failure, and, in most cases, multiple comorbidities, effective management of these patients is crucial. Given the high overall mortality (42–62%) in severe infection, special attention should be focused on patients who require mechanical lung ventilation due to severity of their disease. Mortality in this category of patients ranges from 75 to 90% [1, 2]. Some large epidemiological studies have reported a high rate of invasive mechanical ventilation among all patients with COVID-19 admitted to intensive care units, from 29% in China to 89.9% in the USA [3, 4].

Even before the pandemic, mortality among patients aged 80–90 years with severe comorbidities who underwent mechanical ventilation was high. For example, an epidemiological study conducted in the United States in 2010 has demonstrated a 50% mortality in ventilated patients aged 85 years and older [5].

The ARDS associated with lung injury and severe respiratory failure, which causes 70% of deaths in ICU patients, is the first challenge facing physicians. The second important factor of mortality seen in 28% of severe COVID-19 is the «cytokine storm» resulting from an inadequate immune response to the SARS-CoV-2 virus. While the mechanism of this response has still been unclear, the virus is known to integrate its RNA into the cell through interaction with angiotensin-converting receptor type 2 (ACE-2), which leads to activation of the interferon system and formation of new ACE-2 receptors, and consequently creates new route for the infection [6]. Direct viral damage occurs due to its replication in the respiratory tract, leading to pyroptosis (inflammation-associated programmed cell death) and capillary leakage syndrome. The inflammatory response arising from pyroptosis results in hypercytokinemia, which turns the protective physiological cytokine response of the body into an abnormal one («cytokine storm») [7].

Another mechanism of lung tissue damage is diffuse alveolar lung injury resulting from release of proteases and reactive oxygen species and leading to pulmonary edema [8]. In addition to lung damage, the «cytokine storm» in COVID-19 infection is characterized by cardiovascular, renal, and hepato-

biliary impairment and multisystem organ dysfunction [9–11].

Currently, drug suppression with the interleukin-6 receptor inhibitor tocilizumab is a widely used method for blocking the cytokine storm [12]. However, in several patient categories such as those on a long-term immunosuppression or at risk of a generalized bacterial infection or having this infection, etc., the use of this drug is contraindicated [13]. The use of tocilizumab associates with a high risk of generalized bacterial infection or invasive candidiasis which can dramatically worsen the outcome in patients with severe COVID-19 [14].

Alternative strategies for combating the «cytokine aggression» include the use of extracorporeal blood purification methods such as cascade hemofiltration, high-volume hemofiltration, plasmapheresis, hemoperfusion, extracorporeal liver support, high-adsorption hemofiltration and membrane perfusion with selective filtration of intermediate mass molecules to remove cytokines and chemical mediators from blood of patients with severe COVID-19 [15]. Even before the pandemic, C. Ronco et al. proved the efficacy of various methods of extracorporeal detoxification (ECD) and provided a pathophysiological rationale for their use to restore «immune homeostasis» in sepsis-associated «cytokine storm» [16].

Among ECD methods, anticytokine hemoadsorption demonstrated significant efficacy in treating patients with COVID-19. The use of this technique has been shown to enable extracorporeal elimination of key cytokines (IL-6, IL-10, TNF), which play a significant role in the «cytokine storm» development [17, 18]. The use of extracorporeal purification in patients with severe COVID-19 is reasonable because the elimination of inflammatory mediators from circulation reduces the severity of inflammation causing organ failure and death.

As early as in April 2020, the FDA concluded that selective hemoadsorption using the CytoSorb sorbent is effective in the treatment of patients with severe COVID-19 infection and approved its use in this category [19]. The effectiveness of this ECD in severe COVID-19 infection was confirmed by the studies conducted in the United States and Germany (using Cytosorb) as well as China and Russia (using the HA-330 selective hemosorbent). The results of all studies showed a significant decrease in serum levels of proinflammatory cytokines after the procedure and increased survival rate after hemoadsorption [20–23]. In a series of cases at Noorafshar Hospital in Iran between May 1 and May 31, 2020, hemoadsorption using the HA 380 sorbent (Jafro Biomedical) proved effective in patients with severe disease requiring mechanical ventilation. All the patients who underwent hemoadsorption demonstrated improvement in respiratory

function manifested by increased blood pO_2 and SpO_2 with 5 out of 6 patients subsequently extubated and discharged from the intensive care unit [24].

The benefits of hemoadsorption also include lack of absolute contraindications and significant side effects, as well as efficacy confirmed by the studies conducted in the USA, Germany, Italy, China, and Russia.

Aim of the study. To evaluate the effects of hemoadsorption on clinical and laboratory parameters in patients with severe COVID-19 who required mechanical lung ventilation (MLV) or receiving noninvasive respiratory support.

Material and Methods

We retrospectively studied the longitudinal clinical and laboratory parameters of 49 patients with severe coronavirus infection and «cytokine storm» hospitalized in the First ICU of the Grodno University Hospital from September 2020 to November 2021, who underwent hemoadsorption using the domestic Hemo-Proteasorb sorbent.

All patients were divided into two groups. The first one, «Hemo-Proteasorb + MLV», included 22 patients, of them 14 men (64%) and 8 women (36%), with the mean age of 56 (19.0–89.0) years, Charlson comorbidity index of 4.0 (1.0–8.0) points. The other group, «Hemo-Proteasorb without MLV» comprised 27 patients, of them 16 men (59%) and 11 women (41%) with the mean age of 61 (35.0–86.0) years and Charlson comorbidity index of 4.0 (1.0–9.0) points.

Inclusion criteria were laboratory and clinically confirmed COVID-19 infection complicated by a «cytokine storm». Exclusion criteria were pregnancy, acute cerebrovascular accident, advanced cancer at the time of inclusion, HIV infection, chronic active viral hepatitis B or C with elevated transaminases, pulmonary or extrapulmonary tuberculosis, generalized epilepsy, alcohol or drug abuse, decompensated liver cirrhosis, acute pancreatitis, sepsis.

This study determined 14-day and 30-day survival of patients underwent hemoadsorption, and changes in blood inflammation markers, coagulation parameters, SpO_2/FiO_2 index and the patient's status assessed by NEWS2 scoring at different time points of the study.

All patients in both study groups received standard therapy according to the current guidelines of the Ministry of Health of the Republic of Belarus (Orders No. 393, 690, and 900).

For low-flow oxygen therapy, intranasal cannulas and facial masks were consistently used in all patients with the oxygen flow of 15 l/min. Noninvasive lung ventilation, if necessary, was done using the Mindray SynoVent E3 device (China) in the NIV mode with FiO_2 from 30 to 100%. The invasive lung ventilation was performed using Mindray SynoVent

E3 (China) in P-SIMV mode with FiO_2 from 30 to 100%. The criteria for initiating the next stage of respiratory support included respiratory rate $>22/\text{min}$, $SpO_2/FiO_2 < 60\%$, $SpO_2 < 90\%$ with the ongoing oxygen therapy.

Invasive ventilation was performed in 22 patients (45%), while 27 patients (55%) required oxygen therapy or noninvasive ventilation. Indications for the extracorporeal purification included progressive rise of inflammatory markers (interleukin-6, C-reactive protein, procalcitonin, leukocyte count), D-dimer, and fibrinogen.

The efficacy of the treatment was evaluated using the changes in proinflammatory cytokines (CRP, procalcitonin) levels. Respiratory system assessment in hyperimmune inflammation was performed by monitoring the SpO_2/FiO_2 index. The coagulation system was evaluated by measuring the levels of fibrinogen, which also reflected the severity of inflammation, and D-dimer. The patients' status during hemoadsorption was serially evaluated using the NEWS2 score. Hemoadsorption was performed in all patients using the «Hemo-Proteasorb» antiproteinase biospecific hemosorbent (Republic of Belarus) according to the following procedure. A central vein was punctured and catheterized prior to the start of hemoperfusion. Before the procedure, the extracorporeal circuit was flushed with 5,000 units of unfractionated heparin. The extracorporeal circuit was connected in sterile conditions. Before hemoperfusion, the mass exchangers were flushed with fivefold volume of sterile 0.9% NaCl solution. Thereafter, blood was drawn from a vein into the MCA 0/330-MKV01 single-use hemoperfusion line using a BP-742 roller pump (Fresenius, Germany). Blood was passed through the Hemo-Proteasorb sorbent column and then returned to the previously catheterized peripheral vein. Blood perfusion rate in the line was 80–90 ml/min. The procedure duration was 60 minutes. The average number of sessions was 4.5 (3.0–6.0).

Blood sampling for the study was done 6 hours prior to the procedure of extracorporeal blood purification. Follow-up tests were carried out on days 3 and 5–7 in both groups.

Complete blood count was done using ABX analyzer «Micros» (Roche, France). Levels of fibrinogen and D-dimer were measured by biochemical method on «Architect@c8000 System» (USA). The levels of C-reactive protein (CRP) and procalcitonin (PCT) were determined by enzyme immunoassay on the Abbott AxSYM® system (USA) machine. For a comprehensive assessment of respiratory function, the SpO_2 (pulse oximetry index) to FiO_2 (% of oxygen in the inhaled gas mixture) ratio was calculated.

The results were analyzed using the Statistica 10.0 software (Statsoft Inc., USA). Normally distributed variables were reported as means (M). Medians

Table 1. Changes in the studied parameters in the patient groups, Me (25%, 75%).

Parameter	Study stage	Parameter values in groups			
		Hemo-proteasosorb + MLV, n=22	<i>P</i> -value	Hemo-proteasosorb without MLV, n=27	<i>P</i> -value
CRP, mg/l	Baseline	135.4 (10.6–303.0)		132.6 (30.7–183.0)	0.911 [#]
	On day 3 after hemoadsorption	64.3 (1.2–147.0)	0.003*	28.55 (5.3–182.0)	0.0002* 0.142 [#]
	On days 5–7 after hemoadsorption	107 (19.6–253.0)	0.249*	23.85 (2.2–200.0)	0.0002* 0.003 [#]
PCT, ng/ml	Baseline	0.27 (0.12–2.08)		0.29 (0.14–21.25)	0.499 [#]
	On day 3 after hemoadsorption	0.14 (0.05–1.77)	0.028*	0.14 (0.04–11.91)	0.002* 1.000000 [#]
	On days 5–7 after hemoadsorption	0.27 (0.08–0.45)	0.285*	0.22 (0.05–9.29)	0.721* 0.866 [#]
Leukocyte count, ×10 ⁹ /l	Baseline	15.18 (6.7–26.56)		11.64 (2.1–29.0)	0.031 [#]
	On day 3 after hemoadsorption	12.78 (8.17–26.97)	0.502*	9.13 (2.75–20.9)	0.0008* 0.002 [#]
	On days 5–7 after hemoadsorption	19.6 (6.17–38.4)	0.093*	12.1 (1.34–26.1)	0.677* 0.010 [#]
SpO ₂ /FiO ₂ , %	Baseline	183 (87–448)		238 (88–461)	0.067 [#]
	On day 3 after hemoadsorption	169 (85–471)	0.615*	320 (98–471)	0.012* 0.039 [#]
	On days 5–7 after hemoadsorption	161 (84–467)	0.852*	320 (96–471)	0.002* 0.011 [#]
Fibrinogen, g/l	Baseline	11.7 (4.9–19.49)		10.2 (4.41–15.5)	0.011 [#]
	On day 3 after hemoadsorption	8.2 (3.7–14.7)	0.00004*	6.5 (2.8–11.9)	0.00005* 0.141 [#]
	On days 5–7 after hemoadsorption	9.6 (4.6–17.9)	0.003*	5.11 (2.3–11.5)	0.00006* 0.002 [#]
D-dimer, µg/ml	Baseline	1432.0 (443.0–6390.0)		1445.0 (365.0–4830.0)	0.718 [#]
	On day 3 after hemoadsorption	1087.0 (415.0–3247.0)	0.006*	1049.0 (301.0–3120.0)	0.006* 0.849 [#]
	On days 5–7 after hemoadsorption	1114.0 (481.0–10000.0)	0.650*	1335.0 (335.0–3302.0)	0.179* 0.968 [#]

Note. CRP — C-reactive protein; PCT — procalcitonin; MLV — mechanical lung ventilation; * — *P*-value vs the baseline (Wilcoxon test); [#] — *P*-value vs the same time point in the MLV group (Mann–Whitney test).

(*Me*) and interquartile ranges (values of the 25th and 75th percentiles) were used for parameters with non-normal distribution. The variables not having «close to normal» distribution were reported as Median (*Me*) with upper and lower quartiles. The significance of the results was assessed using the Wilcoxon nonparametric test. Mann–Whitney U-test was applied to compare independent groups with one or two quantitative variables with non-normal distribution. The differences were considered significant at *P*<0.05.

Survival rates in the study groups were assessed by Kaplan–Meier method using the SPSS Statistics software. To identify independent factors influencing mortality in the studied cohort of patients, we performed multivariate analysis using Cox regression method.

Results

The baseline laboratory parameters of patients in both study groups demonstrated a severe inflammatory response associated with a rise in the levels of CRP, PCT, and leukocyte count. On day 3 after hemoadsorption, a decrease in the levels of CRP and PCT was seen in the studied groups. Interestingly, the patients receiving noninvasive res-

piratory support were found to have a significant decrease in the leukocyte count post-hemoadsorption, whereas in those from the MLV group difference between groups was non-significant. On days 5–7, a trend toward a further decrease of CRP and a slight increase in the leukocyte count was seen in the latter group. Meanwhile, in the «Hemo-Proteasosorb + MLV» group, the opposite was observed with the CRP level higher than in the previous time point and the leukocyte count exceeding the baseline (Table 1).

After calculating the baseline SpO₂/FiO₂ index in both study groups, it was found to be lower in the «Hemo-Proteasosorb + MLV» group than in the «Hemo-Proteasosorb without MLV» one, which suggests a more severe patient condition in this group due to more serious respiratory failure. In the same group, there was a trend towards progressive reduction of the index during all the stages of the study, which was considered as worsening respiratory failure. On the contrary, in the «Hemo-Proteasosorb without MLV» group, a significant increase of SpO₂/FiO₂ index was observed on days 3 and 5–7 as compared to the baseline (Table 1).

Respiratory function assessment was also performed by monitoring the changes in the types of

Table 2. The changes in types of respiratory support and clinical condition of patients in the groups, Me (25%, 75%).

Parameter	Study stage	Parameter values in groups			
		Hemo-proteasosorb + MLV, n=22	P-value	Hemo-proteasosorb without MLV, n=27	P-value
Type of respiratory support	Baseline	2.5 (1.0–3.0)		1.0 (1.0–2.0)	0.00003 [#]
	On day 3	3.0 (1.0–3.0)	0.441*	1.0 (0.0–2.0)	0.686*
	after hemoadsorption				0.00004 [#]
	On days 5–7	3.0 (1.0–3.0)	0.169*	1.0 (0.0–2.0)	0.016*
	after hemoadsorption				0.000001 [#]
NEWS 2, points	Baseline	8.0 (4.0–11.0)		7.0 (3.0–9.0)	0.0129 [#]
	On day 3	6.0 (2.0–10.0)	0.0002*	5.0 (1.0–9.0)	0.00002*
	after hemoadsorption				0.002 [#]
	On days 5–7	7.0 (2.0–9.0)	0.011*	3.0 (1.0–8.0)	0.00002*
	after hemoadsorption				0.0001 [#]

Note. * — *P*-value vs the baseline (Wilcoxon test); [#] — *P*-value vs the same time point in the lung ventilation group (Mann–Whitney test). For statistical analysis, each type of ventilatory support was assigned a numerical value from 0 to 3 depending on the level: 0, no oxygen support or support up to 5 l/min; 1, oxygen support up to 15 l/min using nasal cannulas and/or face mask; 2, noninvasive lung ventilation in CPAP mode; 3, invasive ventilation in P-SIMV mode. The data were included in the table accordingly. The value of 1 at different stages in the group with mechanical ventilation is due to the fact that some patients were switched to a less invasive support, while the others had deteriorated. For example, Patient #2 in the group with MLV required only oxygen support up to 15 l/min using nasal cannulas and/or a face mask at the baseline, while on days 5–7, the MLV was required corresponding to deterioration from 1 to 3. In contrast, some patients had the opposite situation: prior to hemoadsorption, they required invasive or noninvasive lung ventilation, and during hemoadsorption, a lower level of respiratory support was required, which corresponded to a positive trend from 3 to 2 or from 2 to 1. For this reason, the range of values in the groups was from 1.0 to 3.0.

respiratory support. The results of this monitoring are shown in Table 2.

The effect of hemoadsorption on hemostasis was evaluated by analyzing the results of coagulation tests (D-dimer, fibrinogen, prothrombin time, APTT, INR) and the platelet count. There were no changes in the levels of prothrombin time, APTT, INR, platelet count during the hemoadsorption, that is why we only analyzed the serial changes of D-dimer and fibrinogen levels universally considered to be markers of disease severity in COVID-19. In both groups, a significant decrease in fibrinogen was seen on day 3 after hemoadsorption and a trend to its reduction was observed on days 5–7. On day 3, both in patients on mechanical ventilation and in those on noninvasive respiratory support, D-dimer level dropped significantly as compared with the baseline values, but on day 3, it rose in both groups (Table 1).

In addition to laboratory parameters, we assessed clinical condition of patients during different periods of the study using the NEWS2 score. In the noninvasive respiratory support group there was a significant decrease of NEWS2 scores on day 3. On days 5–7, the trend towards their further decrease persisted indicating the improvement of the patients' condition. On day 3 after hemoadsorption, the values of the NEWS2 score decreased, while on days 5–7, they increased as compared with the results obtained on day 3, but still remained lower versus baseline (Table 2).

The Kaplan-Meier survival curve was plotted to determine the survival rate in patients receiving hemoadsorption (Fig. a, b). The 14-day survival rate in the «Hemo-Proteasosorb+MLV» group was

64%, while in the «Hemo-Proteasosorb without MLV» group it was 85% (Fig. a).

The 30-day survival rate was 41% in the MLV group and 73% in the noninvasive respiratory support group (Fig. b).

To identify independent factors influencing mortality in the studied cohort, a multivariate Cox proportional hazards regression model was performed. Age, gender, comorbidity did not affect mortality in patients receiving hemoadsorption. However, the impact of invasive ventilation was predictably evident (Table 3).

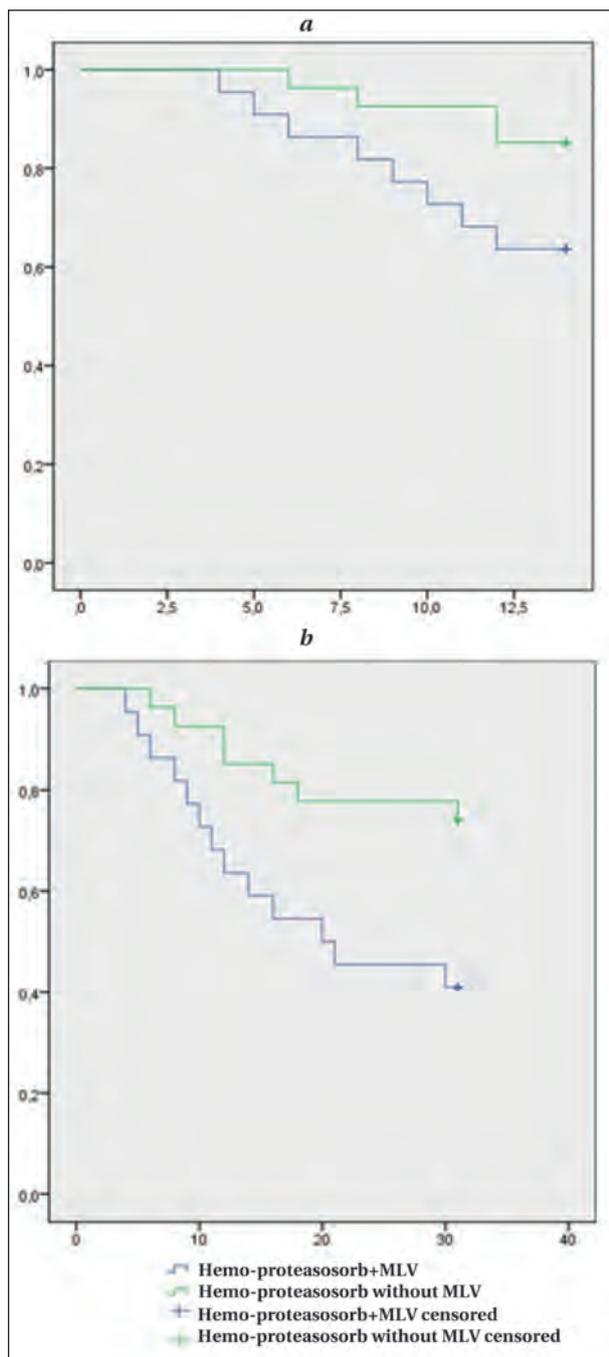
Table 3. Assessment of risk factors for combined endpoint (mortality) in patients with severe COVID-19 who underwent hemoadsorption.

Parameter	HR	95% CI	P-value
Lung ventilation	4.282	1.62–12.05	0.004
Sex	0.78	0.30–2.05	0.61
Age	0.23	0.29–1.89	0.17
Comorbidity	0.54	0.88–3.37	0.51

Note. The results of Cox multiple regression analysis are shown. HR — hazard ratio; CI — confidence interval.

Discussion

Our findings are consistent with the results of a randomized study conducted by Liang Yu (China) on the use of HA-330 hemosorbent in patients with severe COVID-19 which demonstrated higher oxygenation index 72 hours after hemoadsorption (rise from 74.0 to 222.2 mm Hg) vs the control group (rise from 83.0 to 122.9 mm Hg), decrease of APACHE score from 16 to 13.5 (in the control group its increase was seen from 13 to 18), and almost a twofold reduction of pneumonia severity index as



Kaplan–Meier survival curve on day 14 (a) and day 30 (b).

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compared with the control group (from 126.5 to 83 points vs increase from 125 to 164 points in the control group). Mortality of patients in the hemo-adsorption group, as compared with the control group, appeared to be three times lower (15.4% vs. 47.6%, respectively) [21].

Another retrospective study conducted by Ruiz-Rodrigues J.C. between March 3, 2020, and June 22, 2020, which included 343 patients with severe COVID-19 infection, six of whom underwent hemo-adsorption using the CytoSorb® anti-cytokine sorbent while being on mechanical ventilation, significant reductions in D-dimer (from 17,868 µg/mL down to 4,488 µg/mL), C-reactive protein (from 12.9 mg/dL down to 3.5 mg/dL), ferritin (from 1539 µg/L down to 1197 ng/mL), and interleukin-6 (from 17,367 pg/mL down to 2,403 pg/mL) were found as compared to the baseline. After the procedure, an improvement in oxygenation ($\text{PaO}_2/\text{FiO}_2$ rose from 103 to 222 mm Hg) and a decrease in the SOFA score (from 9 at the baseline to 7.7 post procedure) were revealed. The mortality in the intensive care unit was 33.7% [25].

Thus, our results demonstrate the effectiveness of hemo-adsorption using the domestic Hemo-Proteasorb sorbent in patients with severe COVID-19 both on noninvasive respiratory support and on mechanical ventilation. The effectiveness of hemo-adsorption, though, was lower in the group of patients who required invasive ventilatory support. Therefore, the start of hemo-adsorption may be considered more appropriate during the period when invasive respiratory support is not required.

Conclusion

The use of hemo-adsorption in COVID-19 has demonstrated clinical effectiveness in patients on both noninvasive and invasive respiratory support. Positive effects of hemo-adsorption manifesting as increase in $\text{SpO}_2/\text{FiO}_2$ index were more significant in the group of patients without mechanical ventilation. The procedure was associated with a reduced NEWS2 score in both study groups with the changes being more significant in the noninvasive respiratory support group.

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