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Research Article

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Acute Kidney Injury in Patients with Novel Coronavirus Infection COVID-19 After Cardiac Surgery

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RELEVANCE The novel coronavirus (SARS-CoV2) infection (COVID-19) was first identified in China and quickly spread throughout the world, becoming a public health emergency. Acute kidney injury (AKI) occurs in 8–60% of patients with COVID-19 and is associated with significant mortality, especially in patients requiring renal replacement therapy (RRT).

Identification of risk factors for the development of AKI, analysis of the course of this life-threatening condition, study of the use of RRT and extracorporeal hemocorrection (ECHC) in patients with COVID-19 after cardiac surgery is of significant interest.

AIM OF THE STUDY To identify risk factors for the development of AKI, assess the incidence of complications and treatment outcomes in patients with COVID-19 after cardiac surgery. To study the experience of using RRT and ECHC methods.

MATERIAL AND METHODS We examined 23 patients with a confirmed diagnosis of COVID-19 who were treated in the Infectious Diseases Department of the N.V. Sklifosovsky Research Institute for Emergency Medicine in 2021. Of these, 19 were men (82.6%), and 4 — women (17.4%). The mean age of the patients was 42 years. All the patients required emergency cardiac surgery. Depending on the development of AKI, which required the use of RRT and ECHC methods, patients were divided into two groups: in 10 patients with the development of AKI and multiple organ dysfunction, the use of RRT and ECHC methods was required (group 1); in 13 patients without AKI, standard therapy was used (group 2). Twenty-two patients underwent surgery using cardiopulmonary bypass (CPB), and 1 — without CPB. Indications for the use of RRT and ECHC methods in the patients were the development of AKI, including against the background of chronic kidney disease, in accordance with the KDIGO-2012 criteria, as well as sepsis, septic shock, acute respiratory distress syndrome, water-electrolyte imbalance, acid-base imbalance, systemic inflammation and “cytokine storm”.

CONCLUSIONS 1. In patients with COVID-19 who require cardiac surgery, the development of acute kidney injury worsens the prognosis of the disease and is accompanied by a statistically significant increase in the duration of mechanical ventilation, the median was 3.2 days compared to 1.0 day in group 2, and the period of stay in the intensive care unit was 16.5 days and 9 days, respectively.

2. Mortality was 30% in group 1, and 15% in group 2, p=0.475; in patients with acute kidney injury, there was a tendency towards a more frequent development of postoperative complications — thus, acute cerebrovascular accident occurred in 20% and 7.7% of cases, anemia — in 80% and 53.3%, respectively, while mediastinal hematoma developed in 20% of patients in group 1 only.

3. Risk factors for the development of acute kidney injury in the postoperative period were elevated urea levels and a history of chronic kidney disease. In patients of group 1, the level of intraoperative blood loss was 41.7% higher than in group 2, but the differences were not statistically significant.

Keywords: acute kidney injury, renal replacement therapy, novel coronavirus infection COVID-19, cardiac surgery, methods of extracorporeal hemocorrection

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ACVA – acute cerebrovascular accident
AKI – acute kidney injury
ARDS – acute respiratory distress syndrome
AV – aortic valve
BMI – body mass index
CKD – chronic kidney disease
COVID-19 – novel coronavirus (SARS-CoV2) infection
CPB – cardiopulmonary bypass
CRP – C-reactive protein
DM – diabetes mellitus
ECHC – extracorporeal hemocorrection
EF – ejection fraction
GFR – glomerular filtration rate
HR – heart rate
HT – hypertension
ICU – intensive care unit
IgM – Immunoglobulins M
IgG – Immunoglobulins G
IL – interleukin
MAP – mean arterial pressure
MSCT – multislice computed tomography
MV – mitral valve
MVL – mechanical ventilation of the lungs
PE – plasma exchange
RRT – renal replacement therapy
TV – tricuspid valve

RELEVANCE

The novel coronavirus (SARS-CoV2) infection (COVID-19) was first identified in China and quickly spread throughout the world, becoming a public health emergency. Acute kidney injury (AKI) occurs in 8–60% of patients with COVID-19 and is associated with significant mortality, especially in patients requiring renal replacement therapy (RRT) [1, 2]. According to a study by M. Fisher et al. [3], AKI develops in 56.9% of patients with COVID-19, compared to 37.2% who did not suffer from coronavirus infection in 2020. In a meta-analysis by L. Ouyang et al., in seriously ill patients with COVID-19, AKI developed 13.6 times more often than in non-severe cases, and reached 30.7% in deceased patients [4].

The pathogenesis of AKI in COVID-19 is multifactorial. The SARS-CoV-2 coronavirus enters the cells of the proximal tubules and podocytes by endocytosis or using the transmembrane glycoprotein CD147-spike, which leads to a direct cytopathic effect of the coronavirus on the epithelial cells of the proximal tubules and podocytes [5]. SARS-CoV-2 binds to membrane-bound angiotensin-converting enzyme 2 (ACE2) via the S1 subunit. Decreased ACE2 levels lead to unbalanced activation of the renin-angiotensin-aldosterone system, angiotensin II is activated through complement activation and reduction of angiotensin 1–8, which leads to hypercoagulability and microangiopathy, myeloid cells are activated, which further causes the release of cytokines, glomerulopathy and mitochondrial disorders. A pronounced imbalance in the concentrations of pro- and anti-inflammatory mediators, the development of the cytokine storm, causes endothelial and tubular dysfunction, capillary leak syndrome, and disseminated intravascular coagulation, which ultimately leads to the development and progression of AKI as part of multiple organ dysfunction [6–8].

According to M. Gaudino et al., the number of cardiac surgeries during the pandemic decreased by 50–75%, while the number of cardiac beds in intensive care units decreased by more than 50% [9]. The literature describes a small number of patients undergoing cardiac surgery. Thus, in a 2022 meta-analysis [10], after processing 4223 articles, only 44 patients were included with a hospital mortality rate of 27.3%, a length of stay in the intensive care unit (ICU) of 7.4 days, and a hospital stay of 17.8 days.

Acute kidney injury develops in 20–40% of patients after cardiac surgery, in 3% it requires the use of RRT, is accompanied by an increase in the relative risk of death by 5.14 times, and unfavorable long-term outcomes; 5- and 7-year survival rates are 54% and 38%, respectively, and 25% develop chronic kidney disease (CKD) [11–13]. Temporary guidelines “Prevention, diagnosis and treatment of novel coronavirus infection” of the Ministry of Health of the Russian Federation recommend to use methods of extracorporeal hemocorrection (ECHC) in patients with severe COVID-19, progressive respiratory and (or) multiple organ failure [14].

Thus, identifying risk factors for the development of AKI, analyzing the course of this life-threatening condition, studying the use of RRT and ECHC methods in patients with COVID-19 and cardiac surgery is of significant interest.

The aim of our study is to identify risk factors for the development of AKI, assess the incidence of complications and treatment outcomes in patients with COVID-19 after cardiac surgery. To study the experience of using RRT and ECHC methods.

MATERIAL AND METHODS

We examined 23 patients who were treated in the Infectious Diseases Department of the N.V. Sklifosovsky Research Institute for Emergency Medicine in 2021 with a confirmed diagnosis of COVID-19. Of these, 19 were men (82.6%) and 4 women (17.4%). The mean age of the patients was 42 years.

All the patients required emergency cardiac surgical treatment, which included two pathologies: acute infective endocarditis (of native heart valves or previously implanted prostheses) and acute aortic dissection (Table 1). Primary cardiac surgery was performed in 20 (87%) patients, repeated interventions were performed in 3 patients (13%).

Table 1

Distribution of study patients by type of surgery

Type of surgery	Number of patients, n (%)	Mortality, n (%)
MV replacement	2 (9)	0
AV replacement	3 (13)	1 (33)
Repeat AV replacement	1 (17)	1 (100)
TV replacement	8 (35)	1 (12.5)
Combined valve operations:		
MV replacement and TV repair	2 (9)	0
MV and AV replacement	1 (4)	1 (100)
Repeat MV and AV replacement	1 (4)	0
Ascending aorta replacement	1 (4)	0
Ascending aorta and partial arch replacement	2 (9)	0
Ascending aorta and AV replacement	1 (4)	1 (100)
Carotid-subclavian bypass and endoprosthetic repair of the descending thoracic aorta	1 (4)	0
Total	23 (100)	5 (21.7)
CPB /without CPB	22/1	5/0

Notes: AK—aortic valve; MK — mitral valve; TK — tricuspid valve; ИК — artificial blood circulation

22 (96%) patients underwent open-heart surgery under conditions of cardiopulmonary bypass (CPB), 15 patients (64%) were operated on using cardioplegia and in conditions of complete cardiac arrest, and 7 (32%) patients underwent beating-heart surgery. In one case (4%), the operation was performed after carotid-subclavian bypass and endoprosthetic treatment of the descending thoracic aortic rupture.

The range of operations under cardiopulmonary bypass included: interventions on the ascending portion of the aorta and, if necessary, on the aortic arch - 3 (13%) patients, as well as in combination with intervention on the aortic valve - one patient (4%); isolated interventions on the mitral (MV) - 2 (9%), aortic (AV) - 4 (17%), and tricuspid (TV) valves - 9 (39%); combined valve operations on MV and TV - 1 (4%), MV and AV - 2 (9%) patients. A total of 5 patients died, the mortality rate was 21.7% (Table 1).

Depending on the development of AKI, patients were divided into two groups: 10 patients with the development of AKI and multiple organ dysfunction required the use of RRT and ECHC methods (group 1), and 13 patients without AKI received standard therapy (group 2).

Indications for the use of RRT and ECHC methods were the development of AKI, including in case of CKD, in accordance with the KDIGO-2012 criteria [15], as well as sepsis, septic shock, acute respiratory distress syndrome (ARDS), the need to correct water and electrolyte balance, acid-base balance, systemic inflammation and the cytokine storm [16]. The median time from surgery to the start of RRT was 2 days (Table 2). Most often, in 66.7% of cases, hemodiafiltration mode was used; hemofiltration was used in 23.8%; and intermittent extended (12 hours) and long-term (24 hours) hemodialysis - in 8.7%. The duration of RRT procedures was 13.0 (10; 26) hours, the dose achieved was 25.4 (14.2; 42.8) ml/kg/hour.

Table 2

Application of various methods of renal replacement therapy and extracorporeal hemocorrection

Indicators	Values
Hemodiafiltration (long-term+extended), n (%)	14 (66.7)
Hemofiltration (long-term+extended), n (%)	5 (23.8)
Hemodialysis (long-term+extended), n (%)	2 (8.7)
Total RRT procedures	21
Time from surgery to the start of RRT, days	2.0 (2; 7)
Duration of procedures, hours	13.0 (10; 26)
Dose of (long-term/extended) RRT, ml/kg/hour	25.4 (14.2; 42.8)
Number of plasma exchange procedures, n (%)	4 (3)
Number of selective cytokine hemoadsorption procedures, n (%)	1 (1)
Number of selective lipopolysaccharides hemosorption procedures, n (%)	1 (1)

Notes: Data is presented as Me (Q1; Q3); RRT — renal replacement therapy

In 3 patients due to the development of the cytokine storm and septic shock, the following ECHC procedures were performed: in one patient - selective cytokine hemoadsorption using CytoSorb® (Cytosorbents, Corporation, USA), selective lipopolysaccharides hemosorption on a Toraymyxin PMX-20R cartridge (Toray Company, Japan) and one session of plasma exchange (PE), in two others - 3 PE procedures.

The severity of pneumonia in COVID-19 was assessed using chest multislice spiral computed tomography (MSCT) data. Left ventricular ejection fraction (EF) was calculated using echocardiography. Laboratory blood tests included determination of routine biochemical parameters, C-reactive protein (CRP) level, IgM and IgG antibodies. Glomerular filtration rate (GFR) was calculated using the MDRD formula. Blood samples were taken before and after surgical treatment, as well as on the 1st, 3rd, 5th and 7th day of the postoperative period. The severity of the patients' condition was assessed according to the Acute Physiology and Chronic Health Evaluation (APACHE II) scoring system [17] using the worst indicators within 24 hours from the moment of surgery; the surgical risk was assessed using the EuroSCORE risk assessment [18]. Using these scales, the probability of death was also assessed. Body mass index (BMI) was calculated.

Statistical data analysis was performed using the Statistica 12 software package (StatSoft, Inc., USA). All samples were checked for normal distribution using the Kolmogorov–Smirnov test. The median and interquartile range (25th and 75th percentiles) of Me (Q1; Q3) were calculated. To compare variables with a normal distribution, we used the paired Student's t-test (for independent samples). If the distribution was different from normal, the nonparametric Mann–Whitney U test (U) was used for unrelated samples; for comparison of categorical variables – two-tailed Fisher's exact test (F); for the analysis of patient survival - the Kaplan-Meier (K-M) method; for comparing the groups – the log-rank test. The results obtained were considered statistically significant at $p<0.05$.

RESULTS

Comparison of data from the study groups showed that the patients did not differ statistically significantly in age (in the 1st group the median age was 42.5 years, in the 2nd group - 42 years), gender (20% and 15.4% were women, respectively), and duration of the disease (COVID-19 until surgery - 12 days and 10 days, respectively). There were no statistically significant differences in the 1st and 2nd group patients in the severity of the condition according to the APACHE-II and EuroSCORE scales, BMI, volume of administered contrast media, and left ventricular ejection fraction (EF) (Table 3).

Table 3

Characteristics of patients in the compared groups at the time of inclusion in the study

Indicators	Group 1 (n=10)	Group 2 (n=13)	p	Criterion
Age, years	42.5 (35; 51)	42.0 (32; 59)	0.533	U
Gender, m/f	8/2	11/2	1.0	F
Duration of COVID-19 until surgery, days	12.0 (7; 15)	10.0 (3; 16)	0.872	U
EuroSCORE, points	14.0 (14; 15)	13.0 (12; 14)	0.154	U
APACHE II, points	13.0 (12; 17)	12.0 (11; 13)	0.177	U
Risk of unfavorable outcome, %	16,5 (14,6; 26,2)	14.6 (12.8; 16.5)	0.212	U
BMI, kg/m²	23.2 (20.7; 23.9)	26.5 (24.3; 30.9)	0.091	U
Volume of injected contrast, ml	100 (50; 120)	120 (100; 200)	0.172	U
EF, %	65.0 (57; 69)	63.0 (60; 66)	0.301	U
Previous heart surgeries, n (%)	2 (20)	1 (7.8)	0.561	F
Liver diseases, n (%)	4 (40.0)	8 (61.5)	0.413	F
CKD, n (%)	9 (90.0)	6 (46.1)	0.074	F
DM, n (%)	3 (30.0)	2 (15.4)	0.617	F
HT, n (%)	7 (70.0)	7 (53.8)	0.669	F
Oncological diseases, n (%)	1 (10.0)	3 (23.0)	0.603	F
Obesity, n (%)	0	3 (23.0)	0.229	F
Creatinine, μmol/l	108.5 (62; 182)	84.0 (64; 119)	0.307	U
Urea, mmol/l	10.3 (5; 17)	4.0 (4; 9)	0.022	U
GFR, ml/min/1.73 m²	67.0 (37.6; 115.6)	86.5 (54.4; 114.4)	0.459	U
Hematocrit, %	27.0 (25; 33)	29.0 (24; 33)	0.929	U
Leukocytes, ×109/l	12.0 (7; 14)	10.0 (7.5; 15.8)	0.852	U
Lymphocytes, %	10.0 (4; 19.5)	14.5 (11.5; 18)	0.463	U
CRP, mg/l	87.2 (14.3; 211.0)	92.3 (64.0; 134.0)	0.750	U
Lactate, mmol/l	1.6 (1.0; 1.8)	1.5 (1.2; 4.5)	0.874	U
CT 1, n (%)	6 (60)	10 (76.9)	0.650	F
CT 2, n (%)	3 (30)	3 (23.1)	1.0	F
CT 3, n (%)	1 (10)	0	0.435	F
SARS-CoV-2 IgM antibodies (U/ml	0.55 (0.3; 1.9)	0.69 (0.3; 4.1)	0.766	U
SARS-CoV-2 IgG antibodies (U/ml)	177.9 (96.3; 259.2)	77.7 (16.8; 309.4)	0.641	U

Notes: Data is presented as Me (Q1; Q3); HT - hypertension; BMI —body mass index; CT - computer examination of the chest; DM - diabetes mellitus; GFR — glomerular filtration rate; EF —left ventricular ejection fraction; CKD - chronic kidney disease; CRP - C-reactive protein; U—nonparametric Mann–Whitney U test; F - 2-tailed Fisher's exact test

When comparing the frequency of concomitant diseases in patients of the 1st group, diabetes mellitus (DM) and hypertension (HT) were more often detected, and in the 2nd group - liver diseases, cancer and obesity, although no statistically significant differences were found between the groups. CKD was found in 90% of patients in group 1 and only in 46.1% in group 2, but the differences were not statistically significant (p = 0.074). In group 1, there was initially a higher creatinine level - 108.5 and 84.0 µmol/l, respectively, and a lower GFR value - 67.0 and 86.5 ml/min/1.73 m^2, respectively; but the differences were not statistically significant. At the same time, the level of urea in the blood was statistically significantly different between the groups and amounted for 10.3 mmol/l in group 1 compared to 4.0 mmol/l in group 2, p = 0.022.

In the study groups with COVID-19, a computer examination of the chest organs was performed to identify pathological changes in the lungs. As a result, no statistically significant differences were obtained in the study groups. For diagnostic purposes, the patients underwent an examination with intravenous administration of a contrast agent: 100 ml in group 1, 120 ml in group 2, p = 0.172.

The patients of the 1st and 2nd groups did not differ statistically significantly in terms of hematocrit: 27% and 29%, respectively; leukocyte count: 12 and 10x109/l, respectively; relative lymphocyte content: 10% and 14.5%, respectively; CRP content: 87.2 and 92.3 mg/l, respectively; lactate level: 1.6 and 1.5 mmol/l; SARS-CoV-2 IgM antibodies: 0.55 and 0.69, respectively; and SARS-CoV-2 IgG antibodies: 177.9 and 77.7, respectively.

Intraoperatively (Table 4), patients in the study groups did not differ statistically significantly in the volume of infusion therapy, duration of surgery and CPB, and body temperature under artificial hypothermia. In group 1 compared with group 2, there was a statistically insignificant trend toward greater intraoperative blood loss of 1200 ml and 700 ml, respectively, which may be a risk factor for the development of AKI.

The dynamics of nitrogenous wastes, potassium and the rate of diuresis on the 1st, 3rd, 5th, 7th day of the postoperative period were assessed (Table 5). Levels of creatinine and urea increased in patients of group 1 during the 7th day of the postoperative period; in patients of group 2, nitrogen metabolism indicators had normal values during the study period. The groups differed statistically significantly in blood levels of creatinine on the 1st day and urea on the 3rd day. The rate of diuresis on the 1st day was lower in patients of group 1: 1275 ml and 1700 ml, respectively, the differences were not statistically significant.

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Table 4

Intraoperative parameters in the study groups

Indicators	Group 1 (n=10)	Group 2 (n=13)	p	Criterion
Hematocrit on the 1st day after surgery, %	27.0 (24; 30)	29.0 (26; 32)	0,633	U
Hematocrit on the 2nd day after surgery, %	30.0 (28; 31)	28.0 (27; 29)	0,405	U
Blood loss, ml	1200.0 (600; 1600)	700.0 (700; 1200)	0,378	U
Intravenous infusion, ml	2650,0 (1830; 4000)	2610,0 (1975; 3515)	0.482	U
Temperature, °C	35.0 (34; 36)	35.0 (30; 36)	0.666	U
MAP, mmHg	78.4 (67; 90)	83.0 (80; 87)	0.556	U
HR, beats/min	89.0 (80; 90)	89.0 (80; 98)	0.352	U
Operation duration, min	233.5 (165; 246)	210.0 (180; 296)	0.914	U
CPB duration, min	84.5 (74; 137)	101.0 (85; 120)	0.770	U

Notes: Data is presented as Me (Q1; Q3); CPB - cardiopulmonary bypass, MAP — mean arterial pressure, HR — heart rate, U — nonparametric Mann–Whitney U test

Table 5
Dynamics of clinical and laboratory parameters depending on patient groups

Indicators	Group	Research stages				
		Initial	1st day	3d day	5th day	7th day
Creatinine, μmol/l	1	108.5 (62; 182)	129.0 (110; 218) *	145.0 (97; 165)	124.5 (76; 220)	190.0 (58; 220)
	2	84.0 (64; 119)	93.0 (64; 110)	78.5 (63.5; 116)	84.0 (73; 115)	101.0 (56; 154)
Potassium, mmol/l	1	4.0 (3.8; 4.0)	4.0 (3.9; 4.6)	4.5 (3.7; 4.6)	4.0 (3.7; 4.0)	3.9 (3.7; 4.2)
	2	4.0 (3.8; 4.5)	4.1 (3.9; 5.2)	3.9 (3.5; 4.7)	3.8 (3.8; 5.0)	4.0 (3.7; 4.7)
Urea, mmol/l	1	10.3 (5; 17) *	12.0 (12; 24)	17.0 (10; 19) *	14.0 (6; 30)	14.0 (5; 21)
	2	4.0 (3.5; 9)	5.5 (4; 9)	7.3 (5; 9.9)	8.0 (3.5; 12)	6.0 (4; 14)
Diuresis, ml/day	1	–	1275.0 (800; 1700)	2500 (2100; 3100)	2500 (2050; 3500)	2900 (2500; 3200)
	2	–	1700.0 (1500; 2100)	2250 (1800; 2600)	2200 (2000; 2300)	2575 (1550; 3300)

Notes: Data is presented as Me (Q1; Q3); * — statistically significant differences between the groups ($p<0.05$), the significance of the differences was assessed using the non-parametric Mann–Whitney U test

When assessing postoperative complications (Table 6), it was found that in group 1, acute cerebrovascular accident (ACVA) developed more often than in group 2: in 20% and 7.7%, respectively; the presence of blood clots in the atrium was determined in 20% and 7.7%, respectively; mediastinal hematomas developed in 20% and 0%, respectively, and anemia - in 80% and 53.8%, respectively; gastritis and colitis were also more common, although the differences between groups were not statistically significant. Complications identified in the patients with novel coronavirus infection COVID-19 aggravated the severity of the disease (Table 6).

When analyzing treatment outcomes (Table 7), it was revealed that patients in group 1 compared with group 2 required mechanical ventilation of the lungs (MVL) statistically significantly longer: 3.5 and 1.0 days, respectively, $p = 0.014$; there was a tendency towards longer vasopressor support: 2.5 and 1.0 days, respectively, $p = 0.214$; they had a longer ICU length of stay: 16.5 and 9.0 days, respectively, $p = 0.034$ (statistically significant), and length of hospital stay: 24.0 and 18.0 days, respectively, $p = 0.219$.

Table 6
Postoperative complications

Indicators	Group 1 (n=10)	Group 2 (n=13)	p	Criterion
ACVA, n (%)	2 (20)	1 (7.7)	0.559	F
Pulmonary hypertension, n (%)	5 (50)	7 (53.8)	1.0	F
Hydrothorax, n (%)	6 (60)	9 (69.2)	0.685	F
Atrial thrombi, n (%)	2 (20)	1 (7.7)	0.559	F
Mediastinal hematoma, n (%)	2 (20)	0	0.177	F
Pancreatic necrosis, n (%)	1 (10)	0	0.434	F
Anemia, n (%)	8 (80)	7 (53.8)	0.378	F
Colitis, n (%)	3 (30)	3 (23.1)	1.0	F
Gastritis, n (%)	3 (30)	2 (15.3)	0.617	F

Notes: OHMK — acute cerebrovascular accident; F — 2-tailed Fisher's exact test

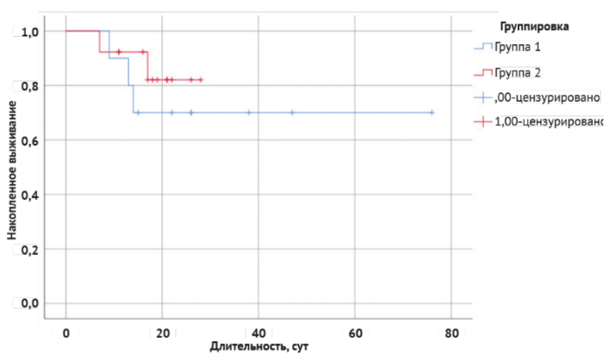
Table 7

Patient outcomes

Indicators	Group 1 (n=10)	Group 2 (n=13)	p	Criterion
MVL duration, days	3.5 (2; 8)	1.0 (1; 2)	0.014	U
Duration of vasopressor support, days	2.5 (1; 4)	1.0 (1; 2)	0.214	U
ICU length of stay, days	16.5 (14; 25)	9.0 (7; 16)	0.034	U
Hospital length of stay, days	24.0 (14; 38)	18.0 (16; 21)	0.292	U
Mortality, n (%)	3 (30%)	2 (15%)	0.475	K–M

Notes: MVL – mechanical lung ventilation; ICU - intensive care unit; U—nonparametric Mann–Whitney U test; K-M – Kaplan-Meier method

Mortality was also higher in group 1 – 30% compared to 15% in group 2, p = 0.473 (Fig. 1).



	Chi-square	Statistical significance, p
Log Rank (Mantel-Cox)	0.511	0.475

Figure. Comparison of survival in the study groups using the Kaplan–Meier method

DISCUSSION

In patients with novel coronavirus infection COVID-19 who required cardiac surgery, the severity of the disease and the risk of adverse outcome increased [19]. Thus, in a large multicenter research conducted in the USA, the results of treatment of 37,769 cardiac surgery patients from 2011 to 2022 were assessed [20]. Of these, 7,269 patients underwent surgery during the pandemic. Compared to the outcomes before the pandemic, they developed AKI significantly more often: 3.2 and 2.5%, respectively; RRT was more often required: 2.5% and 1.7%, respectively; relative risk of death – 1.398 (95% CI 1.179–1.657) – and treatment costs were higher. One of the main risk factors for the development of AKI in patients with COVID-19 is CKD; these same patients also experience a more severe course of COVID-19 with an unfavorable outcome [21, 22]. On the other hand, patients with COVID-19 who have experienced AKI often develop CKD. Thus, according to a study from the UK, 3 months after discharge, 16% of patients developed CKD, 5% required RRT upon discharge from hospital; in-hospital mortality in patients with AKI and COVID-19 was 31.9%, compared with 14% ($p < 0.001$, statistically significant) in patients without renal impairment [23]. In our study, AKI requiring RRT developed in patients of group 1, where 90% of patients had a history of CKD.

To make a decision on starting RRT in a patient after cardiac surgery, the patient's clinical condition, the severity of organ dysfunction, the level of uremia, the need for correction of metabolism, disorders of water-electrolyte metabolism and acid-base balance were assessed. In recent years, a lot of work has been devoted to the timing and indicators that need to be focused on when starting RRT. According to the STARRT-AKI trial [24], when comparing data from the "early" RRT start group and the "standard" RRT start group, there were no statistically significant differences in 90-day mortality: 43.9% and 43.7%, respectively. The "early" RRT group had a shorter ICU stay but more complications such as hypotension and hypophosphatemia. At the same time, if the start of RRT is delayed, the risk of an unfavorable outcome increases. Thus, in the AKIKI-2 trial, when comparing data from stage 3 AKI group with those in later RRT initiation group (urea more than 50 mmol/l, SCr - 521 µmol/l), multivariate analysis showed that 60-day mortality was higher in the "later" group: 44% and 55%, respectively [25]. In a 2021 meta-analysis [26], "earlier" RRT initiation was not associated with a difference in mortality compared with data in the comparison group: 45.5% and 46.6%, respectively; but in the subgroups of surgical ICU patients and RRT, "earlier" RRT resulted in a statistically significant reduction in mortality. In our study, we began to use RRT methods 2 days after surgery, at stages 1–2 of AKI, focusing more on the rate of diuresis, level of hydration, indicators of electrolyte balance and acid-base status of the blood.

The cytokine storm that occurs as a result of SARS-CoV2 infection is the main mechanism leading to the development of acute respiratory distress syndrome (ARDS) and multiple organ failure in COVID-19. To combat the cytokine storm during COVID-19, various pharmacological drugs that block inflammatory mediators are used. At the same time, to eliminate a wide range of inflammatory mediators – chemokines, pro- and anti-inflammatory cytokines, PAMP and DAMP molecules – it is possible to use PE and selective hemoadsorption of cytokines. In patients with COVID-19, the use of PE was accompanied by a decrease in blood levels of interleukin (IL)-6, IL-10, and CRP [27, 28]. A randomized controlled trial [29] on the use of PE in patients with severe COVID-19 (signs of ARDS in accordance with the Berlin definition, severity of the condition on the APACHE II scale more than 20 points) revealed that in the PE group there was a statistically significant decrease in the duration of MVL and ICU stay, and organ dysfunction was eliminated more quickly. Mortality in the PE group was 20.9% compared to 34.1% in the comparison group, p=0.09, statistically significant. In a meta-analysis published in 2023, the use of hemoadsorption of cytokines was accompanied by a decrease of CRP and IL-6 levels in the blood, and hospital mortality was 42.1% [30]. At the same time, in a recently published meta-analysis [31], the use of the selective cytokine hemosorbent CytoSorb (CytoSorbents Corporation, USA) was not accompanied by an improvement in survival either in the overall group of patients: OR = 1.07 (0.88, 1.31) or in the subgroups with sepsis OR=0.98 (0.74; 1.31); against the background of cardiovascular surgery: OR=0.91 (0.74; 1.31); with COVID-19 OR=1.58 (0.50, 4.94). There were no statistically significant changes in lactate and IL-6 levels after hemoperfusion sessions, and no differences in the duration of ICU stay. The authors believe that further research is needed to identify those patients for whom selective cytokine absorption procedures will be indicated. In our study, the timely use of a combination of RRT and ECHC methods made it possible to stop the progression of the cytokine storm and multiple organ dysfunction.

CONCLUSION

The results obtained confirm the need to take into account risk factors for the development of AKI in patients with COVID-19 who have undergone cardiac surgery under cardiopulmonary bypass, constant monitoring of serum creatinine blood levels and diuresis rate to identify early signs of AKI development and to make a timely decision on RRT initiation. Timely use of ECHC and RRT methods prevents the progression of the cytokine storm and multiple organ failure.

FINDINGS

1. In patients with COVID-19 who require cardiac surgery, the development of acute kidney injury worsens the prognosis of the disease, and is accompanied by a statistically significant increase in the duration of mechanical ventilation, the median was 3.2 days compared to 1.0 days in group 2, and the period of intensive care unit stay was 16.5 days and 9 days, respectively.
2. In the 1st group patients, mortality was 30%, in the 2nd – 15%, p = 0.475; patients with acute kidney injury had a tendency towards a more frequent development of postoperative complications – for example, acute cerebrovascular accident occurred in 20% and 7.7% of cases, respectively, the differences were not statistically significant, anemia - in 80% and 53.3%, the differences were also not statistically significant, mediastinal hematoma developed in 20% of patients in group 1 only.
3. Risk factors for the development of acute kidney injury in the postoperative period were elevated urea levels and a history of chronic kidney disease. In patients of group 1, the level of intraoperative blood loss was 41.7% higher than in group 2, but the differences were not statistically significant.

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