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RESEARCH ARTICLE

Effect of Previous Coronavirus Disease 2019 Infection on Patients Undergoing Open-Heart Surgery

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ABSTRACT

Objectives: This study aimed to evaluate the effects of previous coronavirus disease 2019 (COVID-19) infection on mortality, factors influencing mortality, and potential postoperative complications in on-pump cardiac surgery.

Methods: This single-center, retrospective, observational study included 233 adult patients who underwent on-pump cardiac surgery between June 2021 and February 2022. Patients with preoperative history of COVID-19 infection confirmed by nasopharyngeal swab polymerase chain reaction (PCR) test were compared to those without COVID-19 history.

Results: Patients' mean age was 60.12±11.26 years (range, 23–81 years), and 77.3% were male. The mean time from PCR positivity to surgery was 191.11±169.9 days (median, 108 days). No between-group differences were observed in anesthesia, cross-clamp time, pump time, operative time, extubation time, length of intensive care unit and hospital stay, or mortality (p>0.05). The post-COVID-19 group had higher rates of preoperative acute neurologic events and arrhythmias, pump lactate levels, and intraoperative inotropic scores (p<0.05). These factors were not associated with survival. Postoperative pneumothorax was more frequent in the post-COVID-19 group (p=0.002) and associated with longer length of hospital stay. No significant difference was observed in preoperative, postoperative, or changes in neutrophil/lymphocyte ratio (NLR) between groups.

Conclusion: Patients with and without COVID-19 history had similar outcomes after open-heart surgery. Nevertheless, the former had increased frequency of postoperative pneumothorax and prolonged length of hospital stay. Open-heart surgery seems safe after COVID-19. However, larger, prospective studies including inflammatory markers other than NLR are needed to further investigate the potential complications.

Keywords: Complications, neutrophil/lymphocyte ratio, open heart surgery, post-COVID-19,

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Introduction

Coronavirus disease 2019 (COVID-19), which is caused by the SARS-CoV-2 virus, was first reported in Wuhan, China, in December 2019 and declared a pandemic by the World Health Organization on March 11, 2020. It spread rapidly worldwide, causing an unprecedented global health crisis.[1] Early in the pandemic, the presence of COVID-19 was associated with sevenfold higher mortality in patients undergoing heart surgery (24.5% vs. 3.5%, p<0.0001).[2] In addition, COVID-19 infection after open-heart surgery was associated with increased rates of pneumonia and mortality.[3] At present, many patients with COVID-19 history are undergoing cardiac surgery. One study indicated that COVID-19 history in patients undergoing cardiothoracic surgery was not associated with significant mortality and morbidity, but 92.86% of these patients underwent beating-heart surgery.[4]

Regarding the safety of on-pump cardiac surgery in patients who recovered from COVID-19, literature data are limited. Thus, the present study aimed to determine the 30-day mortality rate and assess the factors influencing mortality and postoperative complications.

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Methods

This single-center, retrospective, observational study was approved by the Izmir Katip Celebi University Ataturk Training and Research Hospital Non-Interventional Clinical Research Ethics Committee (decision number 0147, dated March 24, 2022). A total of 233 patients who underwent open-heart surgery between June 2021 and February 2022 in the cardiovascular surgery clinic were retrospectively evaluated. Patients with COVID-19 confirmed by polymerase chain reaction (PCR) test of a nasopharyngeal swab sample in the preoperative period were included in the post-COVID-19 group. Meanwhile, those without history of PCR-confirmed COVID-19 were included in the non-COVID-19 group. Patients who exhibited the clinical symptoms of COVID-19 and/or fever, who had a positive COVID-19 PCR test from a single nasopharyngeal swab sample 48 h before surgery, and who underwent off-pump (beating heart) surgery were excluded. The data were obtained from the hospital information system, patient history, and patient records.

Data including demographic data, European System for Cardiac Operative Risk Evaluation II score, risk factors, intraoperative variables, postoperative clinical outcomes, complications (pneumothorax, acute kidney injury, thrombosis, coagulopathy, acute neurological event, revision surgery, bleeding), length of hospital stay, length of intensive care unit (ICU) stay, and 30-day mortality were noted. Preoperative and postoperative 24-h leukocyte, lymphocyte, and neutrophil levels were determined, and the neutrophil/lymphocyte ratio (NLR) was calculated.

With regard to the post-COVID-19 group, the time from COVID-19 infection to surgery and the clinical presentation of COVID-19 were also recorded. Renal failure was defined according to Kidney Disease: Improving Global Outcomes staging. The inotrope score (IS) was determined using the following formula: dopamine dose (mcg/kg/min)+dobutamine dose (mcg/kg/min)+100×epinephrine dose (mcg/kg/min).[4] This study was conducted in accordance with the tenets of the 1964 Declaration of Helsinki and its later revisions.

Statistical Methods

Statistical analysis was performed using IBM SPSS version 26 software. Categorical variables were expressed as number and percentage, whereas continuous variables as mean, standard deviation, range, median, and interquartile range (25th–75th percentile). Pearson's chi-square and Fisher's exact tests were used for comparison of categorical variables between groups. The Mann–Whitney U test was used for pairwise comparisons of continuous variables because the data were not normally distributed (Kolmogorov–Smirnov $p<0.05$). Univariate logistic regression analysis was used to evaluate variables thought to be associated with mortality. Statistical significance was considered at $p<0.05$.

Results

A total of 233 patients (61 in the post-COVID-19 group, 172 in the non-COVID-19 group) who underwent on-pump open-heart surgery were evaluated. The mean age was 60.12±11.26 years (range, 23–81 years), and 77.3% of patients were male. The mean ejection fraction was 53.57%±10.41%. The mean length of ICU and hospital stay was 4.38±3.99 days (range, 2–40 days) and 15.63±6.63 days (range, 3–54 days), respectively.

In the post-COVID-19 group, the clinical course of COVID-19 infection was as follows: nine patients (14.8%) were asymptomatic, 40 patients (65.6%) were mildly symptomatic requiring home care, 10 patients (16.4%) had moderate symptoms requiring hospitalization, and 2 patients (3.3%) had severe symptoms requiring ICU admission. Among all patients, 81.7% had received at least one dose of COVID-19 vaccine, whereas 18.3% were unvaccinated. No statistically significant difference was observed in the vaccination rate between the two groups (Table 1).

The mean number of days from PCR positivity to surgery was 191.11±169.9 days, and the median interval was 108 days (range, 8–523 days). The post-COVID-19 group had significantly higher preoperative acute neurological events and arrhythmias than the non-COVID-19 group ($p=0.037$ and $p=0.012$, respectively). Meanwhile, the non-COVID-19 group had higher frequency of coronary artery bypass graft (CABG) surgery compared with the post-COVID-19 group. Most cases (89.5%) were elective, whereas the remaining 10.5% were emergency surgeries. Table 1 shows a comparison of preoperative characteristics, demographic data, and surgical types.

The 30-day mortality rate was 3.3% in the post-COVID-19 group and 2.9% in the non-COVID-19 group ($p>0.05$). Table 2 shows a comparison of mortality rates and cause of death.

No difference was observed in the anesthesia time, cross-clamp time, pump time, or operative time between groups ($p>0.05$). However, the post-COVID-19 group had significantly higher pump lactate levels and intraoperative IS than the non-COVID-19 group ($p=0.000$ and $p=0.037$, respectively). Table 3 shows the intraoperative data.

The prevalence of postoperative pneumothorax was higher in the post-COVID-19 group than in the non-COVID-19 group ($p=0.002$) (Table 4). Patients in the post-COVID-19 group who developed pneumothorax had longer hospital stays, and the frequency of pneumothorax was higher in patients admitted to the ICU ($p<0.05$) (Table 5).

Table 1. Preoperative characteristics, demographic data, and types of operation

	Post-COVID-19 group (n=61)		Non-COVID-19 group (n=172)		X^2/Z	p
	n	%	n	%		
Age (years)	61	20.5	60.5	14	–0.085	0.932
Sex (male)	42	68.9	138	80.2	3.319	0.068
EuroSCORE	2	1.28	2	1.58	–0.648	0.517
EF	55	10	60	10	–0.778	0.437
BMI (kg/m²)	28 (3.5)		27.4 (4)		–0.134	0.893
DM	24	39.3	68	39.5	0.001	0.979
Smoking	25	41	92	53.5	2.817	0.093
HT	39	63.9	106	62.4	0.048	0.826
COPD	8	13.1	32	18.8	1.022	0.312
Acute neurological event	8	13.1	8	4.7	5.044	**0.037**
Pneumothorax	2	3.3	–	–	5.410	0.068
At least 1 dose of vaccine	53	86.9	72	78.3	1.825	0.177
Arrhythmia	20	32.8	30	17.4	6.291	**0.012**
NLR	2.36 (1.89)		2.48 (1.63)		–0.737	0.461
PaO_2 (mmHg)	92 (25.65)		90.5 (23.23)		–2.797	0.056
Lactate (mmol/L)	1.2 (0.6)		1.1 (0.6)		–1.341	0.180
Surgery type						
Emergency	6	9.8	18	10.5	0.019	0.890
Elective	55	90.2	154	89.5		
Surgical procedure						
CABG	35	57.4	123	71.5	4.122	**0.042**
If CABG, no. of vessels	3	1	3	1	–0.513	0.608
AVR	9	14.8	12	7	3.321	0.068
MVR	6	9.8	17	9.9	0.000	0.991
AVR+MVR	1	1.6	5	2.9	0.288	1.000
Valve+CABG	4	6.6	10	5.8	0.044	0.763
Ascending aortic aneurysm	6	9.8	8	4.7	2.143	0.205
Aortic dissection	3	4.9	4	2.3	1.039	0.382

EuroSCORE: European System for Cardiac Operative Risk Evaluation; EF: Ejection fraction; BMI: Body mass index; DM: Diabetes mellitus; HT: Hypertension; COPD: Chronic obstructive pulmonary disease; NLR: Neutrophil/lymphocyte ratio; PaO_2: Arterial partial pressure of oxygen; CABG: Cardiac artery bypass graft; AVR: Aortic valve repair; MVR: Mitral valve repair

Table 2. Rates and causes of mortality

	Post-COVID-19 group (n=61)		Non-COVID-19 group (n=172)		Total		X^2	p
	n	%	n	%	n	%		
Mortality								
Yes	2	3.3	5	2.9	7	3	0.021	1.000
No	59	96.7	167	97.1	226	97		
Cause of death								
MODS	2	100	3	60	5	71.4	1.12	1.000
ARDS	0	0	2	40	2	28.6		

MODS: Multiorgan dysfunction syndrome; ARDS: Acute respiratory distress syndrome

Table 3. Intraoperative findings

	Post-COVID-19 group (n=61)	Non-COVID-19 group (n=172)	X²/Z	p
Anesthesia time (min)	240 (75)	240 (85)	−1.091	0.275
Operative time (min)	220 (70)	220 (85)	−0.520	0.603
Pump time (min)	82 (48.5)	80 (36.5)	−0.946	0.344
Cross-clamp time (min)	47 (35.5)	44 (22.5)	−1.713	0.087
Total blood loss (mL)	400 (250)	400 (200)	−1.364	0.172
IS	10 (15)	5 (13.5)	−2.086	**0.037**
Pump PO_2 (mmHg)	271 (68.5)	270 (58.25)	−0.140	0.889
Pump lactate (mmol/L)	1.3 (1.05)	1 (0.6)	−3.510	**0.000**

IS: Inotrope score; PO_2: Partial pressure of oxygen

Table 4. Postoperative data and complications

	Post-COVID-19 group (n=61)	Non-COVID-19 group (n=172)	X²/Z	p
Extubation time (h)	9 (3.75)	9.15 (4.28)	−1.078	0.281
Prolonged weaning (>24 h)	7 (11.5)	18 (10.6)	0.037	0.848
Length of ICU stay (days)	4 (2)	3 (2)	−1.366	0.172
Length of hospital stay (days)	15 (5)	15 (7)	−1.066	0.286
AKI	12 (19.7)	30 (17.6)	0.124	0.725
Pneumothorax	12 (19.7)	10 (5.9)	9.907	**0.002**
Pneumonia	4 (6.6)	6 (3.5)	0.994	0.298
Arrhythmia	19 (31.1)	41 (24.1)	1.154	0.283
Acute neurological event	2 (3.3)	2 (1.2)	1.166	0.285
Revision surgery	8 (13.1)	27 (15.9)	0.267	0.605
Postoperative bleeding	13 (21.3)	54 (31.8)	2.382	0.123
PO_2 (mmHg)	101 (42)	102 (45.78)	−2.208	0.067
Lactate (mmol/L)	1.6 (1.4)	1.4 (1.2)	−1.691	0.091
Hematocrit (%)	29.5 (4.75)	29 (5.15)	−0.318	0.751
NLR	19 (17.13)	16.51 (12.86)	−1.468	0.142

h: Hour; ICU: Intensive care unit; AKI: Acute kidney injury; PO_2: Partial pressure of oxygen; NLR: Neutrophil/lymphocyte ratio

In univariate logistic regression analysis of variables that may affect survival in the post-COVID-19 group, NLR was not a significant predictor of survival (Table 6).

Postoperative NLR was significantly higher than preoperative NLR in both groups ($p<0.05$). When the post-COVID-19 and non-COVID-19 groups were compared, there was no statistically significant difference between groups in terms of preoperative and postoperative NLR or change in NLR ($p>0.05$) (Table 7). Figure 1 shows the mean preoperative and postoperative NLR of all patients and both groups. Figure 2 shows the difference between preoperative and postoperative NLR in both groups.

Discussion

In this study, similar clinical outcomes and mortality rates were observed in patients undergoing on-pump open-heart surgery with and without history of COVID-19 infection. However, the post-COVID-19 group had more frequent postoperative pneumothorax, and those who developed pneumothorax postoperatively had longer hospital stays. Moreover, the post-COVID-19 group had higher rates of acute neurological events and arrhythmia preoperatively and increased intraoperative IS and pump lactate levels. The results showed that the inflammatory marker NLR and postoperative changes in NLR were not associated with mortality.

A study comparing COVID-19-positive patients and those without COVID-19 infection undergoing open-heart surgery early in the pandemic showed that the former had longer length of ICU stay and higher mortality than the latter.[2] In the same study, comparison of patients with preoperative COVID-19 and those without COVID-19 history revealed

Table 5. Distribution of preoperative and demographic variables in recovered COVID-19 patients with and without postoperative pneumothorax

Pneumothorax	No (n=12)	Yes (n=49)	X^2/Z	p
Vaccination	41 (83.7)	12 (100)	2.255	0.337
Sex				
Female	16 (32.7)	3 (25)	0.263	0.737
Male	33 (67.3)	9 (75)		
Age (years)	61 (21.5)	62.5 (15.25)	–0.5	0.617
EF	60 (10)	55 (8.75)	–0.5	0.616
EuroSCORE	4 (4.27)	1.75 (2.8)	–1.52	0.127
Smoking	22 (44.9)	3 (25)	1.578	0.328
COPD	6 (12.2)	2 (16.7)	0.165	0.650
Obesity	13 (26.5)	3 (25)	0.012	1.000
BMI	27 (4)	28 (3.75)	–0.58	0.559
COVID-19 severity				
Asymptomatic at home	6 (12.2)	3 (25)	1.247	0.361
Symptomatic at home	35 (71.4)	5 (41.7)	3.782	0.088
Intensive care admission	0 (0)	2 (16.7)	8.444	**0.036**
Inpatient admission	8 (16.3)	2 (16.7)	0.001	1.000
Days from PCR positivity to surgery	97 (293.5)	220.5 (384)	–1.45	0.147
Preoperative pneumothorax	1 (2)	1 (8.3)	1.204	0.357
Change in NLR	15.67 (19.96)	15.18 (8.77)	–0.4	0.690
Surgical procedure				
CABG	28 (57.1)	7 (58.3)	0.006	0.940
If CABG, no. of vessels	3 (2)	3 (1)	–0.93	0.352
AVR	7 (14.3)	2 (16.7)	0.043	1.000
MVR	5 (10.2)	1 (8.3)	0.038	1.000
AVR+MVR	1 (2)	0 (0)	0.249	1.000
Valve+CABG	2 (4.1)	2 (16.7)	2.492	0.170
Aneurysm	6 (12.2)	0 (0)	1.63	0.588
Dissection	3 (6.1)	0 (0)	0.773	1.000
Postoperative outcomes				
Duration of MV (h)	9 (3.75)	9 (3.75)	–0.05	0.956
Length of ICU stay (days)	3 (2)	4.5 (2.75)	–1.05	0.294
Length of hospital stay (days)	14 (5.5)	18 (6)	–2.28	**0.023**

EF: Ejection fraction; EuroSCORE: European System for Cardiac Operative Risk Evaluation; COPD: Chronic obstructive pulmonary disease; BMI: Body mass index; PCR: Polymerase chain reaction; NLR: Neutrophil/lymphocyte ratio; CABG: Coronary artery bypass graft; AVR: Aortic valve repair; MVR: Mitral valve repair; MV: Mechanical ventilation; ICU: Intensive care unit

no significant difference in terms of mortality.[2] In the present study, the 30-day mortality rate in the post-COVID-19 group was similar to that in the non-COVID-19 group (3.3% vs. 2.9%, respectively, p>0.05). Similarly, in another study that evaluated cardiothoracic surgery in post-COVID-19 and non-COVID-19 patients, previous COVID-19 infection was not associated with mortality. However, this study evaluated 35 post-COVID-19 patients, of whom 28 underwent CABG and only two had on-pump cardiac surgery. The complications and survival rates were similar in both groups.[5] In another study, cardiac surgery could be performed safely in patients who had preoperative COVID-19 infection, especially after asymptomatic or clinically mild infection. This study demonstrated the early effects of the pandemic, with a mean of 46.3 days from COVID-19 PRC test to surgery.[6] In the present study, the mean time from PCR positivity to surgery was 108 days (range, 8–523 days). Thus, our results reflect the later effects of the pandemic. There are few data in literature on whether on-pump cardiac surgery can be safely performed in patients who have recovered from COVID-19, making our study an important contribution to literature.

When complications were compared between groups in the present study, the results showed that postoperative pneumothorax occurred more frequently in the post-COVID-19 group than in the non-COVID-19 group (19.7%

Table 6. Results of univariate logistic regression analysis of factors that may be associated with mortality in the post-COVID-19 group

Post-COVID group	B	p	OR	95% CI	
Postoperative pneumothorax	–18.046	0.999	0.000	0.000	
Preoperative acute neurological event	–17.964	0.999	0.000	0.000	
Preoperative arrhythmia	0.744	0.606	2.105	0.125	35.5
Postoperative arrhythmia	0.823	0.568	2.278	0.135	38.469
Preoperative NLR	–0.001	0.995	0.999	0.770	1.297
Postoperative NLR	–0.220	0.240	0.803	0.556	1.158
Preoperative lactate	–0.584	0.672	0.557	0.037	8.365
Pump lactate	–7.988	0.152	0.000	0.000	18.706
Postoperative lactate	–3.597	0.166	0.027	0.000	4.452
Days from PCR positivity to surgery	0.001	0.803	1.001	0.993	1.009

OR: Odds ratio; CT: Computed tomography; NLR: Neutrophil/lymphocyte ratio; PCR: Polymerase chain reaction

Table 7. Preoperative and postoperative values and postoperative changes in NLR

	Post-COVID-19 group		Non-COVID-19 group		
	Median (IQR)	p^1	Median (IQR)	p^1	p^2
Preoperative NLR	2.36 (1.89)	**<0.001**	2.48 (1.63)	**<0.001**	0.461
Postoperative NLR	19 (17.13)		16.51 (12.86)	0.142	
Change in NLR	15.67 (17.28)		13.76 (11.44)	0.209	

P^1: Preop vs. postop; P^2: Post-COVID-19 vs. non-COVID-19 groups. The preoperative to postoperative change in NLR was statistically significantly in both groups (p1<0.05). Postoperative NLR was significantly higher than preoperative NLR. Both groups did not differ significantly in terms of preoperative, postoperative, or change in NLR (p2>0.05). NLR: Neutrophil/lymphocyte ratio; IQR: Interquartile range

vs. 5.9%) (p=0.002). However, this did not have a significant impact on survival, despite a significantly longer mean length of hospital stay in recovered COVID-19 patients with postoperative pneumothorax. Other complications occurred at similar rates in both groups. One study indicated that 7.4% of post-COVID-19 patients develop pneumomediastinum, and 8.6% develop pneumothorax.[7]

Although many case reports cite an increase in the rate of pneumothorax in post-COVID-19 patients,[8–10] data on this finding after cardiac surgery are limited. In their study evaluating the effect of COVID-19 infection on cardiac surgery outcomes, Thomas et al.[5] evaluated preoperative chest computed tomography (CT) findings and detected emphysematous and fibrotic changes in 2.85% and 42.8% of patients, respectively. In our clinic, routine chest CT was not performed in all patients who recovered from COVID-19. Therefore, we do not have clear data regarding preoperative emphysematous and fibrotic findings in our patients. Of course, many factors related to the surgical technique and anesthesia administration in the preoperative, perioperative, and postoperative period can lead to respiratory complications (including pneumothorax) in patients undergoing heart surgery.[11] It is difficult to say whether this finding is associated with previous COVID-19 infection. However, the increase in postoperative pneumothorax independent of surgical procedure in patients with COVID-19 history may be a late complication. Moreover, the longer hospital stays in these patients suggest that this finding warrants further investigation.

The long-term effects of COVID-19 are a result of endothelial dysfunction characterized by macro- and microvascular thrombosis secondary to inflammation, especially in the cardiovascular and respiratory system.[7,11,12] Previous COVID-19 infection has been proven to be a high-risk factor for cardiovascular problems (especially cardiac rhythm disorders) and cerebrovascular events.[7,13] This is supported by the higher rates of preoperative arrhythmia and neurological events in the post-COVID-19 group in the present study.

The NLR changes in both groups were compared to evaluate a possible relationship between endotheliopathy and increase in pneumothorax. However, this parameter was not found to be associated with pneumothorax development or survival.

According to the results of a cohort study involving approximately 3,000 patients, a postoperative increase in NLR in patients undergoing cardiac surgery was associated with

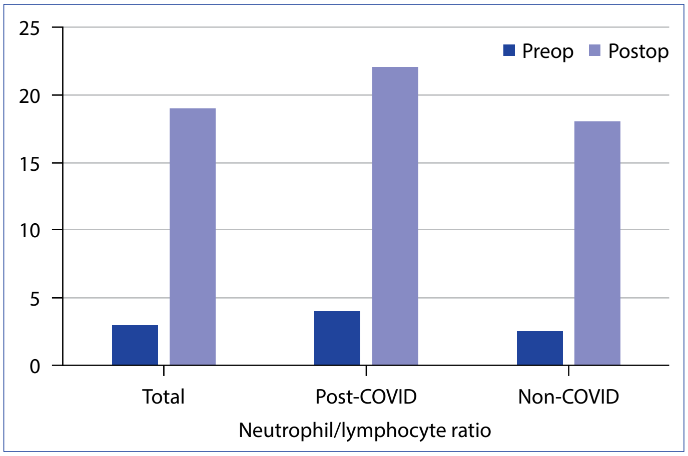

Figure 1. Preoperative and postoperative neutrophil/lymphocyte ratio (NLR).

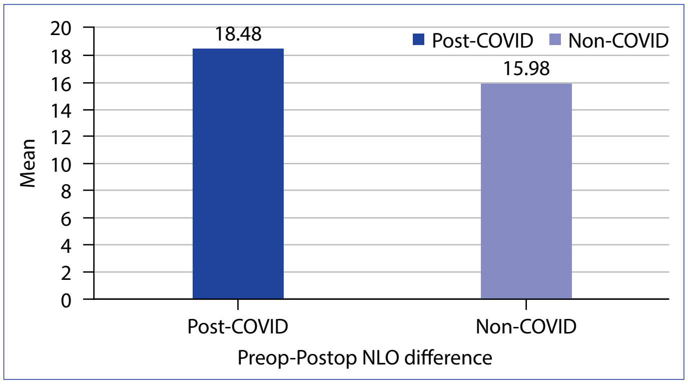

Figure 2. Preoperative to postoperative change in neutrophil/lymphocyte ratio (NLR) in the post-coronavirus disease 2019 (COVID-19) and non-COVID-19 groups.

higher mortality and longer hospital and ICU stay, and was found to be an independent prognostic biomarker.[14] In the present study, postoperative NLR was significantly higher than preoperative NLR in both groups ($p<0.05$). However, NLR and its change had no effect on survival in either group. This finding is inconsistent with literature and may be related to our small patient series.

Early-onset hyperlactatemia after cardiac surgery is related to many common hypoxic and non-hypoxic factors associated with major morbidity and mortality (e.g., drug therapy, cardioplegia, cardiopulmonary bypass, and hypothermia).[15] In one study, a threefold or greater increase in baseline intraoperative lactate level in adult cardiac surgery was found to be an important determinant of length of ICU stay, postoperative renal failure, and mortality.[16] Another study of on-pump CABG surgery showed that the risk of postoperative complications increased in patients with elevated lactate levels after high IS.[17] In the present study, pump lactate levels and IS were higher in the post-COVID-19 group than in the non-COVID-19 group but did not have a significant effect on survival. Studies with larger sample sizes may elucidate the clinical significance of this finding.

Limitations

This study was retrospective. Therefore, the findings must be supported by prospective randomized controlled studies. The small patient sample may also limit the generalization of the results reported here. In addition, NLR was the only inflammatory marker that could be evaluated in this study. The results of laboratory tests such as serum fibrinogen, D-dimer, C-reactive protein, and procalcitonin were not available. The ability to perform advanced preoperative imaging in patients who recovered from COVID-19 may provide guidance regarding potential postoperative complications.

Conclusion

Patients with and without a history of COVID-19 had similar outcomes after open-heart surgery. However, the increased frequency of postoperative pneumothorax and the prolonged length of hospital stay in post-COVID-19 patients who developed pneumothorax are noteworthy. Open-heart surgery seems safe after COVID-19. Nevertheless, larger, prospective studies including inflammatory markers other than NLR are needed to further investigate the potential complications.

Disclosures

Ethics Committee Approval: The study was approved by The İzmir Katip Çelebi University Non-interventional Clinical Research Ethics Committee (Date: 24/03/2022, No: 0147).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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