

Outcomes of COVID-19 infection occurring in the recovery period of the open-heart surgery

Açık kalp ameliyatının iyileşme döneminde ortaya çıkan COVID-19 enfeksiyonunun sonuçları

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ABSTRACT

Background: In this study, we aimed to examine the effect of novel coronavirus 2019 disease (COVID-19) on the healing process of patients undergoing open-heart surgery.

Methods: Between October 2020 and May 2021, a total of 22 patients (14 males, 8 females; mean age: 60±15 years; range, 18 to 82 years) who developed COVID-19 within the first 30 days after open-heart surgery were retrospectively analyzed. Since the study was conducted in the pre-vaccination period, all of the patients were unvaccinated. Demographic, operative, and laboratory data of the patients were analyzed, and morbidity and mortality rates were evaluated.

Results: Postoperative COVID-19 infection occurred in 22 of 1,171 patients who underwent open-heart surgery. Pneumonia developed in 14 (64%) patients and mechanical ventilation support was required in 50% (n=7) of them. Mortality was seen in eight (36%) patients. Only procalcitonin level (p=0.003) and age (p=0.005) had significant effects on survival.

Conclusion: Postoperative COVID-19 infection is associated with high pneumonia and mortality rates in unvaccinated patients. Protocols that can prevent false polymerase chain reaction negativity and early contamination can be life-saving.

Keywords: Cardiopulmonary bypass, COVID-19, mortality, open-heart surgery.

ÖZ

Amaç: Bu çalışmada yeni koronavirüs 2019 hastalığının (COVID-19) açık kalp ameliyatı yapılan hastaların iyileşme sürecine olan etkisi incelendi.

Çalışma planı: Ekim 2020 - Mayıs 2021 tarihleri arasında açık kalp ameliyatından sonra ilk 30 gün içinde COVID-19 gelişen toplam 22 hasta (14 erkek, 8 kadın; ort. yaş: 60±15 yıl; dağılım, 18-82 yıl) retrospektif olarak incelendi. Çalışma aşılanma öncesi dönemde yapıldığı için, hastaların tamamı aşısızdı. Hastaların demografik, ameliyat ve laboratuvar verileri incelendi ve morbidite ve mortalite oranları değerlendirildi.

Bulgular: Ameliyat sonrası COVID-19 enfeksiyonu açık kalp ameliyatı yapılan 1171 hastanın 22'sinde saptandı. Hastaların 14'ünde (%64) pnömoni gelişti ve bunların %50'sinde (n=7) mekanik ventilasyon gereksinimi oldu. Mortalite sekiz hastada (%36) görüldü. Yalnızca prokalsitonin düzeyi (p=0.003) ve yaşın (p=0.005) sağkalım üzerinde etkisi izlendi.

Sonuç: Ameliyat sonrası COVID-19 enfeksiyonu, aşılanmamış hastalarda yüksek pnömoni ve ölüm oranları ile ilişkilidir. Yanlış polimeraz zincir reaksiyon negatifliğini ve erken kontaminasyonu önleyebilen protokoller hayat kurtarıcı olabilir.

Anahtar sözcükler: Kardiyopulmoner baypas, COVID-19, mortalite, açık kalp ameliyatı.

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The COVID-19 pandemic has devastating effects all over the world. Undoubtedly, heart surgery was affected by the pandemic period. It is recommended that all elective operations should be postponed in patients infected with the novel coronavirus 2019 disease (COVID-19). However, in the case of false-negative polymerase chain reaction (PCR) test results in asymptomatic patients or early postoperative contamination, patients may suffer from COVID-19 during the recovery period. In a multi-center study consisting of 826 patients, the incidence of postoperative COVID-19 was reported as 5.8% after cardiac surgery.^[1]

The number of studies on the outcomes of COVID-19 occurring in the recovery period of open-heart surgery is very limited.^[2] In the present study, we aimed to examine the effect of COVID-19 on the healing process of patients undergoing open-heart surgery.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Health Sciences University, Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Department of Cardiovascular Surgery between October 21st, 2020 and May 9th, 2021. Patients who underwent open-heart surgery and developed COVID-19 within the first 30 days after the operation were included. Those with COVID-19 test positivity preoperatively and after the 30th postoperative day were excluded from the study. Since the study was conducted in the pre-vaccination period, all the patients were unvaccinated. During the study period, the total number of open-heart surgeries performed in our hospital was 1,171 and COVID-19 was diagnosed in 22 (2%) patients (14 males, 8 females; mean age: 60±15 years; range, 18 to 82 years).

Demographic, operative, and laboratory data were obtained from the patient files and hospital electronic registry systems. The discharged patients were called for outpatient control. The patients who did not come to the outpatient clinic due to the pandemic were interviewed by phone. Data were analyzed and the data of surviving and non-surviving patients were compared. The morbidity and mortality rates were detected.

In the preoperative period, severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) reverse transcriptase-PCR assays were routinely performed in patients within 48 h before all elective cardiac operations according to the Recommendations of the Ministry of Health of the Republic of Türkiye. The

patients with negative SARS-CoV-2 PCR tests were taken for cardiac surgery. The patients with positive SARS-CoV-2 PCR tests were consulted by the infectious diseases specialists, and their operations were postponed if not urgent.

In the postoperative period, patients were not routinely screened for SARS-CoV-2 PCR. Patients who had symptoms, pneumonic infiltration on chest X-ray, or increased acute phase reactants underwent SARS-CoV-2 PCR tests. Patients with positive PCR tests were followed in the isolated COVID-19 inpatient wards or intensive care unit (ICU). The follow-up and treatment of these patients were tailored by a team of infectious diseases and ICU specialists according to the protocols of the Republic of Türkiye, Ministry of Health.

No routine SARS-CoV-2 PCR test was applied to the individuals accompanying the patients during their hospital stay. Those with symptoms or a history of contact were not accepted as patient care attendants.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were presented in mean ± standard deviation (SD) or median (25th-75th percentile) for continuous variables and in number and frequency for categorical variables. The distribution of parameters that did not fit the normal distribution was considered abnormal. The Mann-Whitney U test was used for quantitative data comparisons. To compare qualitative data, the chi-square test was used. A *p* value of <0.05 was considered statistically significant.

RESULTS

Of a total of 22 patients, 19 (86%) were operated electively and three were operated in the emergency setting. The initial symptoms were fever (n=9), dyspnea (n=1), and fever and cough (n=2). In the remaining 10 patients, COVID-19 disease was suspected due to elevated acute phase reactants and pneumonic infiltrates on chest X-rays. In eight of the patients, the disease was developed after discharge. The mean time of SARS-CoV-2 PCR test positivity after cardiac surgery was 10.6±7.3 (range, 2 to 29) days. Demographic data of the patients are summarized in Table 1 and the types of operations in Table 2.

Pneumonia developed in 14 (64%) patients. Mechanical ventilation support was required in seven (32%) patients. Renal failure requiring dialysis was not observed, except in four (18%) patients who developed

Table 1. Demographical data of the patients (n=22)

	n	%	Mean±SD	Min-Max
Age (year)			60±15	18-82
Sex				
Female	8	36		
Male	14	64		
Diabetes mellitus	6	27		
Hypertension	8	36		
Chronic obstructive pulmonary disease	4	18		
Smoking	14	64		
Body surface area			2.0±0.2	1.5-2.2
Ejection fraction (%)			52.1±9.3	30.0-65.0
EuroSCORE II			2.0±1.9	0.5-7.5
Time to be COVID PCR (+) after the operation (day)			10.6±7.3	2.0-29.0

SD: Standard deviation; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II; PCR: Polymerase chain reaction.

multiple organ failure (MOF). Multiple organ failure was detected in six (27%) patients. The mean duration of ICU and hospital stay was 9.8±17.5 days and 22.2±20.1 days, respectively.

Eight of the 22 patients included in the study died. The overall mortality rate was 36%. No mortality was observed in emergency patients. The patients who needed mechanical ventilation support did not recover. The most common cause of death was MOF (n=6). One patient died from sepsis and the other due to possible thromboembolic complications. Detailed information on patients with mortality is shown in Table 3.

Furthermore, COVID-19 occurred in four patients during the ICU stay. Although one patient was transferred to the inpatient ward and cure was

obtained, three patients died due to MOF. During the inpatient care, COVID-19 was detected in 10 patients. Four patients needed re-admission to ICU and two of them required mechanical ventilation support. While two patients died from MOF and sepsis, recovery was achieved in the remaining eight patients. After discharge, COVID-19 developed in eight patients. Two of these patients needed re-admission to the ICU and both required mechanical ventilation support. Multiple organ failure occurred in these patients and cure was unable to be obtained. In addition, one patient died from sudden cardiac arrest during the inpatient care.

When the acute phase reactants of the patients were compared, only procalcitonin levels were significantly increased in the non-surviving patient

Table 2. Types of surgical procedures

	n	%
Coronary bypass surgery	14	64.0
Aortic valve replacement	2	9.0
Mitral valve replacement	1	4.5
Coronary bypass surgery and mitral valve replacement	1	4.5
Aortic and mitral valve replacement and coronary bypass surgery	1	4.5
Adult congenital heart surgery	1	4.5
Ascending aorta replacement	1	4.5
Ascending aorta and hemiarch replacement	1	4.5
Total	22	100.0

Table 3. Detailed information on patients with mortality

Age and Sex	Type of operation	COVID + timing	Mortality after COVID +	Cause of mortality	Morbidity	EuroSCORE II	Discharge from hospital
69/M	CABG	Postoperative 8	5 days	MOF	Pneumonia Dialysis	1.39	No
66/M	Ascending aorta replacement + CABG	Postoperative 29	2 days	Sepsis	Sternal dehiscence Pneumonia	7.46	No
72/F	CABG	Postoperative 4	4 days	MOF	Dialysis Pneumonia	2.15	No
54/F	CABG	Postoperative 10	6 days	MOF	Pneumonia	1.27	No
82/M	CABG + MVR	Postoperative 22	4 days	MOF	Dialysis Pneumonia	4.69	Yes
65/M	CABG	Postoperative 15	19 days	MOF	Pneumonia	0.87	Yes
74/M	AVR	Postoperative 10	10 days	Sudden cardiac arrest	Pneumonia	1.59	Yes
74/M	CABG	Postoperative 9	73 days	MOF	Tracheostomy Dialysis Pneumonia	1.73	No

EuroSCORE II: European System for Cardiac Operative Risk Evaluation II; CABG: Coronary artery bypass grafting; MOF: Multiple organ failure; MVR: Mitral valve replacement; AVR: Aortic valve replacement.

Table 4. The effect of serum acute phase reactants on mortality

	Surviving patients (n=14)		Non-surviving patients (n=8)		p
	Median	25 th -75 th percentile	Median	25 th -75 th percentile	
Serum fibrinogen (mg/dL)	635.0	560.0-768.0	569.5	549.0-602.0	0.404
Serum C-reactive protein (mg/L)	81.9	25.2-132.8	132.7	69.4-177.4	0.082
Serum procalcitonin (ng/mL)	0.11	0.1-0.2	2.1	0.9-5.8	0.003
Serum D-dimer (µg/mL)	2.9	2.2-7.0	4.3	0.4-7.8	0.966

(0.11 ng/mL vs. 2.1 ng/mL, respectively; p=0.003). Evaluation of the effect of serum acute phase reactants on mortality is listed in Table 4.

When the demographic and operative data were compared, there was a significant difference only in terms of age (p=0.005). Comorbidity rates of groups such as diabetes mellitus, chronic obstructive pulmonary disease, hypertension, European System for Cardiac Operative Risk Evaluation (EuroSCORE) values, the cardiopulmonary bypass, and cross-clamp times were similar (Table 5).

Fourteen patients who had COVID-19 and recovered from it after open-heart surgery did not have any cardiac complaints and did not experience any thromboembolic events during follow-up.

DISCUSSION

During this period, many centers postponed elective surgeries, and some centers were converted into COVID-19 treatment centers. Since our center is a tertiary cardiac surgical center, open-heart surgeries continued in line with the recommendations and measures of the Republic of Türkiye, Ministry of Health during the pandemic.

Except for case reports, studies on COVID-19 developing after cardiac surgery is scarce in the literature.^[3,4] To the best of our knowledge, our study is one of the largest series on this subject. Furthermore, the majority of the studies concern emergency patients.^[4,5] These patients have high surgical mortality even under normal conditions. Our study group mostly consisted

Table 5. The effect of demographic and operative data on mortality

	Surviving patients (n=14)				Non-surviving patients (n=8)				p		
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD		Median	Min-Max
Age (year)			54±15	56	18-71			70±8	71	54-82	0.402
Sex											0.005
Female	6					2					
Male	8					6					
Diabetes mellitus	3	21				3	38				0.416
Hypertension	5	36				3	38				0.933
Chronic obstructive pulmonary disease	3	21				1	13				1.000
Smoking	10	71				4	50				0.315
Cross clamping time (min)			59±56	41	15-230			55±35	52	17-117	0.920
Cardiopulmonary bypass time (min)			99±49	88	37-240			97±45	108	26-150	0.764
EuroSCORE II			1.7±1.6	0.9	0.5-5.7			2.6±2.3	1.7	0.9-7.5	0.145

SD: Standard deviation; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II.

of electively operated patients. Therefore, the effect of COVID-19 on the healing process of open-heart surgery can be seen more clearly.

The present study revealed that COVID-19 after open-heart surgery caused high pneumonia and mortality rates. All patients who were re-intubated due to COVID-19 pneumonia died. In a case series of Fattouch et al.^[5] from Italy, patients who underwent cardiac surgery during the pandemic and developed COVID-19 after the operation were evaluated. In this series of 18 patients, the mortality rate was 17%. The patients with elevated D-dimer and fibrinogen and lymphopenia after COVID-19 had worse outcomes. In our study, the mortality rate was found to be 36%. Although elevated levels of serum acute phase reactants and lymphopenia were observed during COVID-19, a significant difference was only detected in procalcitonin levels in non-survivors.

Previous studies have shown that COVID-19 is more severe in elderly, diabetic, and hypertensive patients.^[6] However, in our study, only age was significantly different between surviving and non-surviving patients. This discrepancy can be explained by the small number of our series which may reduce the reliability of the statistical analysis.

Thrombophilia due to COVID-19 is a crucial consequence.^[7] In a multi-center study conducted in China, the frequency of D-dimer elevation in patients with COVID-19 was 46%, which may be a precursor of mortality.^[8] To prevent thromboembolic complications, the anticoagulation protocol with low-molecular-weight heparin recommended by the guidelines was applied to all the patients included in the study.^[9] Based on the results, it can be speculated that the protocol is quite successful. Thromboembolic complications developed in only one (4.5%) of 22 patients. Although not confirmed by autopsy, the sudden death of the patient who was followed in the ward indicates that such a complication may have been developed.

There is still no definitive recommendation for cases requiring cardiac surgery during pandemic.^[10] Although preoperative patient preparation and postoperative follow-up were performed according to the criteria determined by the Republic of Türkiye, Ministry of Health, we encountered 22 COVID-19 cases after open-heart surgery. In three of these patients, COVID-19 was detected on the second postoperative day. We believe that infections occurring in the very early period are due to preoperative false PCR negativity. These patients may have been operated at the time

of their asymptomatic period. Alternative protocols, such as two SARS-CoV-2 PCR negative test results taken 24 to 48 h apart in asymptomatic patients or operating patients who are negative for SARS-CoV-2 PCR after one week of isolation, may reduce false PCR negativity.

The current study shows that COVID-19 which occurs after the patient is discharged may also have a very severe course. Of eight patients after discharge, three died. Undoubtedly, preventing early transmission depends on the meticulous implementation of the protocols of the Republic of Türkiye, Ministry of Health, as well as the attitudes of the patients and their relatives. Emphasizing the importance of this situation during discharge can help to prevent early transmission.

The main limitation of the present study is that it is conducted during the pre-vaccination period. Therefore, our study does not provide information about the course of vaccinated patients. The pandemic seems to be controlled by vaccination, and these developments may also make positive changes during postoperative COVID-19. However, we do not have any information about this subject yet. Moreover, a recent publication has advocated that SARS-CoV-2 antibody titers substantially decrease after open-heart surgery, leading to the impairment of the effectiveness of the vaccine.^[11] Another limitation of the study is the small number of cases which reduces the reliability of the statistical analysis. Finally, this study has a single-center, retrospective design.

In conclusion, COVID-19 occurring in the recovery period after open-heart surgery is associated with high pneumonia and mortality rates in unvaccinated patients. Protocols that can prevent false polymerase chain reaction negativity and early contamination can be life-saving.

Ethics Committee Approval: The study protocol was approved by the Health Sciences University, Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee (date/no: 13.07.2021/2021/56) and the Ministry of Health (04/06/2021/ T10_13_37). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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