Clinical and Experimental Health Sciences

Evaluation of Perioperative Complications and Mortality in Covid-19 Patients Who Had Emergency Surgery

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ABSTRACT

Objective: The risk for adverse outcomes in COVID-19 patients necessitates further scrutiny in Covid 19 patients in providing appropriate surgical indications and perioperative surgical safety precautions. In this study, we aimed to contribute to elective surgery resumption about infection with early and late postoperative complications and mortality in patients with RT-PCR (+) and clinically suspicious COVID-19 who underwent emergency surgery in our hospital.

Methods: A total of 86 patients who have been operated on in our institution for emergency surgery over the age of 18 who were diagnosed with SARS-CoV-2 infection seven days before or 30 days after surgery were enrolled in the study. In this retrospective study, the primary outcome has been established as mortality factors and survival within postoperative 30 days.

Results: Regarding the primary outcome as 30-day survival, every 1-year increase in age increased the risk of death by two folds. Patients with one or more comorbidities have an increased risk of death 13 times and those with two or more have an increased risk of death 23 times. Patients in intensive care units increase the risk of death by 8.5 times compared to those who are not hospitalized. On the contrary, an increase in hemoglobin level was shown to reduce the risk of death by 0.8 times.

Conclusion: The need for intensive care and mortality is high, especially after emergency surgery, in patients with COVID19 symptoms and more than one comorbidity. Surgical indications of such patients should be well investigated.

Keywords: COVID-19, PCR, emergency surgery, surgery complications, pandemic

1. INTRODUCTION

Coronavirus disease 2019 *(COVID-19)* was first detected in Wuhan City, China. COVID-19 was caused by a novel coronavirus called severe acute respiratory syndrome coronavirus 2 *(SARS-CoV-2)* and has caused a worldwide pandemic *(1)*. Although most patients survive the disease with mild to moderate symptoms, almost one-third of the individuals are at risk of developing acute respiratory distress syndrome *(ARDS)* due to COVID-19. This group of severe patients may require mechanical ventilation *(MV)*, intensive care, and their diseases may even result in death *(2,3)*.

The rapidly spreading epidemic has caused severe difficulties in the effectiveness and sustainability of health systems. There was a significant increase in admissions to emergency services, hospitalization to inpatient services, and admissions to intensive care units. Coronavirus disease 2019 *(COVID-19)* can lead to severe viral pneumonia. Characteristic computerized tomography *(CT)* findings in affected patients include bilateral, multilobar ground-glass opacities *(GGO)* and peripheral and posterior dispersed consolidations *(4,5)*. In addition to common symptoms such as dry cough, fever, myalgia, and/or fatigue, recent studies have identified severe secondary complications such as acute respiratory distress syndrome *(ARDS)*, acute kidney or heart injury, secondary infection, and liver dysfunction *(6,7)*.

According to most health care professionals, elective surgeries and endoscopic procedures other than emergency and oncological surgeries should be postponed to a later date during the COVID-19 pandemic. Although there is no sufficient scientific evidence yet, surgical procedures to be performed on patients diagnosed with COVID-19 involve a high risk in the postoperative period *(8)*. It is convenient to proceed with a safe non-operative treatment approach that should be considered in patients *(9)*.

Although the utilization of resources, such as hospital and intensive care unit *(ICU)* admission, is well documented in patients with COVID-19, data on surgical needs and outcomes are limited. The unexpectedly high rate of postoperative mortality in patients infected with SARS COV-2 in the global

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literatüre requires perioperative surgical safety measures like evaluating the necessity and emergency of surgery, assuring the personal protective equipment and isolated operation rooms, lastly extubating the patients in the COVID-ICUs *(10)*.

Viral pneumonia is a condition that requires treatment, but infected patients may require emergency surgery. Coronavirus infection is associated with a marked inflammatory and prothrombotic state and cytokine storm plays a vital role in critical patient groups with SARS-CoV-2 infection *(11,12)*. The inflammatory and prothrombotic process in severe COVID-19 infection may be exacerbated by surgery and immobilization, complicating postoperative recovery. It is essential to document the necessity and diversity of surgical procedures in this population in estimating risk for patients *(10,11)*.

1.2. Study Hypothesis

The risk for adverse outcomes in the perioperative period in individuals infected with SARS-CoV-2 remains uncertain. Some studies have published that the perioperative risk is high in COVID-19 patients, while some studies have no difference. It necessitates further scrutiny in Covid 19 patients to provide appropriate surgical indications and perioperative surgical safety precautions *(13)*.

In this study, we aimed to contribute to the resumption of elective surgery following hospital resources, service and ICU beds by investigating the relationship of infection with early and late postoperative complications and mortality in patients with COVID-19 who underwent emergency surgery in our hospital. The primary outcome has been established as mortality factors within 30 days postoperatively, and the secondary outcome was pneumonia, acute respiratory distress syndrome, or pulmonary complications requiring postoperative mechanical ventilation.

2. METHODS

A total of 86 patients who applied to Bursa Training and Research Hospital between 1st of April 2020 to 31st of March 2021 and who have been operated in our institution as emergency surgery via general, regional or local anesthesia were evaluated in the scope of this research. Subjects over 18 diagnosed or suspected of SARS-CoV-2 infection seven days before or 30 days after surgery were enrolled in the study. SBU Bursa Training and Research Hospital Ethics Committee approval was granted in 2021 *(protocol number: 2011-KAEK-25 2021/04-02)* and informed consent was not obtained from patients.

The study had a retrospective nature. PCR could not be evaluated in all patients. Emergency patients were operated without waiting for test results. Those with clinical and radiological findings were considered suspicious. Age, gender, and American Society of Anesthesiologists *(ASA)* physical status classification have been interpreted as the demographic variables of the study population. The time from the PCR positivity or the onset of symptoms to surgery was recorded.

The patient's preoperative symptoms *(fever, respiratory distress, etc.),* baseline characteristics such as preoperative oxygen saturation or requirement for invasive mechanical ventilation, previous medication *(antiviral agents, anticoagulants, steroids, antibiotics)* have been investigated via the hospital database. Surgery type, surgical urgency, initial laboratory values, initial radiological findings, preoperative Sequential Organ Failure Assessment *(SOFA)* score, and intraoperative variables were obtained from the patient files.

Primary outcome parameter was recorded 30-day survival and secondary outcomes were classified as postoperative respiratory complications *(atelectasis, pneumonia, Acute Respiratory Distress Syndrome [ARDS] and pulmonary aspiration),* non-pulmonary infectious complications, acute kidney injury, thrombosis-related complications (pulmonary embolism, myocardial infarction, stroke, and cardiac arrest). Duration of hospital stay, 30-day mechanical ventilation-free days, 30-day organ dysfunction-free days, and any new ICU admissions were also recorded.

The data set has interpreted the preoperative, operative and postoperative information of 96 procedures conducted between 1 April 2020 and 31 March 2021. Ten individuals were operated on twice for various reasons, and of these patients, the procedure closest to the diagnosis of SARS-CoV-2 infection was evaluated.

2.1. Statistical Analysis

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences *(SPSS)* for Windows 23.0 *(IBM Corp., Armonk, NY)* package program. Frequency and percentage were given for categorical data and median, minimum and maximum descriptive values for continuous data. "Mann Whitney-U Test" was utilized for comparisons between groups, *"Chi-Square Test"* was used for comparison of categorical variables, and *"Cox Regression Analysis"* was used for examining risk factors affecting survival. The results were considered statistically significant when the *p*-value was less than 0.05.

3. RESULTS

A total of 86 patients were enrolled in the study, and the 30-day postoperative information of all patients, except for one, was obtained. A patient whose data information could not be retrieved was transferred to another center because there was no room in intensive care units of our hospital. The study population consisted of 4 *(5%)* children, 52 men *(60%)* and 30 *(35%)* women.

We could not reach 11 PCR results due to the loss of the samples. Thirty-nine patients were negative for Sars-Cov-2 PCR. Thirty patients were positive preoperatively and six were positive postoperativly.

Table 1. *Baseline demographics and clinical features of the patients*

Characteristics (n=86)	Alive (n=61) Median (Min-Max) or n (%)	Exitus (n=25) Median (Min-Max) or n (%)	P-value
Age (years)	51 (1-92)	69 (36-90)	<0.001
<29	15 (24.6)	0 (0.0)	0.005
30-49	14 (23.0)	2 (8.0)	
50-69	18 (29.5)	12 (48.0)	
>70	14 (23.0)	11 (44.0)	
Gender			0.923
Female	22 (36.1)	10 (40.0)	
Male	39 (63.9)	15 (60.0)	
Smoking	5 (8.2)	3 (12.0)	0.686
PCR positive	38 (62.3)	13 (52.0)	0.522
ICU admission	23 (37.7)	22 (88.0)	<0.001
Duration of hospital stay (days)	7 (1-66)	13 (1-58)	0.095
Time to surgery from diagnosis	5 (1-55)	3 (1-40)	0.599
COVID-19 adherent radiology	33 (54.1)	23 (92.0)	0.002
Number of Comorbidities			<0.001
None	31 (50.8)	1 (4.0)	
1	14 (23.0)	8 (32.0)	
2 or more	16 (26.2)	16 (64.0)	
Concomitant Disease			
Hypertension	17 (27.9)	13 (52.0)	0.060
Heart Failure	5 (8.2)	4 (16.0)	0.438
Atrial Fibrillation	4 (6.6)	3 (12.0)	0.409
Coronary Artery Disease	9 (14.8)	6 (24.0)	0.353
Diabetes Mellitus	8 (13.1)	8 (32.0)	0.065
Neurologic Diseases	5 (8.2)	5 (20.0)	0.146
COPD	1 (1.6)	2 (8.0)	0.201
Malignity	5 (8.2)	3 (12.0)	0.686
Obesity	1 (1.6)	1 (4.0)	0.499
Thyroid Disease	1 (1.6)	2 (8.0)	0.201
Chronic Renal Failure	2 (3.3)	3 (12.0)	0.145
Deep Vein Thrombosis	2 (3.3)	1 (4.0)	1.000
ASA Score			<0.001
1	24 (39.3)	0 (0.0)	
2	20 (32.8)	4 (16.0)	
3	16 (26.2)	12 (48.0)	
4	1 (1.6)	9 (36.0)	
Chronic Medication	31 (50.8)	23 (92.0)	0.001
Hemoglobin g/dL	12.7 (7.5-18.4)	10.8 (6.7-14.8)	0.006
White Blood Cells 10^3/mL	11.21 (2.4-35.3)	12.99 (4.09-59.55)	0.351
Lymphocytes 10^3/mL	1.41 (0.14-13.72)	0.9 (0.16-5.06)	0.061
Plateles 10^3/mL	240 (68-612)	250 (108-637)	0.326
Neutrophil 10^3/mL	8.43 (2.22-213.00)	9.65 (2.25-57.41)	0.219
CRP mg/L	19.5 (3.11-278.0)	77 (9-493)	0.003
Fibrinogen mg/dl	494 (104-778)	466.5 (292-812)	0.914
Ferritin ng/mL	192.19 (19.91-637.00)	843 (20.5-2000)	0.013
LDH U/L	254 (100-1145)	403 (229-862)	0.104
ALT U/L	14.5 (4.0-472)	19 (5-109)	0.522
AST U/L	22 (8-611)	23 (10-196)	0.333
BUN mg/dL	15.89 (5.84-73.32)	29.77 (12.9-111.0)	<0.001
Creatinine mg/dL	0.87 (0.36-5.19)	1.08 (0.31-11.72)	0.040
INR kU/L	0.98 (0.87-11.6)	1.05 (0.1-1.23)	0.107
Hemoglobin g/dL	3.61 (0.25-80.0)	5.43 (0.98-25.82)	0.303

The overall mortality rate was 29.6% and most of these originated due to respiratory complications were 75.86%. The distribution of demographic and clinical findings of the participants within the scope of the study was given in *Table 1*. When the table is examined, there were a statistically significant difference between alive and deceased individuals in terms of age, duration of stay in intensive care, presence of radiology compatible with COVID-19, number of comorbidities, ASA score, chronic drug use, hemoglobin, CRP, ferritin, urea and creatinine counts. It was determined that there was a statistically significant relationship *(p<0.05)*. ICU admission was a strong denominator and observed in 88% of the deceased patients compared to alive subjects *(p<0.001)*. The number of comorbid diseases was another significant predictor of survival, and the deterioration has increased with the number of comorbid conditions *(p<0.001)*. On the other hand, none of the concomitant diseases had any clinically significant effect on the 30-day survival.

Table 2 indicates the distribution of the participants' preoperative evaluation results. When the table was examined, it was seen that there was a statistically significant relationship between the two groups in terms of preoperative COVID-19 symptoms such as fatigue/myalgia, respiratory distress, and encephalopathy *(p<0.005, p<0.031 and p<0.022, respectively)*. It was determined that there was a significant relationship between survival status and anesthesia type and intraoperative variables *(p<0.025)* and the majority of the deceased subjects were operated via general anesthesia *(76%)*. The intraoperative status of the patient *(stable or unstable)* has been significant as 76% of the deceased individuals were unstable cases by no means. However, no statistical significance has been observed regarding the type of surgery.

Postoperative complications were also a significant determinant of mortality. The 88% of the deceased cases had respiratory *(px-thorax tube)* problems *(p<0.001)*, 84% had infection *(p<0.001),* 80% had acute renal injury *(p<0.001)* and 96% has acute thrombotic disease *(p<0.001) (Table 3).*

Individuals in intensive care units increase the risk of death by 8.5 times compared to those who are not admitted to ICU. A COVID-19 adherent radiological findings elevated the risk of death by 7.5 times compared to those who do not *(p<0.006) (Table 4)*.

Table 2. *Distribution of participants pre-operational evaluation results*

Characteristics (n=86)	Alive (n=61)	Exitus (n=25)	P-value
	Median (Min-Max) or n (%)	Median (Min-Max) or n (%)	
Pre-operative COVID-19 Symptoms			
Headache	2 (3.3)	1 (4.0)	1.000
Fatigue/myalgia	10 (16.4)	12 (48.0)	0.005
Cough	2 (3.3)	1 (4.0)	1.000
Respiratory Distress	7 (11.5)	8 (32.0)	0.031
Fever	6 (9.8)	4 (16.0)	0.467
Diarrhea	2 (3.3)	0 (0.0)	1.000
Encephalopathy	0 (0.0)	3 (12.0)	0.022
COVID-19 Treatment	31 (50.8)	20 (80.0)	0.024
Surgery Type			0.688
Minor	19 (31.1)	6 (24.0)	
Major	42 (68.9)	19 (76.0)	
Anesthesia Type			0.025
Spinal	27 (44.3)	4 (16.0)	
Local + Sedatives	1 (1.6)	2 (8.0)	
General	33 (54.1)	19 (76.0)	
Intraoperative Status			<0.001
Stabile	45 (73.8)	6 (24.0)	
Unstabile	16 (26.2)	19 (76.0)	

Chronic medication enhanced the risk of death 8.7 times compared to non-users. On the other hand, it has been determined that those who received COVID-19 treatment had 3.4 higher risk of death times compared to those who did not *(p<0.003) (Table 4)*.

Table 3. *Distribution of post-operational complications*

Characteristics (n=86)	Alive (n=61)	Exitus (n=25)	P-value
	Median (Min-Max) or n (%)	Median (Min-Max) or n (%)	
Postoperative complications			
Respiratory (px-thorax tube)	7 (11.5)	22 (88.0)	<0.001
Infection	7 (11.5)	21 (84.0)	<0.001
Acute Renal Injury	5 (8.2)	20 (80.0)	<0.001
Acute Trombotic Disease	7 (11.5)	24 (96.0)	<0.001

Fatigue/myalgia, which was one of the preoperative symptoms, increased the risk of death 3.6 times *(p<0.001)* compared to those who did not have, and 2.8 times the risk of death compared to those who did not have respiratory distress *(p<0.017) (Table 4)*.

Table 4. *Analysis of risk factors affecting mortality*

Characteristics (n=86)	Mortality	
	Odds ratio (%95 GA)	P-value
Age (years)	1.04 (1.02-1.06)	0.001
PCR positive		
No	1.0	-
Yes	0.75 (0.34-1.65)	0.477
Number of Comorbidities		
None	1.0	-
1	13.23 (1.65-105.82)	0.015
2 or more	23.03 (3.05-173.87)	0.002
ICU admission		
No	1.0	-
Yes	8.54 (2.55-28.58)	0.001
COVID-19 adherent radiology		
No	1,0	-
Yes	7.49 (1.76-31.80)	0.006
Chronic Medication		
No	1.0	-
Yes	8.66 (2.04-36.75)	0.003
Pre-op COVID-19 Symptoms		
Fatigue/myalgia		
No	1.0	-
Yes	3.60 (1.63-7.90)	0.001
Respiratory Distress		
No	1.0	-
Yes	2.81 (1.21-6.53)	0.017
COVID Treatment		
No	1.0	-
Yes	3.35 (1.26-8.94)	0.016
Surgery Type		
Minor	1.0	-
Major	1.34 (0.53-3.35)	0.535
Hemoglobin g/dL	0.80 (0.66-0.95)	0.012
CRP mg/L	1.01 (1.00-1.02)	0.003
Ferritin ng/mL	1.001 (1.00-1.01)	0.007
BUN mg/dL	1.02 (1.01-1.04)	0.001
Creatinine mg/dL	1.24 (1.07-1.43)	0.004
INR kU/L	0.58 (0.03-7.58)	0.578
D-dimer microg/mL	0.98 (0.94-1.03)	0.449

An increase in hemoglobin level was shown to reduce the risk of death by 0.8 times *(p<0.012)*. On the contrary, it was observed that each increase in CRP *(p<0.003)*, ferritin *(p<0.007)*, urea *(p<0.001),* and creatinine *(p<0.004)* levels deteriorated the risk of death approximately by two folds *(Table 4)*.

Table 4 and figure 1 denoted the Cox Regression Analysis results conducted the risk factors affecting the 30-day survival of individuals. According to the results every increase, in age increased the risk of death by two folds. Individuals with one or more comorbidities have an increased risk of death 13 times compared to those without any, and those with two or more have an increased risk of death 23 times compared to those without.

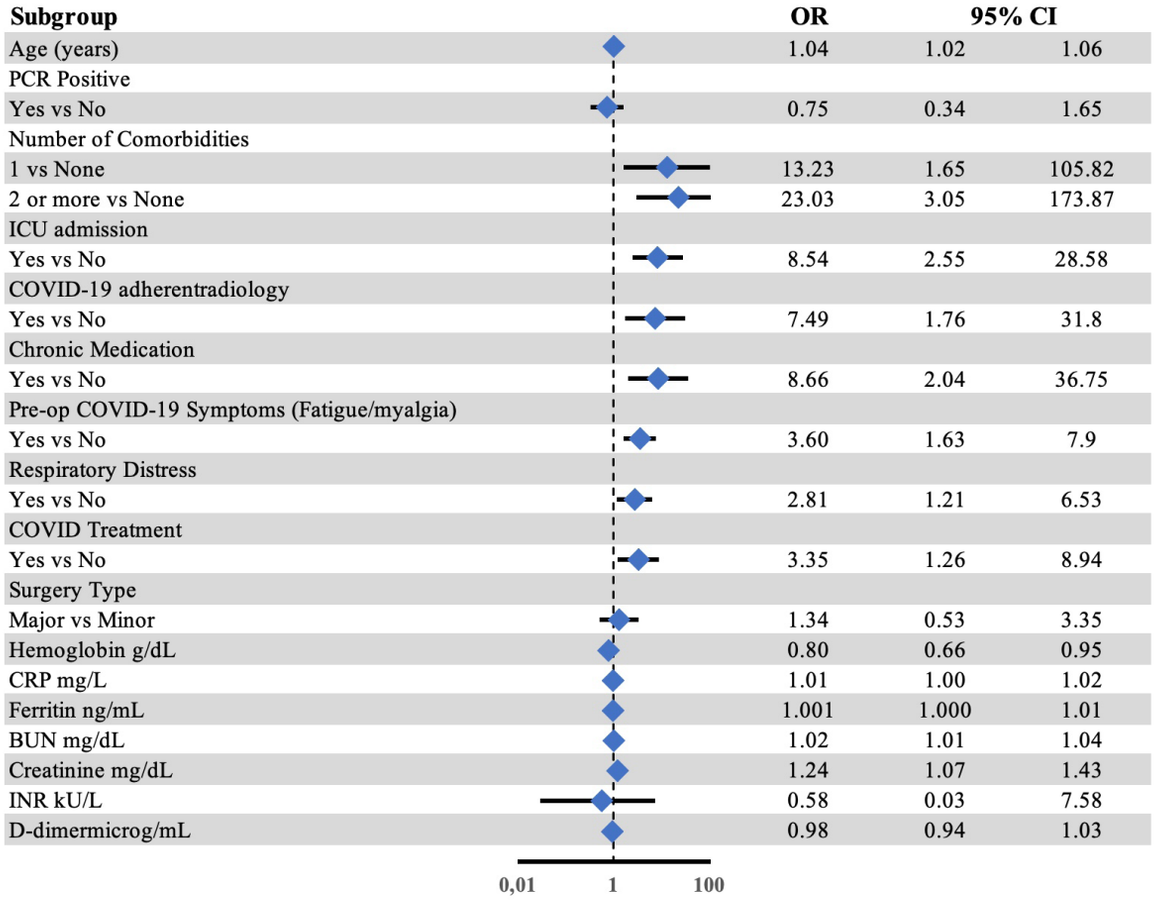

Figure 1. *Analysis of Risk Factors Affecting Mortality – Odds ratio graphic*

4. DISCUSSION

In this study, the need for intensive care is higher in advanced elderly patients who have symptoms of COVID-19 and require emergency surgery, and the mortality of these patients was found to be higher. The frightening aspect of COVID 19 infection is the lack of proven treatment and the unknowns about the disease. The global literature's high postoperative mortality rate in patients infected with SARS COV-2 warrants further scrutiny in providing appropriate surgical indications and perioperative surgical safety measures in this vulnerable patient cohort. During the COVID-19 epidemic, elective surgeries were canceled as a health management policy, Hospital organizations were urgently changed, and notable in-hospital routes and special operating rooms for COVID-19 patients were created. These practices are essential for using hospital bed capacity, providing personal protective equipment (PPE), and protecting patients and healthcare workers. The COVIDSurg Collaborative has created a predictive model regarding these pandemic originated conditions and stated that the three-month cancellation rate was 72.3% *(14)*. Most of these cancellations were situations *(90.2%) (14)*.

According to the results of COVID Surg collaborative study, the 30-day mortality rate was 23.8% for all patient groups.

The breakdown of all-cause mortality has been elaborated as 18.9% in elective operations, 25.6% in emergency patients, 16.3% in minor surgery and 26.9% in major surgery *(13)*. In the current study, we have focused on the factors affecting and found that every 1-year increase in age increased the risk of death by two folds. Individuals with one or more comorbidities have an increased risk of death 13 times compared to those without any, and those with two or more have an increased risk of death 23 times compared to those without. Individuals in intensive care units increase the risk of death by 8.5 times compared to those who were not admitted to ICU. On the contrary, an increase in hemoglobin level was shown to reduce the risk of death by 0.8 times. Nevertheless, the overall mortality rate was 29.6%, in line with the results of the COVIDSurg Collaborative international cohort study and a majority of these originated due to respiratory complications were 75.86%.

The main reason for mortality in SARS-CoV-2-infected patients in the postoperative period was pulmonary complications, accounting for 50% of the cases *(13)*. This rate of mortality was considerably high when compared to the pre-pandemic healthcare environment. The POPULAR study conducted in 211 institutions from 28 European Union Countries reported that the mortality rate due to pulmonary complications was 8% *(15)*. ARDS has been observed 50% among postoperative pulmonary complications mortality in COVIDSurg Collaborative international cohort study. The 30-day mortality was deferred in subjects with postoperative pulmonary complications *(38% versus 23.8%) (13)*. This rate has been 20% higher than the results surgical Outcomes Study published results-by Biccard et al. *(2018)* in pre-pandemic conditions *(16)*. This study found that 88% of the deceased cases had respiratory *(px-thorax tube)* problems as postoperative complications. Respiratory distress was also a statistically significant predictive factor affecting mortality. This rate was quite similar to the one of COVIDSurg Collaborative, which was 83% *(13)*.

Infection stands as another game-changing player in the streamline of SARS-CoV-2 positive individuals. COVIDSurg Collaborative international cohort study declared that 71.5% of the infections were proclaimed in the postoperative period. Only one-third of them were detected in the preoperative period as GGO in the CT scan *(13)*. In this study, the mortality rate *(84% – p<0.001)* due to infection was statistically significant for mortality. One can derive these data that perioperative SARS-CoV-2 infection is associated with high mortality. The remaining postoperative complications could be elaborated as infection, acute renal injury and acute thrombotic disease.

Nashon et al. (2020) have reviewed for COVID-19 patients asymptomatic or not tested in the preoperative period. The postoperative mortality rate of these studies has been pooled as 27.5% *(17)*. Lei et al. *(2020)* published that the postoperative death rate was 20.5%, ICU admission was 44.1%, and pulmonary complications were 100% among 34 asymptomatic COVID-19 patients who underwent elective surgery. All patients who were inadvertently scheduled for elective surgery in the incubation period of COVID-19 developed COVID-19 pneumonia with abnormal findings on computed tomography scans in the early postoperative period. *(18)*. In an Italian study by Luca et al. (2020), they reported that 32% of the cases had ICU admissions, 33.8% had postoperative pulmonary complications and 22% had acute respiratory distress in a retrospective analysis. The emergency and oncological surgeries postoperative mortality rate were 14.7%, considerably low compared to prospective data *(19)*. In our study, six patients had PCR positivity after the surgery. Four of these patients were admitted to ICU and dead in ICU. This study observed that the mortality of the patients who underwent surgery during the incubation period was high. However, this situation cannot be directly attributed to this because the comorbidities and surgeries of these patients are different.

The SARS-CoV-2 infection is associated with high rate of mortality over the globe. A majority of the severely ill patients die due to this disease. At this stage, the surgery decision should be taken by a multidisciplinary approach and conducted in benign, not postponable diseases or emergency operations. It was recommended to follow a conservative approach as delaying surgery in most cases. Thus the pandemic was an extraordinary situation and had caused multifactorial obstacles for the health institutions via limiting resources. The medical team should evaluate each case separately and conduct the surgery if the medical urgency is life-threatening such as perforation, trauma, intestinal ischemia etc.

Canceling or delaying oncological surgeries worsens patients' condition should remain throughout the pandemic. When the rate of COVID-19 infection decreases, the resumption of elective surgeries should be considered if hospital resources, service and ICU beds are sufficient to meet the demand.

The main limitation of the study could be attributed to its retrospective nature. Unfortunately, a randomized prospective study could not be conducted due to the emerging health conditions and increased patient burden with scarce sources.

5. CONCLUSION

It may be appropriate to postpone elective surgical procedures in patients with COVID19 symptoms or PCR positivity. It should be kept in mind that complications that may develop in the postoperative period and the symptoms of COVID19 may worsen, especially in patients who require urgent interventions. The urgency of the operation should be reconsidered, especially in those with the additional disease. As no one knows the exact date of COVID-19 infection eradication, this subject will require further studies and the establishment of guidelines.

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Competing interests

The authors declare that they have no competing interests.

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