

Biomarkers predicting the 30-day mortality of patients who underwent elective surgery and were infected with SARS-CoV-2 during the post-operative period: A retrospective study

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Abstract. The coronavirus disease 2019 (COVID-19) pandemic is a significant global concern that has had major implications for the healthcare system. Patients with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) undergoing elective or emergency surgical procedures have a substantial risk of mortality and peri-operative complications. The present study aimed to describe the characteristics of patients who underwent elective surgery and developed nosocomial SARS-CoV-2 infection post-surgery. Patients who underwent thoracic, upper and lower abdominal or peripheral elective surgery with a polymerase chain reaction diagnosis of COVID-19, at 3-7 days after the surgery, were enrolled in the present retrospective study. Demographics, vaccination status against SARS-CoV-2, Charlson comorbidity index (CCI) and laboratory data were recorded upon admission to the hospital unit. In total, 116 subjects (80 males, 36 females; mean age, 67.31±16.83 years) fulfilling the inclusion criteria were identified. Among the

116 participants, 14 (12.1%) were intubated. From the 116 individuals analyzed, 84 were alive after 30 days (survivors), and 32 had succumbed to the disease (non-survivors). The mortality rate was 27.6% (32/116). The non-survivors had an older age and a higher CCI score. At the evaluation upon admission to the hospital unit, the survivors presented with higher serum albumin levels and a higher number of blood lymphocytes. In addition, the survivors exhibited lower levels of lactate dehydrogenase, aspartate aminotransferase, alkaline phosphatase (ALP) and C-reactive protein (CRP), as well as a higher neutrophil to lymphocyte ratio (NLR) and CRP to albumin ratio (CAR) ($P<0.05$). The patients that were intubated had higher levels of gamma glutamyl-transferase (GGT), ALP and ferritin, as well as a higher NLR and platelet to lymphocyte ratio upon admission to the hospital unit ($P<0.05$). According to the Cox proportional hazards multivariate regression analysis, the only independent predictors of mortality and intubation were ALP and GGT upon admission, respectively ($P<0.05$). On the whole, the findings of the present study suggest that more stringent guidelines are required in order to prevent infection during the post-operative period.

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic is a major global concern that has had significant implications for the healthcare system (1). Elective surgeries have been canceled or postponed in certain hospitals worldwide, and the threshold for emergency surgery has been increased (2).

While surgical delays were frequently caused by hospital capacity and infection transmission concerns, there was also

ambiguity as regards the peri-operative hazards of individuals infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (3).

It should be noted that COVID-19 infection is linked to significant pulmonary and cardio-circulatory complications, such as respiratory failure, pneumonia, venous thromboembolism, cardiac arrhythmias, or other coagulation issues; thus, a more difficult recovery is anticipated, particularly after the performance of aggressive surgical procedures (4). As a result, major surgical societies recommended that surgeons deliver surgical care that requires local epidemiological, logistical and patient-related aspects into account. Of note, the guidelines that were created in the initial phase of the pandemic used a pragmatic approach and were based on expert opinions, as limited data were available at that time (5).

Previous studies have reported that patients with severe SARS-CoV-2 infection who underwent elective surgery had a high risk of post-operative mortality and of developing complications (6-8). According to other researchers, SARS-CoV-2-positive patients undergoing emergency surgical procedures had a substantial risk of mortality and of developing peri-operative complications as well (4). Furthermore, in a retrospective cohort study of patients undergoing surgery during the incubation period of SARS-CoV-2 infection, a significant number of patients required admission to intensive care units and had a high mortality rate (9).

However, data on the outcomes of patients undergoing surgery and becoming infected with SARS-CoV-2 during the post-operative period are limited. The present study thus aimed to describe the characteristics of patients who underwent elective surgery and developed nosocomial SARS-CoV-2 infection post-surgery, as well as to identify determinants of mortality and other unfavorable outcomes in these patients.

Patients and methods

Study design. The present study was a single-center retrospective study of patients with COVID-19 admitted to the Department of Infectious Diseases-COVID-19 Unit of Laiko General Hospital, Athens, Greece between September 21, 2020 and April 15, 2022. The study was conducted in line with the Declaration of Helsinki and was approved by the Institutional Review Board of Laiko General Hospital (protocol no. 765/12-2021). Written informed was obtained from the patients for inclusion in the study.

The following criteria were required for inclusion in the study: Patients who underwent thoracic, upper and lower abdominal or peripheral elective surgery with a polymerase chain reaction (PCR) diagnosis of COVID-19, at 3-7 days post-surgery, who had been tested negative during the pre-operative evaluation and were admitted to the Department of Infectious Diseases-COVID-19 Unit on the day of COVID-19 diagnosis. Thoracic surgery included esophagectomy. Upper abdominal surgeries included the open repair of an aortic stent leak, the resection of retroperitoneal sarcoma, gastrectomy, splenectomy, hepatectomy, nephrectomy, pancreatectomy and choleptic anastomosis.

Lower abdominal surgeries included segmental colectomy, the surgical repair of ureteroarterial fistula, cystectomy, hysterectomy, umbilical hernia repair, abdominal wall hernia repair, low anterior resection, abdominoperineal resection and renal transplantation. Peripheral surgeries included orthopedic surgeries, such as the repair of knee, hip and metatarsal fractures, and amputations due to limb gangrene.

The patients were classified into the following categories according to the severity of COVID-19 infection: Asymptomatic, mild/moderate, severe and critical, based on the clinical spectrum of SARS-CoV-2 infection (10). All patients were uniformly treated according to the National Institutes of Health (NIH) protocols (10). Some of the participants had a follow-up appointment at 1 month after their admission to the post-COVID-19 outpatient clinic of Laiko General Hospital, and if that was not possible, a telephone call was made to determine the 30-day mortality rate. The exclusion criteria were an age <18 years and a lack of data available on survival at 1 month post-diagnosis.

Investigations. Data regarding demographics, vaccination status against SARS-CoV-2 and the Charlson comorbidity index (CCI) were recorded. Hemoglobin (Hb), white blood cells, blood neutrophils, lymphocytes and immature granulocytes, neutrophil to lymphocyte ratio (NLR), platelets (PLTs), platelet to lymphocyte ratio (PLR), C-reactive protein (CRP), serum albumin, CRP to albumin ratio (CAR), serum lactate dehydrogenase (LDH), d-dimer levels, ferritin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gamma glutamyl-transferase (GGT) were recorded upon admission to the Department of Infectious Diseases-COVID-19 Unit. Charts were evaluated for the implementation of intubation and all-cause mortality at 30 days.

Statistical analysis. Continuous variables are presented as the mean (standard deviation). The assessment of the normal distribution of variables was performed with the use the Kolmogorov-Smirnov test. The comparison of normally distributed variables was performed using an independent samples Student's t-test on variables with two groups and not normally distributed variables were examined using an unpaired non-parametric two-tailed Mann-Whitney test. Categorical variables were examined using the Fischer's exact test or the Chi-squared test and are shown as absolute numbers (frequency, percentage). The CCI data were numerically recorded. To identify predictors of event(s) (event=intubation, or mortality at 30 days), statistically significant factors were subsequently examined using Cox proportional hazards multivariate regression analysis. The goodness of fit of the log-likelihood ratio was evaluated. The discriminative ability of variables was evaluated using the area under the receiver operating characteristic curve (ROC). The log-rank (Mantel-Cox) test was used to plot survival curves utilizing significant variables. Kaplan-Meier survival analysis was used to analyze time to event data and to compare two groups of subjects. Participants were censored at 30 days. P-values <0.05 were considered to indicate statistically significant differences. Statistical analysis

Table I. Demographics and baseline characteristics of the study population.

Parameter	No. of patients	Value
Age, years; mean (SD)	116	67.31 (16.83)
Sex, n (%)		
Female	36	31
Male	80	69
Mortality, n (%)		
No	84	72.4
Yes	32	27.6
Intubation, n (%)		
No	102	87.9
Yes	14	12.1
Type of surgery, n (%)		
Thoracic	10	8.6
Upper abdominal	32	27.6
Lower abdominal	35	30.2
Peripheral	39	33.6
Disease severity, n (%)		
Asymptomatic	26	22.4
Mild/moderate	30	25.9
Severe	27	23.3
Critical	33	28.3
Vaccination status, n (%)		
Unvaccinated	72	62.1
Fully vaccinated	44	37.9

SD, standard deviation.

was conducted using IBM SPSS-Statistics version 26.0 (IBM Corp.).

Results

In total, 116 subjects (80 males, 36 females; mean age, 67.31±16.83 years) fulfilling the inclusion criteria were identified. Among the 116 participants, 14 (12.1%) were intubated. From the 116 individuals examined, 84 were alive after 30 days (survivors), and 32 had succumbed to the disease (non-survivors). The mortality rate was 27.6% (32/116). The Demographics and baseline data of the study population are presented in Table I.

The non-survivors had an older age and a higher CCI score. At the evaluation upon admission to the hospital unit, the survivors presented with higher serum albumin levels and a higher number of blood lymphocytes. In addition, the survivors exhibited lower levels of LDH, AST, ALP, CRP, NLR and CAR ($P<0.05$; Table II). It was also found that the patients that were intubated had higher levels of GGT, ALP, ferritin, NLR and PLR on admission to the hospital unit ($P<0.05$; Table III).

All parameters with significant differences in the univariate analysis were analyzed using the Cox proportional hazards multivariate regression analysis. The

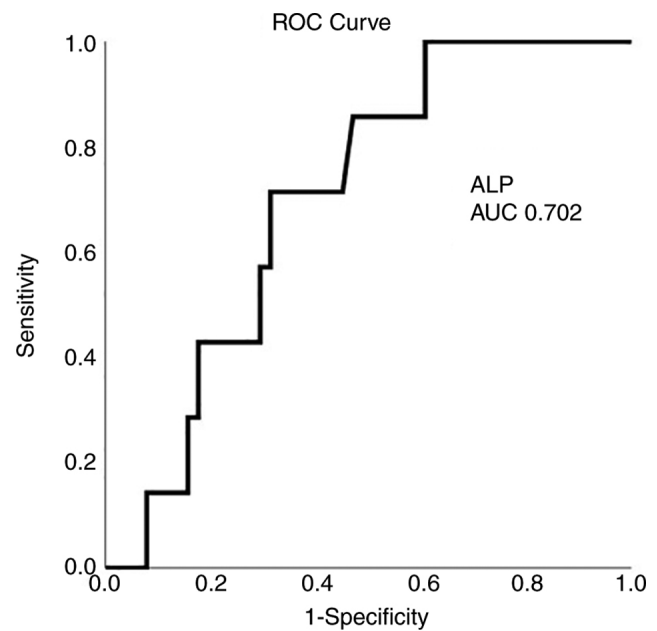


Figure 1. Receiver operating characteristic curve for ALP predicting the mortality rate of patients who underwent elective surgery and were infected with COVID-19 post-operatively. AUC, 0.702 ($P<0.05$). ALP, alkaline phosphatase; AUC, area under the curve.

outcome was all-cause mortality, and cases were censored at 30 days. The results demonstrated that the only independent predictor of mortality was the ALP levels upon admission ($P<0.05$; Table IV). The ALP levels were found to be significant predictors of mortality, as also shown by ROC curve analysis (Fig. 1). A value of ALP >122.5 U/l predicted mortality with 71.4% sensitivity and 69.6% specificity (AUC, 0.702). Kaplan-Meier survival analysis based on cut-off values for ALP revealed a worse survival for subjects with ALP levels >122.5 U/l (log-rank test for trend, $P<0.05$; Fig. 2).

Cox proportional hazards multivariate regression analysis with intubation as the outcome, identified GGT levels as a significant biomarker for the prediction of intubation ($P<0.05$; Table V). The GGT levels were also found to be significant predictors of mortality by ROC curve analysis (Fig. 3). A value of GGT >139 U/l predicted intubation with 66.7% sensitivity and 71.6% specificity (AUC, 0.742).

Discussion

According to the results of the present study, the mortality rate of patients who underwent elective surgery and were infected with SARS-CoV-2 during the post-operative period was high. In the study by Kader *et al* (11), the risk of mortality following elective orthopedic surgery was low. On the contrary, in a multicenter retrospective study by Clement *et al* (12) on mortality and risk factors related to COVID-19 following orthopedic and trauma surgery, the mortality rate of patients infected with SARS-CoV-2 was 32.4%, while in another study by the same researchers on the rate of COVID-19-associated mortality following elective hip and knee arthroplasty, the mortality rate was 20% (13).

Table II. Univariate analysis (outcome, mortality).

Parameter	Outcome	No. of patients	Mean	SD	P-value
Age, years	Recovery	84	64.95	17.97	0.03
	Mortality	32	73.50	11.48	
CCI	Recovery	80	4.30	2.61	0.01
	Mortality	36	5.94	2.37	
Hb (g/dl)	Recovery	80	10.40	1.63	0.97
	Mortality	36	10.44	1.63	
WBCs (K/ μ l)	Recovery	84	8.99	4.26	0.20
	Mortality	32	10.16	4.82	
IGs (10 ⁹ /l)	Recovery	84	0.17	0.24	0.80
	Mortality	32	0.18	0.19	
Lymphocytes (K/ μ l)	Recovery	84	1.10	0.58	0.04
	Mortality	32	0.86	0.57	
Neutrophils (K/ μ l)	Recovery	84	7.08	3.97	0.06
	Mortality	32	8.75	4.56	
PLTs (K/ μ l)	Recovery	84	396.52	420.25	0.10
	Mortality	30	269.60	111.01	
Fibrinogen (mg/dl)	Recovery	64	561.00	160.48	0.10
	Mortality	30	499.13	184.99	
Albumin (g/l)	Recovery	82	32.55	5.00	0.01
	Mortality	32	28.00	5.82	
GGT (U/l)	Recovery	82	135.76	194.38	0.26
	Mortality	32	182.00	203.80	
LDH (U/l)	Recovery	84	266.26	105.29	0.01
	Mortality	32	397.75	287.10	
ALT (U/l)	Recovery	84	36.76	31.76	0.21
	Mortality	30	81.20	191.30	
d-Dimers (μ g/ml)	Recovery	56	3.32	2.74	0.92
	Mortality	30	3.80	3.29	
Creatinine (mg/dl)	Recovery	80	1.14	0.80	0.54
	Mortality	36	1.42	1.41	
AST (U/l)	Recovery	80	35.48	27.46	0.03
	Mortality	36	150.44	284.95	
ALP (U/l)	Recovery	80	118.02	90.68	0.005
	Mortality	36	181.77	149.97	
Ferritin (ng/ml)	Recovery	66	733.74	559.13	0.06
	Mortality	32	1367.28	1917.45	
CRP (mg/l)	Recovery	78	74.74	58.34	0.003
	Mortality	36	131.87	110.36	
NLR	Recovery	80	10.16	17.31	0.01
	Mortality	36	14.56	11.43	
PLR	Recovery	80	517.53	872.83	0.33
	Mortality	34	439.11	287.33	
CAR	Recovery	76	2.40	2.03	0.004
	Mortality	36	5.44	5.58	
Sex					0.61
Female	Recovery	26			
	Mortality	10			
Male	Recovery	54			
	Mortality	26			
Type of surgery					0.15
Thoracic	Recovery	6			
	Mortality	4			

Table II. Continued.

Parameter	Outcome	No. of patients	Mean	SD	P-value
Upper abdominal	Recovery	22			0.15
	Mortality	8			
Lower abdominal	Recovery	30			
	Mortality	10			
Peripheral	Recovery	22			
	Mortality	14			
Vaccination status					
Unvaccinated	Recovery	46			
	Mortality	26			
Fully vaccinated	Recovery	34			
	Mortality	10			

SD, standard deviation; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CCI, Charlson comorbidity index; CRP, C-reactive protein; CAR, CRP to albumin ratio; GGT, gamma glutamyl-transferase; Hb, hemoglobin; IGs, immature granulocytes; LDH, lactate dehydrogenase; NLR, neutrophil to lymphocyte ratio platelets; PLTs, platelets; PLR, platelet to lymphocyte ratio; WBCs, white blood cells.

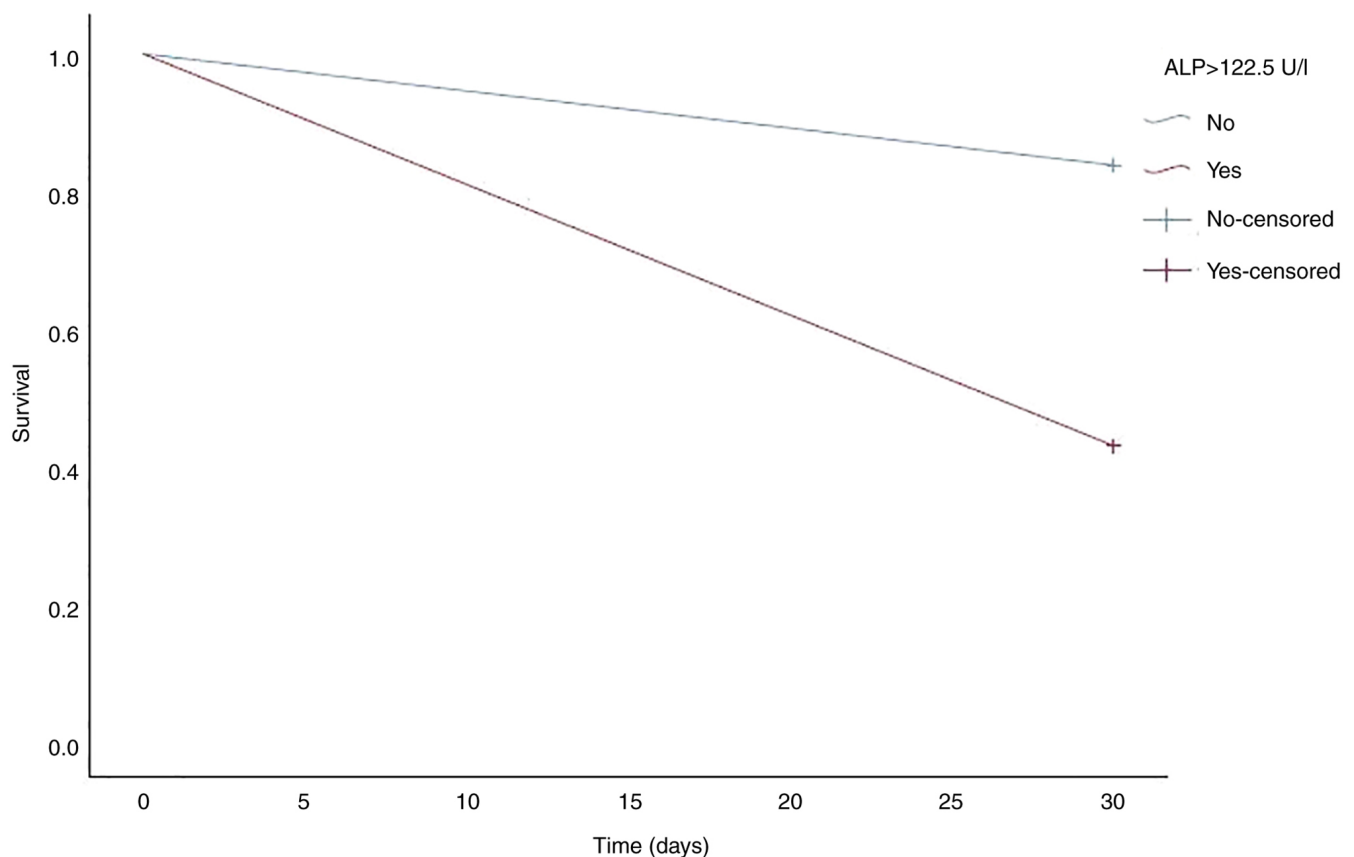


Figure 2. Kaplan-Meier survival curve. A significantly worse survival was observed for patients with ALP levels >122.5 U/l ($P < 0.05$). ALP, alkaline phosphatase.

In their study on the clinical outcomes of patients with COVID-19 following thoracic surgery, Al Masri *et al* (14) reported that the mortality rate was 25%. In that same study, fatal outcomes were associated with decreased levels of serum albumin, and an open surgical procedure, the

oxygen desaturation at the time of the COVID-19 diagnosis, and a PCR cycle threshold (Ct) value <20 were related to mortality (14). Furthermore, in their study on patients who underwent cardiac surgery and were then incidentally detected with COVID-19 post-surgery, Uysal *et al* (15)

Table III. Univariate analysis (outcome, intubation).

Parameter	Outcome	No. of patients	Mean	SD	P-value
Age, years	Non-intubated	102	67.16	17.34	0.79
	Intubated	14	68.43	12.97	
CCI	Non-intubated	102	4.73	2.61	0.57
	Intubated	14	5.43	2.92	
Hb (g/dl)	Non-intubated	102	10.43	1.62	0.83
	Intubated	14	10.31	1.70	
WBCS (K/ μ l)	Non-intubated	102	9.33	4.41	0.91
	Intubated	14	9.19	4.78	
IGs (10 ⁹ /l)	Non-intubated	102	0.17	0.24	0.75
	Intubated	14	0.15	0.14	
Lymphocytes (K/ μ l)	Non-intubated	102	1.07	0.58	0.07
	Intubated	14	0.78	0.54	
Neutrophils (K/ μ l)	Non-intubated	102	7.48	4.18	0.69
	Intubated	14	8.00	4.37	
PLTs (K/ μ l)	Non-intubated	100	369.34	392.23	0.63
	Intubated	14	318.71	91.4	
Fibrinogen (mg/dl)	Non-intubated	80	541.37	173.04	0.98
	Intubated	14	540.57	158.73	
Albumin (g/l)	Non-intubated	100	31.64	5.45	0.06
	Intubated	14	28.65	6.20	
GGT (U/l)	Non-intubated	102	130.04	179.00	0.04
	Intubated	12	307.67	273.40	
LDH (U/l)	Non-intubated	102	300.14	190.32	0.70
	Intubated	14	320.00	127.92	
ALT (U/l)	Non-intubated	100	51.56	108.86	0.39
	Intubated	14	26.28	24.13	
d-Dimers (μ g/ml)	Non-intubated	72	3.53	3.14	0.40
	Intubated	14	3.24	1.54	
Creatinine (mg/dl)	Non-intubated	102	1.21	1.05	0.48
	Intubated	14	1.34	0.89	
AST (U/l)	Non-intubated	102	70.80	174.49	0.90
	Intubated	14	73.71	108.91	
ALP (U/l)	Non-intubated	102	134.27	119.99	0.015
	Intubated	14	163.57	74.89	
Ferritin (ng/ml)	Non-intubated	84	770.47	655.04	0.015
	Intubated	14	1961.42	2635.74	
CRP (mg/l)	Non-intubated	100	89.84	80.17	0.46
	Intubated	14	113.80	98.18	
NLR	Non-intubated	102	11.00	16.30	0.02
	Intubated	14	15.36	11.36	
PLR	Non-intubated	100	482.76	791.23	0.008
	Intubated	14	575.44	273.55	
CAR	Non-intubated	98	3.21	3.62	0.47
	Intubated	14	4.53	5.04	
Sex					0.90
Female	Non-intubated	32			
	Intubated	4			
Male	Non-intubated	70			
	Intubated	10			
Type of surgery					0.46
Thoracic	Non-intubated	8			
	Intubated	2			

Table III. Continued.

Parameter	Outcome	No. of patients	Mean	SD	P-value
Upper abdominal	Non-intubated	28			0.13
	Intubated	2			
Lower abdominal	Non-intubated	30			
	Intubated	8			
Peripheral	Non-intubated	34			
	Intubated	2			
Vaccination status					
Unvaccinated	Non-intubated	46			
	Intubated	26			
Fully vaccinated	Non-intubated	34			
	Intubated	10			

SD, standard deviation; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CCI, Charlson comorbidity index; CRP, C-reactive protein; CAR, CRP to albumin ratio; GGT, gamma glutamyl-transferase; Hb, hemoglobin; IGs, immature granulocytes; LDH, lactate dehydrogenase; NLR, neutrophil to lymphocyte ratio platelets; PLTs, platelets; PLR, platelet to lymphocyte ratio; WBCs, white blood cells.

Table IV. Cox regression multivariable analysis (outcome, mortality).

Parameter	P-value	Exp(B)	95% CI for Exp(B)	
			Lower	Upper
Age (years)	0.275	1.018	0.986	1.051
CCI	0.972	0.997	0.837	1.187
Lymphocytes (K/ μ l)	0.052	0.384	0.146	1.010
AST (U/l)	0.494	1.001	0.998	1.004
ALP (U/l)	0.045	1.003	1.000	1.007
LDH (U/l)	0.926	1.000	0.997	1.003
CRP (mg/l)	0.631	0.995	0.976	1.015
ALB (g/l)	0.413	0.955	0.855	1.067
NLR	0.565	0.991	0.963	1.021
CAR	0.555	0.131	0.751	1.703

Values in bold font indicate a statistically significant difference ($P < 0.05$). ALP, alkaline phosphatase; ALB, albumin; AST, aspartate aminotransferase; CCI, Charlson comorbidity index; CRP, C-reactive protein; CAR, CRP to albumin ratio; LDH, lactate dehydrogenase; NLR, neutrophil to lymphocyte ratio.

reported a mortality rate of 20.7%, while in that same study, increased neutrophil and decreased lymphocyte counts were associated with poor outcomes.

Tabourin *et al* (16), in a post-operative assessment of the nosocomial transmission of COVID-19 following robotic surgery for urinary and gynecological cancer, as well as Bacalbasa *et al* (17) in a post-operative assessment of the nosocomial transmission of COVID-19 following surgery for ovarian cancer, found low mortality rates. Of note, the present study did not include patients who underwent robot-assisted surgery or surgery for ovarian cancer.

Prasad *et al* (18), in their study on patients who underwent different types of elective surgery who tested positive for

COVID-19 post-surgery, reported increased complications, providing no data however, on the predictors of intubation and mortality. To the best of our knowledge, the present study is the first to report data on the predictors of poor outcomes of patients who underwent several different types of surgery and were infected with SARS-CoV-2 during the post-operative period.

Of note, association was found between the type of surgery and poor outcomes. It is known that thoracic and abdominal surgery are more frequently related to adverse events and pulmonary complications in particular (19).

In the present study, liver biomarkers were associated with patient outcomes. It is known that SARS-CoV-2 is a

Table V. Cox regression multivariable analysis (outcome, intubation).

Parameter	P-value	Exp(B)	95% CI for Exp(B)	
			Lower	Upper
NLR	0.209	1.060	0.968	1.162
PLR	0.278	0.999	0.997	1.001
GGT (U/l)	0.015	1.006	1.001	1.012
Ferritin (ng/ml)	0.736	1.000	0.990	0.999
ALP (U/l)	0.294	0.994	0.982	1.005

ALP, alkaline phosphatase; GGT, gamma glutamyl-transferase; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio.

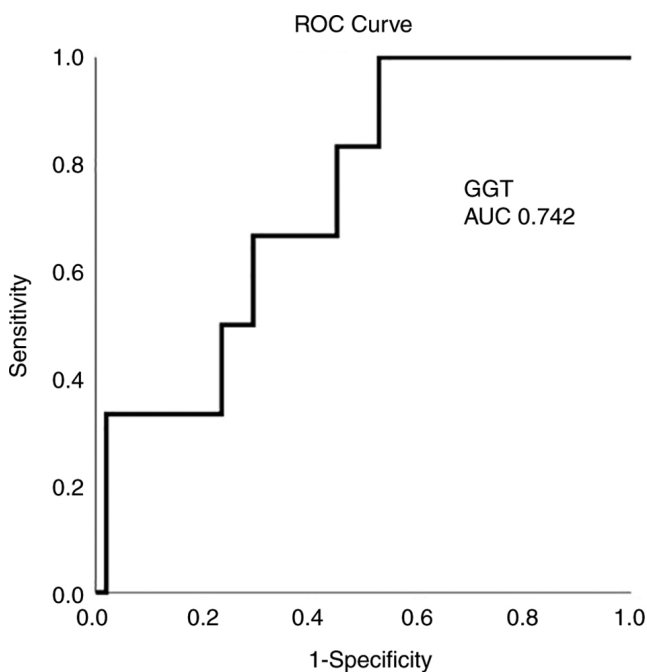


Figure 3. Receiver operating characteristic curve for GGT predicting intubation in patients who underwent elective surgery and were infected with COVID-19 post-operatively. AUC, 0.742. GGT, gamma glutamyl-transferase; AUC, area under the curve.

systemic infection that affects numerous organs, including the kidneys, pancreas, liver and heart (20-23). Liver impairment is present in more than half of individuals infected with SARS-CoV-2, and this impairment becomes more severe as the disease progresses. Moreover, SARS-CoV-2 RNA has been observed in the blood and hepatocytes of infected patients. The high density of ACE2 receptors on cholangiocytes and bile duct cells of the liver, and bile duct cells of the liver apparently facilitates the access of SARS-CoV-2 to the cells where they proliferate, resulting in the disruption of liver function (24). Additionally, there is evidence to support the hypothesis that the majority of viruses that attack the respiratory system can injure liver cells via the CD8⁺-mediated immune response (24). Moreover, liver enzymes have been shown to be associated with poor outcomes of patients with COVID-19 (25-28). To the best of

our knowledge, the present study is the first to report GGT and ALP as biomarkers predicting poor outcomes of patients who underwent elective surgery.

The present study has certain limitations. The present study had a retrospective design, and there no control group was included. Furthermore, it is possible that the negative results obtained in the present study (all-cause mortality) are attributable to other etiologies in addition to severe COVID-19 (thromboembolism, sepsis, or coexisting diseases). In addition, another important limitation is the heterogeneity of the cohort, which underwent lower and upper gastrointestinal surgery or other complex procedures. Finally, the present study did not include patients who underwent other types of surgery, such as neurosurgery or robot-assisted laparoscopy surgery.

The advantages of the present study however, are the relatively large number of patients who underwent surgery, as well as the fact that the participants were patients who underwent several different types of surgery. Other additional strong points of the study are the reliable follow-up and the availability of 30-day data.

In conclusion, in the present retrospective study, mortality occurred in 27.6% of the patients who underwent elective surgery and who were infected with SARS-CoV-2 during the post-operative period. The predictors of mortality and intubation were ALP and GGT levels, respectively. Survival did not differ among patients who underwent different types of surgery. Given that the pandemic crisis is ongoing, closer post-operative follow-up periods for COVID-19-related manifestations, and stricter guidelines in order to prevent infection in the post-operative period are required. Larger studies on mortality and risk factors for poor outcomes of patients undergoing surgery and who are infected with SARS-CoV-2 during the post-operative period are also warranted.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

KT, GF and VEG conceptualized the study. VEG, DB, PMV, GK, IE, SP and CVP advised on patient care and medical treatment, were involved in data analysis and wrote and prepared the draft of the manuscript. NM, KT, DAS, PP, GF and NVS analyzed the data and provided critical revisions. VEG and NVS confirm the authenticity of all the data. All authors contributed to manuscript revision and have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was conducted in line with the Declaration of Helsinki and was approved by the Institutional Review Board of Laiko General Hospital (protocol no. 765/12-2021). Written informed was obtained from the patients for inclusion in the study. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Patient consent for publication

Not applicable.

Competing interests

DAS is the Editor-in-Chief for the journal, but had no personal involvement in the reviewing process, or any influence in terms of adjudicating on the final decision, for this article. The other authors declare that they have no competing interests.

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