CIRUGIA Y CIRUJANOS

ORIGINAL ARTICLE

Postoperative complications and predictors of mortality in patients with COVID-19

Complicaciones posoperatorias y predictores de mortalidad en pacientes con COVID-19

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Abstract

Background: *There are limited data about the perioperative outcomes of coronavirus disease 2019 (COVID-19) patients that needed emergency general surgery. The aim of the present study was to describe the perioperative outcomes and mortality of patients with COVID-19 who underwent emergency surgery.* **Materials and methods:** *Retrospective study of COVID-19 patients symptomatic versus asymptomatic from March 2020 to February 2022 that needed an emergency surgery in a national referral hospital.* **Results:** *Forty-four patients were included in this study. Patients with symptomatic COVID-19 have higher ICU admissions and prolonged length of stay (LOS) as compared with asymptomatic COVID-19 patients. The 90-day survival probability of the entire cohort was 70.1% (60.3-79.9) and was significantly lower in patients with COVID-19 symptomatic 63.4% (50.5-76.2). The cut-off preoperative values for the prediction of mortality: Ferritin ≥ 438.5 ng/mL (Area under the curve [AUC] = 0.908), C-reactive protein (CRP) ≥ 12.5 mg/dL (AUC = 0.715), leukocyte ≥ 13.8 × 10^3/μL (AUC = 0.706), and albumin ≤ 2.78 g/dL (AUC = 704). Furthermore, a cut-off value of CRP of ≥ 12.5 mg/dL yielded an accuracy of 82.9% for the prediction of postoperative complications (p < 0.001).* **Conclusion:** *Patients with symptomatic COVID-19 who needed emergency surgery have higher ICU admissions, prolonged LOS, and decreased 90-day survival as compared with asymptomatic COVID-19 patients. Preoperative ferritin, CRP, leukocytes, and albumin could be used as predictors of mortality.*

Keywords: *Coronavirus disease 2019. Severe acute respiratory syndrome coronavirus 2. Perioperative complications. Mortality.*

Resumen

Antecedentes: *Hay datos limitados sobre los pacientes con COVID-19 que necesitaron cirugía de emergencia. El objetivo del presente estudio fue describir los resultados perioperatorios y la mortalidad de pacientes con COVID-19 que se sometieron a cirugía de emergencia.* **Material y métodos:** *Estudio retrospectivo de pacientes con COVID-19 sintomáticos vs. asintomáticos de marzo 2020 a febrero 2022 que requirieron cirugía de emergencia en un Hospital de Referencia Nacional.* **Resultados:** *Se incluyeron 44 pacientes. Los pacientes con COVID-19 sintomático tienen más admisiones en la UCI y estancia hospitalaria prolongada en comparación con los pacientes con COVID-19 asintomático. La supervivencia a 90 días de la cohorte fue del 70,1% (60,3-79,9) y fue menor en los pacientes con COVID-19 sintomáticos del 63.4% (50.5-76.2). Los valores preoperatorios para la predicción de mortalidad: ferritina ≥ 438.5 ng/mL (AUC = 0.908), PCR ≥ 12.5 mg/dL (AUC = 0.715), leucocitos ≥ 13.8 × 10^3/μL (AUC = 0.706) y albúmina ≤ 2.78 g/dl (AUC = 704). La PCR de ≥ 12.5 mg/dL tiene una precisión del 82.9% para la predicción de complicaciones posoperatorias (p < 0.001).* **Conclusión:** *Los pacientes con COVID-19 sintomático tienen más admisiones en la UCI, estancia hospitalaria prolongada y menor supervivencia en comparación con los*

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Date of reception: 14-10-2022
Date of acceptance: 15-02-2023
DOI: 10.24875/CIRU.22000512

Cir Cir. 2023;91(3):344-353
Contents available at PubMed
www.cirugiaycirujanos.com

pacientes con COVID-19 asintomáticos. La ferritina, PCR, leucocitos y albúmina preoperatoria pueden utilizarse como predictores de mortalidad.

Palabras clave: *Coronavirus disease 2019. Severe acute respiratory syndrome coronavirus 2. Complicaciones perioperatorias. Mortalidad.*

Introduction

A novel coronavirus (severe acute respiratory syndrome coronavirus 2, [SARS-CoV-2]) emerged in China, in December 2019, causing a new disease named (coronavirus disease 2019 [COVID-19])[1]. SARS-CoV-2 rapidly spread across the world and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020[1]. In Mexico, until March 31, 2022, a total of 2,455,219 suspected COVID-19 patients were registered, of which 1,993,629 were treated in Mexico City[2].

This pandemic originated unprecedented changes for health systems, hospitals and surgical departments. In the world, the non-essential surgical procedures or elective surgeries were cancelled and postponed. In our country, hospitals and institutions were converted to specialized units for attention to COVID-19 patients. Our hospital and surgical department maintained only emergency surgery, so patients with surgical emergencies with and without SARS-CoV-2 infection were treated.

Early reports suggested an increased risk of morbidity and mortality for COVID-19 patients who underwent surgical procedures[3-7]. Patients with acute abdomen or surgical emergencies plus concomitant COVID-19 started to present to the emergency department. The effects of SARS-CoV-2 infection in patients that needed emergency surgery are still poorly described and few evidence have been published[8].

Recently published data suggested an overall postoperative 30-day mortality of 23.8%, with more than half of the patients developing postoperative pulmonary complications. Emergency in comparison to elective surgery was associated with 30-day mortality (1.67 [1.06-2.63], $p = 0.026$)[6]. Furthermore, recent data suggested that surgery performed $\geq$ 7 weeks after SARS-CoV-2 diagnosis was associated with a similar mortality risk to baseline, so when possible, surgery should be delayed for at least 7 weeks[9]. However, several diseases or abdominal emergencies required fast or early treatment.

Until now, there are limited published data describing the perioperative outcomes of patients that needed an emergency general surgery procedure with concomitant COVID-19. The aims of the present study were to describe the perioperative outcomes of patients with COVID-19 that underwent emergency general surgery and to determine possible predictors of mortality and postoperative complications.

Materials and methods

Study population

This is a retrospective study of a prospectively collected data of adult patients with confirmed COVID-19 diagnosis that required emergency general surgery procedures from March 2020 to February 2022. Patients were admitted to Hospital General Dr. Manuel Gea González, in Mexico City, Mexico. COVID-19 was diagnosed according to the WHO COVID-19 case definitions[1]. We enrolled symptomatic and asymptomatic SARS-CoV-2 positive patients (asymptomatic carriers) that required emergency surgery. We only included patients with the SARS-CoV-2 infection confirmed either by reverse-transcriptase polymerase chain reaction assay of a nasopharyngeal swab, a rapid antigenic test, or with a highly suspicious computed tomography (CT) findings (COVID-19 Reporting and Data System [CO-RADS] category $\geq$ 5)[10,11]. All patients had chest CT scans before surgery patients that developed COVID-19 after surgery, but during the same admission (< 7 days after surgery), were included. We enrolled patients that underwent emergency general surgery procedures including gastrointestinal or abdominal emergencies, and wound debridement for necrotizing soft-tissue infections (NSTI). We excluded patients that required thoracic, neurosurgical, or head and neck surgical procedures, we also excluded patients with negative laboratory tests or CT scans with CO-RADS < 4. The study protocol was approved by the ethics and research committee of the hospital and conducted in accordance with the principles of the Declaration of Helsinki. Prospective informed consent was waived by competent authorities due to the use of anonymous data.

Data collection

Several variables were recorded including demographic parameters, preoperative quick Sequential Organ Failure Assessment (qSOFA) score[12], type of surgical procedure, preoperative laboratory studies, type of postoperative complications, data regarding intensive care, hospital length of stay (LOS) (days), and 90-day mortality.

Demographic data included age (years), gender, body mass index (BMI), comorbidities (including: diabetes, hypertension, chronic obstructive pulmonary disease, chronic renal disease), smoking status, the American Society of Anesthesiology classification (ASA). We calculated the preoperative qSOFA score and divided the patients in high risk (> 2 point) or not high-risk patients (0-1 points)[12]. The emergency general surgeries included gastrointestinal pathologies (abdominal) and wound debridements for NSTI. Abdominal surgeries were divided in laparoscopic, open or converted. All surgical procedures were performed in a separated theater dedicated to COVID-19 patients. Preoperative laboratory data consisted of a complete blood count, C-reactive protein (CRP) expressed in mg/dL, lactate dehydrogenase (LDH) in IU/L, serum ferritin ng/mL, and albumin in g/dL. Postoperative complications were classified and presented according with the Clavien-Dindo classification[13]. The need for intensive care (ICU), vasopressors and invasive mechanical ventilation, timing of ICU in relation to surgery (pre- or post-operative) as well as organ failures were recorded. The hospital LOS in days was registered. Survival was calculated at 90-days.

COVID-19-related symptoms included fever, cough, dyspnea, fatigue, myalgia, and headache. Pneumonia was diagnosed by clinical symptoms (fever, dyspnea, and cough) and a confirmatory CT scan imaging (consolidation and pleural effusion)[14,15].

Statistical analysis

All data were collected prospectively in a digital database. For the purpose of the analysis, we divided the patients in the following groups: based on COVID-19 related symptoms (asymptomatic vs. symptomatic), based on their survival status (survivors vs. non-survivors) and based on the presence or absence of postoperative complications (postoperative complicated vs. non-complicated). Comparisons of baseline preoperative and postoperative variables were performed. Categorical data were presented as totals (n) and proportions as percentages (%). Categorical data were compared using the Pearson's Chi-square test or Fisher's exact test. Univariate analysis was performed in order to identify possible risk factors for mortality and postoperative complications. All variables with a p-value inferior to 0.10 in the univariate analysis were considered as potential risk factors and were entered into multivariate backward logistic regression analysis. The variables representing the lowest risk for each complication was considered to be the reference group (OR = 1). Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated for the risk of postoperative complications. Kaplan–Meier method was employed to perform survival analysis (90-day survival) and the differences were compared with the log-rank test. Cox proportional hazards (Hazard ratios [HR]) regression model was employed to identify possible independent prognostic factors for 90-day mortality. To evaluate the discriminatory ability (accuracy) of each risk factor, receiver operating characteristic (ROC) curves were generated, and the areas under the curve (AUC) were calculated. The optimal cut-offs were determined by ROC analysis. The sensitivity, specificity, and positive and negative likelihood ratios (LR), of each cut-off value were calculated. A two-tailed $p < 0.05$ was considered to be statistically significant. All data were analyzed using SPSS statistic version 22.0 (IBM Corporation, Armonk, New York, NY).

Results

We prospectively collected data of 44 COVID-19 confirmed patients that needed an emergency general surgery procedure during the pandemic at our institution. The baseline characteristics of the included patients are presented in tables 1 and 2. Concerning the entire cohort, 52.3% were males, the mean age was 53.5 years, the mean BMI was 28.8, 43.2% were current smokers, 59.1% have comorbidities, and 63.6% were classified as High Risk qSOFA score (Table 1). Regarding COVID-19 timing of diagnosis, 30 (68.2%) were diagnosed preoperatively and 14 (31.8%) postoperatively.

The surgical procedures performed in this cohort were abdominal (n = 39, 88.6%) and soft tissue debridements for NSTI (n = 5, 11.4%). Regarding the abdominal procedures, there were 11 appendectomies, 10 cholecystectomies, and 18 emergency laparotomies. The causes of emergency laparotomies

Table 1. Characteristics of positive SARS-CoV-2 patients with and without symptomatic disease, that underwent emergency general surgery

Variables	All patients (n = 44)	Asymptomatic patients (n = 14)	Symptomatic patients (n = 30)	p-value
Sex, n (%)				
Female	21 (47.7)	6 (42.9)	15 (50)	0.659
Male	23 (52.3)	8 (57.1)	15 (50)	
Age, mean (SD)	53.5 (17)	42.2 (18.8)	58.7 (2.4)	0.002
BMI, mean (SD)	28.8 (6.8)	26.2 (7.08)	30 (6.48)	0.093
BMI, n (%)				
< 29.9	24 (54.5)	11 (78.6)	13 (43.3)	0.029
≥ 30	20 (45.5)	3 (21.4)	17 (56.7)	
Smoking, n (%)				
Yes	19 (43.2)	2 (14.3)	17 (56.7)	0.008
No	25 (56.8)	12 (85.7)	13 (43.3)	
ASA classification				
I	5 (11.4)	5 (35.7)	0	< 0.001
II	20 (45.5)	8 (57.1)	12 (40)	
III	19 (43.2)	1 (7.1)	18 (60)	
Comorbidities, n (%)				
Yes	26 (59.1)	4 (28.6)	22 (73.3)	0.005
Comorbidities, n (%)				
Diabetes	16 (36.4)	2 (14.3)	14 (46.7)	0.038
Hypertension	25 (56.8)	4 (28.6)	21 (70)	0.01
COPD	3 (6.8)	0	3 (10)	0.220
CRD	9 (20.5)	2 (14.3)	9 (20.5)	0.488
Preoperative qSOFA score				
Not high risk (0–1)	16 (36.4)	9 (64.3)	7 (23.3)	0.009
High risk (> 2)	28 (63.6)	5 (35.7)	23 (76.7)	
Index surgery, n (%)				
Appendectomy	11 (25)	6 (42.8)	5 (16.7)	0.061
Cholecystectomy	10 (22.7)	4 (28.6)	6 (20)	0.527
Emergency Laparotomy	13 (29.5)	3 (21.4)	10 (33.3)	0.420
PDCI	5 (11.4)	0	5 (16.7)	0.160
Soft-tissue debridement	5 (11.4)	1 (7.1)	4 (13.3)	0.546
Modality of abdominal surgery, n (%)				
Laparoscopic	16 (41)	8 (61.5)	8 (30.8)	0.065
Open	20 (51.3)	5 (38.5)	15 (57.7)	0.320
Converted to open	3 (7.7)	0	3 (11.5)	0.537

BMI: body mass index; ASA: American Society of Anesthesiology; PDCI: peritoneal dialysis catheter insertion; CRD: chronic renal disease; COPD: chronic obstructive pulmonary disease.

were perforated gastroduodenal ulcer (n = 3), strangulated inguinal hernia (n = 1), acute mesenteric ischemia (n = 2), penetrating abdominal trauma (n = 2), strangulated ovarian cyst (n = 1), non-penetrating abdominal trauma (n = 1), perforated diverticulitis (n = 2), peritoneal dialysis catheter insertion or revision (n = 5), and necrotizing pancreatitis (n = 1). Abdominal surgeries were performed open (n = 20, 51.3%), laparoscopic (n = 16, 41%), and laparoscopic converted to open (n = 3, 7.7%). Five patients (11.4%) had necrotizing soft-tissue infection that required surgical exploration and several surgical debridements.

Comparisons between COVID-19 patients with symptomatic versus asymptomatic disease

Of the total of patients, 30 (68.1%) had SARS-CoV-2 associated symptoms (Table 1). Patients with symptomatic COVID-19 were significantly associated with older age, higher BMI, were current smokers, had higher ASA score, had more comorbidities (more diabetes and hypertension), and had higher preoperative qSOFA score. Regarding preoperative studies, patients with symptomatic

Table 2. Characteristics of positive SARS-CoV-2 patients that underwent emergency general surgery. Two comparisons based on 90-day mortality status and presence or absence of postoperative complications

Variables	90-day survivors (n = 32)	90-day non survivors (n = 12)	p-value	No postoperative complications (n = 21)	Postoperative complications (n = 23)	p-value
Sex, n (%)						
Female	15 (46.9)	6 (50)	0.853	10 (47.6)	11 (47.8)	0.989
Male	17 (53.1)	6 (50)		11 (52.4)	12 (52.2)	0.171
Age, mean (SD)	52.1 (18.2)	56.5 (13.5)	0.121	49.6 (17.9)	57.1 (15.7)	0.755
BMI, mean (SD)	28.0 (6.6)	30.9 (7.1)	0.216	28.4 (7.2)	29.1 (6.5)	
BMI, n (%)						
< 29.9	21 (65.6)	3 (25)	0.016	13 (61.9)	11 (47.8)	0.349
≥ 30	11 (34.4)	9 (75)		8 (38.1)	12 (52.2)	
Smoking, n (%)						
Yes	12 (37.5)	7 (58.3)	0.214	6 (28.6)	13 (56.5)	0.062
ASA classification						
I	5 (15.6)	0	0.105	5 (23.8)	0	0.023
II	16 (50)	4 (33.3)		10 (47.6)	10 (43.5)	
III	11 (34.4)	8 (66.7)		6 (28.6)	13 (56.5)	
Comorbidities, n (%)						
Diabetes	11 (34.4)	5 (41.7)	0.654	7 (33.3)	9 (39.1)	0.690
Hypertension	17 (53.1)	8 (66.7)	0.419	11 (52.4)	14 (60.9)	0.570
COPD	2 (6.3)	1 (8.3)	0.807	0	3 (13)	0.086
CRD	6 (18.8)	3 (25)	0.647	6 (28.6)	3 (13)	0.202
Preoperative qSOFA score						
Not high risk (0-1)	13 (40.6)	3 (25)	0.337	7 (33.3)	9 (39.1)	0.690
High risk (> 2)	19 (59.4)	9 (75)		14 (66.7)	14 (60.9)	
Index surgery, n (%)						
Appendectomy	9 (28.1)	2 (16.7)	0.434	6 (28.5)	5 (21.7)	0.601
Cholecystectomy	9 (28.1)	1 (8.3)	0.162	4 (19)	6 (26.1)	0.577
Emergency laparotomy	8 (25)	5 (41.7)	0.080	4 (19)	9 (39.1)	0.144
PDCI	2 (6.3)	3 (25)	0.080	4 (19)	1 (4.3)	0.124
Soft tissue debridement	4 (12.5)	1 (8.3)	0.698	3 (14.3)	2 (8.7)	0.559
Modality of abdominal surgery, n (%)						
Laparoscopic	13 (46.4)	3 (27.3)	0.273	9 (50)	7 (33.3)	0.291
Open	13 (46.4)	7 (63.6)	0.333	9 (50)	11 (52.4)	1.000
Converted	2 (7.2)	1 (9)	0.837	0	3 (14.3)	0.234

BMI: body mass index; ASA: American Society of Anesthesiology; SOFA: Sequential Organ Failure Assessment; PDCI: peritoneal dialysis catheter insertion; CRD: chronic renal disease; COPD: chronic obstructive pulmonary disease.

disease had lower hemoglobin and albumin levels, and had higher CRP, LDH and ferritin levels. Postoperative complications were more frequent in patients with symptoms, as well as more incidences of ARDS, septic shock and MOF. Patients with symptoms require more ICU admissions, mechanical ventilation, vasopressors, and had more prolonged LOS. Mortality was more frequent in patients with symptomatic disease (7.1 vs. 36.7%, p = 0.041).

Comparisons between survivors versus non-survivors

Of the 44 patients, 32 survived (72.7%) and the rest were died at 90 days (n = 12, 27.3%). Patient's baseline characteristics were similar between these two groups (Table 2). Only BMI was different, being more obese the group of patients that died (BMI ≥ 30: 34.4 vs. 75%, p = 0.016). Comorbidities as well as the preoperative qSOFA score were similar in both groups. Non-survivors had higher rates of pneumonia (59.4 vs. 91.7%, p = 0.041). Regarding the preoperative laboratory studies, non-survivors had higher CRP, leukocyte count and ferritin, and lower albumin. The rate of postoperative complications was similar between both groups; however, patients in the non-survivors group developed more ARDS, septic shock, and multi-organic failure. In addition, non-survivors required more ICU admissions, invasive mechanical ventilation, and vasopressors.

Table 3. Clinical evolution of COVID-19 patients that underwent emergency general surgery. Comparisons between survivors and non-survivors and complicated and non-complicated patients

Variables	90-day survivors (n = 32)	90-day non survivors (n = 12)	p-value	No post operative complications (n = 21)	Postoperative complications (n = 23)	p-value
Preoperative studies, mean (SD)						
Hemoglobin	12.1 (3.1)	11.7 (2.5)	0.682	12.6 (3.3)	11.4 (2.4)	0.171
CRP	16.2 (11.4)	27.4 (15.4)	0.013	11.1 (9.1)	26.8 (12.4)	< 0.001
Platelets	275.9 (122.8)	261.4 (123.0)	0.728	279.4 (101.5)	265.2 (139.5)	0.704
Leukocytes	12.1 (5.2)	16 (6.3)	0.045	11.4 (4.3)	14.7 (6.5)	0.063
Lymphocytes	1.35 (0.9)	1.45 (1.3)	0.807	1.48 (1.0)	1.29 (1.1)	0.556
Neutrophils	13.4 (20.0)	13.7 (7.0)	0.952	9.4 (4.6)	17.2 (23.2)	0.142
Monocytes	1.85 (2.7)	1.40 (2.8)	0.626	2.29 (3.4)	1.22 (1.7)	0.197
LDH	247.8 (130.9)	262.5 (138.4)	0.745	222.6 (120.5)	278.5 (138.1)	0.161
Ferritin	536.0 (210.3)	1167.9 (388.8)	< 0.001	614.8 (344.7)	278.5 (138.1)	0.129
Albumin	3.16 (0.9)	2.56 (0.7)	0.050	3.24 (1.0)	2.78 (0.7)	0.087
Symptomatic COVID-19						
Yes	19 (59.4)	11 (91.7)	0.041	9 (30)	21 (70)	0.001
Organ Failures, n (%)						
ARDS	16 (50)	11 (91.7)	0.011	7 (33.3)	20 (87)	< 0.001
ARF	5 (15.6)	5 (41.7)	0.066	4 (19)	6 (26.1)	0.578
Septic shock	8 (25)	7 (58.3)	0.038	2 (9.5)	13 (56.5)	0.001
MOF	1 (3.1)	12 (100)	< 0.001	4 (19)	9 (39.1)	0.145
Mechanical ventilation, n (%)						
Not required	16 (50)	1 (8.3)	0.037	14 (66.7)	3 (13)	< 0.001
Preoperative	9 (28.1)	7 (58.3)		6 (28.6)	10 (43.5)	
Postoperative	7 (21.9)	4 (33.3)		1 (4.8)	10 (43.5)	
ICU Admission, n (%)						
No	16 (50)	1 (8.3)	0.03	14 (66.7)	3 (13)	< 0.001
Preoperative	8 (25)	7 (58.3)		6 (28.6)	9 (39.1)	
Postoperative	8 (25)	4 (33.3)		1 (4.8)	11 (47.8)	
Hospital LOS, mean (SD)	26.7 (28.3)	41.5 (25.2)	0.121	21.8 (26.9)	38.8 (27.1)	0.043
Mortality	-	-	-			
90-day mortality, n (%)				4 (19)	8 (34.8)	0.242
90-day survival probability (Kaplan–Meier) (95% CI)				75.3 (62.2-88.4)	65.3 (51.2-79.5)	0.278

SD: standard deviation; CRP: C-reactive protein; LDH: lactate dehydrogenase, ARDS: acute respiratory distress syndrome; ARF: acute renal failure; MOF: multi organic failure; LOS: length of stay; GPS: Glasgow prognostic score; PI: prognostic index; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet to lymphocyte ratio; LMR: lymphocyte to monocyte ratio; PNI: prognostic nutritional index.

Comparisons between patients with postoperative complications and patients without postoperative complications

A total of 23 (52.3%) patients developed at least one postoperative complication (Tables 2 and 3). Postoperative complications were classified according to Clavien–Dindo and are presented in table 4. The majority of baseline and demographic data were similar between complicated and uncomplicated patients. Patients that developed postoperative complications had higher ASA classification, elevated preoperative CRP, and higher rate of pneumonia. In addition, complicated patients were associated with higher incidence of ARDS and septic shock, requiring more mechanical ventilation, ICU admission, and vasopressors. The hospital LOS was shorter in patients without postoperative complications (21.8 vs. 38.8 days, p = 0.043).

Predictors of mortality and postoperative complications

The overall mortality rate was 27.3% (12/44). Concerning the causes of death, 9 patients died due to ARDS complications, and 3 patients due to abdominal sepsis and septic shock (1 abdominal blunt trauma, 1 pancreatic necrosis, and 1 perforated gastric ulcer).

The 90-day survival probability after surgery of the entire cohort was 70.1% (95% CI 60.3-79.9) (Tables 3 and 4). The 90-day survival probability was

Table 4. Description of postoperative complications according with the Clavien-dindo classification (n = 44)

Clavien-Dindo classification	n (%)
Grade I, n (%)	20 (45.4)
Grade II, n (%)	
Blood transfusion	16 (36.3)
Total parenteral nutrition	17 (38.6)
Postoperative Ileus	12 (27.2)
Pneumonia	21 (47.7)
Delirium	11 (25)
Superficial surgical infection	12 (27.2)
Deep surgical infection	5 (11.3)
Post-chole biliary leak	1 (2.2)
Pancreatic fistula	1 (2.2)
Grade IIIa, n (%)	
Percutaneous peripancreatic collection drainage	1 (2.2)
Percutaneous drainage of intra-abdominal collection	2 (4.5)
Grade IIIb, n (%)	
Evisceration	1 (2.2)
Bleeding	2 (4.5)
Intestinal occlusion	1 (2.2)
Pancreatic necrosis	2 (4.5)
Negative pressure therapy	1 (2.2)
Appendicular stump leak	1 (2.2)
Anastomotic leak	1 (2.2)
Need of ERCP	4 (9.0)
Grade IVa, n (%) Single organ dysfunction	20 (45.5)
Grade IVb, n (%) Multiorgan dysfunction	13 (29.5)
Grade V, n (%) Mortality	12 (27.3)

significantly lower in patients with SARS-CoV-2 symptoms (63.4 [95% CI: 50.5-76.2]) in comparison with patients without symptoms (84.5 [95% CI: 74.3-94.3]).

The 90-day survival probability was similar between patients with (65.3 [95% CI: 51.2-79.5]) and without (75.3 [95% CI: 62.2-88.4]) postoperative complications. The univariate analysis revealed that higher BMI (HR = 4.2 [1.14-15.66]), developing ARDS (HR = 8.4 [1.08-65.17]), need of vasopressors (HR = 10.4 [1.34-80.65]), and invasive ventilation (HR = 8.41 [1.08-65.17]), as well as higher values of preoperative ferritin (HR = 1.003 [1.002-1.005]), CRP (HR = 1.05 [1.01-1.10]) and preoperative leukocytes (HR = 1.097 [1.003-1.198]) were risk factors for decreased 90-day survival. Multivariate analysis identified high preoperative ferritin values as independent risk factor (HR = 1.003 (1.002-1.005); $p < 0.001$) for decreased 90-day survival as shown in table 5.

To assess the discriminatory capacity of each risk factor, ROC curves were constructed for survival status and postoperative complications at 90 days. The area under the ROC curve (AUC), sensitivity, specificity, and LR were calculated for mortality and postoperative complications, as displayed in table 6.

Regarding the accuracy of prediction, we found the following cut-off values associated with decreased 90-day survival (preoperative studies): ferritin ≥ 438.5 g/mL (AUC = 0.908, $p < 0.001$), CRP value ≥ 12.5 mg/dL (AUC = 0.715, p = 0.030), leukocyte count ≥ 13.8 × 10^3/μL (AUC = 0.706. p = 0.037), and albumin ≤ 2.78 g/dL (AUC = 704, p = 0.039).

Regarding the probability for postoperative complications, univariate and multivariate analysis revealed those higher levels of preoperative CRP (OR = 0.022 [0.013-0.032], $p < 0.001$) was associated with increased risk of postoperative complications. We found that a cut-off value of CRP of ≥ 12.5 mg/dL yielded an accuracy of 82.9% for the prediction of postoperative complications in COVID-19 patients ($p < 0.001$).

Discussion

We found in the present study that symptomatic COVID-19 patients that needed an emergency general surgery procedure had worse postoperative outcomes, increased postoperative complications, higher ICU admissions, prolonged LOS, and decreased 90-day survival probability as compared with asymptomatic COVID-19 patients. We also found that preoperative ferritin value of ≥ 438.5 g/mL, CRP value of ≥ 12.5 mg/dL, total leukocyte count of ≥ 13.8 × 10^3/μL and albumin of ≤ 2.78 g/dL, could be used as predictor factors for decreased 90-day survival with acceptable accuracy. Furthemore, a preoperative CRP value of ≥ 12.5 mg/dL predicted the development of postoperative complications.

To date, there are limited data that describes outcomes of COVID-19 patients that underwent surgery. The firsts published studies regarding the impact of COVID-19 on surgical outcomes analyzed elective and emergency surgeries together and included several specialties together[8,16]. A series of 34 patients from China, at the beginning of the pandemic, with occult COVID-19 infections at the time of surgery reported the development of pneumonia in all patients, ARDS in 32%, 44.1% were admitted to the ICU and a 20.5% postoperative mortality rate[4]. However, this study included several types of surgeries including neurosurgery, orthopedics, ophthalmology and general surgery. In the cohort of Doglietto et al., they described factors associated with surgical mortality and complications among patients with and without COVID-19 in Italy[17]. They concluded that the surgical

Table 5. Logistic regression analysis of factors associated with postoperative mortality and development of postoperative complications in patients with COVID-19

Factors	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	**p-value**	**Hazard ratio (95% CI)**	**p-value**
Univariate and multivariate analysis for factors associated with 90-day survival (Cox regression)				
BMI, n (%) ≥ 30	4.23 (1.14-15.66)	0.030		
COVID-19 Pneumonia	6.03 (0.78-46.77)	0.085		
ARDS	8.41 (1.08-65.17)	0.042		
ARF	2.94 (0.93-9.34)	0.066		
Septic shock	2.87 (0.90-9.06)	0.072		
Invasive ventilation	8.41 (1.08-65.17)	0.042		
Vasopressors	10.40 (1.34-80.65)	0.025		
Cox regression analysis for laboratory parameters associated with 90-day survival				
Factors	**Hazard ratio (95% CI)**	**p-value**	**Hazard ratio (95% CI)**	**p-value**
Ferritin	1.003 (1.002-1.005)	< 0.001	1.003 (1.002-1.005)	< 0.001
CRP	1.05 (1.01-1.10)	0.016		
Leukocytes	1.097 (1.003-1.198)	0.042		
Albumin	0.511 (0.246-1.062)	0.072		
Linear regression analysis for laboratory parameters associated with postoperative complications				
Factors	**Odds ratio (95% CI)**	**p-value**	**Odds ratio (95% CI)**	**p-value**
CRP	0.022 (0.013-0.032)	< 0.001	0.022 (0.013-0.032)	< 0.001
Leukocytes	0.025 (−0.001-0.050)	0.063		
Albumin	−0.145 (−0.312-0.022)	0.087		

BMI: body mass index; ARDS: acute respiratory distress syndrome; ARF: acute renal failure; CRP: C-reactive protein. For uni- and multivariable logistic regression analysis odds ratio (OR) and 95% confidence interval (CI) are presented. Odds ratios of factors associated to 90-day survival. Only significant results are shown in the multivariate analysis. The reference category has an odds ratio of 1.00.

mortality and complications were higher in patients with COVID-19 (19.5%) compared with patients without COVID-19, where pulmonary (14.6%) and thrombotic complications (9.7%) are significantly associated with it. The meta-analysis conducted by Abate et al.,[7] revealed a very high global rate of postoperative mortality among COVID-19 patients of 20% (95% CI: 15-26) and a postoperative ICU admission rate of 15% (95% CI: 10-21). However, this meta-analysis included patients of several specialties (mostly orthopedics), and included elective and emergency procedures.

There are some published studies regarding outcomes after emergency or acute surgery in COVID-19 patients. Seeliger et al.,[8] described 13 patients with acute surgical condition and concomitant COVID-19. They concluded that co-infection did not result in more complications for emergency abdominal surgery, although an acute abdomen with severe COVID-19 had dismal prognosis. In a multi-center cohort study conducted by Carrier et al.,[18] they analyzed 44 patients with COVID-19, with 31 surgeries (71%) being urgent. They described that the postoperative 30-day mortality in COVID-19 patients undergoing surgery was high (15.9%). This mortality was higher in patients with symptoms (23.1%) compared to those without symptoms (5.6%), although not statistically significant. Fallani et al.,[19] reported a higher rate of postoperative complications during the COVID-19 pandemic in patients with peritonitis. They found that the ASA score, severity of peritonitis, qSOFA score, diagnosis other than appendicitis, and COVID period resulted independent predictors of complications.

Table 6. ROC analysis for prediction of postoperative mortality and postoperative complications in COVID-19 patients that underwent emergency surgery

Variables	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)	LR+	LR-	p-value
ROC analysis for prediction of postoperative mortality							
Ferritin	0.908 (0.785-1.000)	438.5	91.7	62.5	1.47	0.22	< 0.001
CRP	0.715 (0.522-0.908)	12.5	83.3	62.5	1.40	0.41	0.030
Leukocytes	0.706 (0.528-0.884)	13.8	75	31.3	2.40	0.36	0.037
Albumin	0.704 (0.534-0.875)	2.78	66.7	37.5	1.78	0.53	0.039
ROC analysis for prediction of postoperative complications							
CRP	0.829 (0.702-0.956)	12.5	91.3	38.1	2.40	0.14	< 0.001

ROC: receiver operator curve; AUC: area under the curve; LR: likelihood ratios; CRP: C-reactive protein.

One strength of the present study is that we limited the procedures to general surgeries (mostly abdominal emergencies). Furthermore, all our patients had confirmed COVID-19. We noted that patients with COVID-19 were at a substantially higher risk of postoperative morbidity and mortality. In our study, 52.3% of patients experienced at least one complication, the postoperative mortality rate was 27.3%, the mean hospital stay was 30.7 days, and 61.4% required ICU admission. It is important to mention that patients in our cohort have high rates of comorbidities (59.1%), almost the half of the patients were classified as ASA III (43.2%), and the majority of patients (63.6%) have a high-risk preoperative qSOFA score. This could contribute to the high rate of surgical complications, need of ICU, prolonged LOS, and decreased survival rate.

The data analyzed in the present study suggest that patients with COVID-19 who needed emergent gastrointestinal or soft-tissue surgery have an increased risk of postoperative morbidity and mortality. These findings have several important implications. First, it is necessary to rule out COVID-19 in all patients that are admitted with an acute surgical disorder, to inform the patients or relatives about the potential impact of COVID-19 on surgical complications, LOS, need of ICU, and mortality. Second, we consider that laparoscopy can be safely performed in patients with diseases commonly treated by laparoscopy (such as appendicitis and cholecystitis), with all the isolation and protective measures needed to avoid unnecessary infections to the health personnel. Third, we found a high prevalence of comorbidities, obesity, and smoking, that could impact on the severity of COVID-19 thus affecting postoperative outcomes.

We would like to add that there is no scientific evidence concerning the risk of transmission of COVID-19 by laparoscopic surgery[20-22]. A recent systematic review of 22 articles concluded that laparoscopic surgery can be used with the recommended precautions because of its benefits compared to open surgery[20]. In our study, we performed 19 laparoscopic procedures. All these laparoscopic procedures were performed in a special theater and within an area dedicated to only SARS-CoV-2-positive patients. We employed a special filter for gas evacuation and all staff had personal protective equipment. We would like to add that after following protocols recommended by scientific societies and our internal protocols, no staff members (surgeons, anesthesiologist, and nurses) were infected with COVID-19 after laparoscopic surgeries[23].

There are some limitations to our study that need to be mentioned. The most important limitation is the fact that is a single-center observational study, with a small sample size, which predisposes to all the biases inherent to the design. Another important limitation is the inherent problems with the criteria for diagnosing COVID-19. For example, CT-scan findings depend on the criteria of the radiologists.[10] Other limitation was that although a comprehensive review of all medical records was performed, we cannot exclude the possibility that some clinical parameters, including symptoms and comorbidities, were not correctly registered. An additional limitation of the study is the fact that it is difficult to evaluate the unmixed contribution of SARS-CoV-2 infection to the morbidity and mortality considering the diversity of pathologies and operations included in the study. However, despite these limitations we consider that the results of this study could help us to better understand the implications of SARS-CoV-2 in patients that needs emergency gastrointestinal and soft-tissue surgery.

Conclusion

We found in our study that positive SARS-CoV-2 patients who needed an emergency general surgery with concomitant COVID-19 related symptoms had worse postoperative outcomes, increased postoperative complications, higher ICU admissions, prolonged length of hospital stay, and decreased 90-day survival rate as compared with asymptomatic COVID-19 patients. Also, preoperative serum ferritin, CRP, leukocytes, and albumin values could be used as accurate predictors of decreased 90-day survival.

Acknowledgments

The authors would like to thank the ethics and research committee for the approval of this work.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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