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Short-term perioperative outcomes among patients with concurrent asymptomatic and mild SARS-CoV-2 infection: A retrospective, multicenter study

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ABSTRACT

Background: Previous studies report high rates of postoperative morbidity and mortality among patients with SARS-CoV-2 (COVID-19). With routine preoperative screening, we are identifying an increasing number of patients with asymptomatic and mild COVID-19. Based on these prior studies, we hypothesized that patients with asymptomatic and mild COVID-19 infections have low perioperative morbidity and mortality. The purpose of this study was to determine the risk of perioperative morbidity and mortality associated with operations performed on patients diagnosed with asymptomatic or mild COVID-19.

Methods: A multicenter, retrospective study of patients with asymptomatic/mild SARS-CoV-2 (COVID-19) infection diagnosed within 8 days of surgery from March 2020 to February 2021. The primary outcome was 30-day mortality, and secondary outcomes included pulmonary complications and perioperative morbidity. The Chinese Center for Disease Control and Prevention criteria of COVID severity was used for categorization.

Results: The initial cohort included 53 patients. COVID-19 infection was detected preoperatively in 86.8%. At admission, 90.5% of patients were asymptomatic, 7.5% had mild COVID-19 symptoms, and 1.9% were unknown due to obtundation and later determined to be asymptomatic. Of the 53 cases, 35.8% were general surgical and 18.9% orthopedic; the remaining 54.7% were other surgical subspecialties. Overall mortality was 0%. New COVID-19 symptoms developed in 13.2% of patients postoperatively, with only 11.3% developing postoperative pulmonary complications.

Conclusion: Postoperative morbidity and mortality rates were low among patients with asymptomatic and mild COVID-19. The risks of nonoperative management should be weighed against these operative risks in such patients with surgical indications.

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Introduction

Early in the SARS-CoV-2 (COVID-19) pandemic, reports suggested that perioperative morbidity and mortality were significantly increased in patients with COVID-19.^{1–3} Relying on these data, many surgical societies recommended the consideration of nonstandard, nonoperative treatment in patients with COVID-19.^{4,5} However, as testing capabilities improve, more patients who need surgery are found to have asymptomatic or mild COVID-19.¹ In this subgroup of patients, the risks of COVID-19 associated complications may be less

than the risk of avoiding or delaying surgical intervention. The purpose of our study was to better characterize the rates of morbidity and mortality in patients who undergo operations who have concomitant mild or asymptomatic COVID-19.

Previous studies report rates of postoperative morbidity and mortality in COVID-19 patients as high as 58% and 24%, respectively, after elective and emergency operations.^{1,2,6,7} However, these studies included patients with all levels of COVID-19 disease severity.^{2,6–8} Furthermore, it remains unclear whether undergoing an operation and/or general anesthesia directly precipitates the increased risks reported in COVID-19 surgical patients or if we were observing the natural history of COVID-19 infection in patients with an indication for surgery. There are conflicting reports regarding perioperative outcomes of COVID-19 patients with asymptomatic disease.^{1,9–12}

We hypothesized that patients with mild or asymptomatic COVID-19 would have relatively low rates of perioperative

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morbidity and mortality. We performed a multicenter cohort study to evaluate the risk of 30-day perioperative morbidity and mortality among patients with asymptomatic or mild COVID-19 diagnosed within 7 days of surgery.

Methods

Study population and data source

We retrospectively reviewed adult patients >18 years of age who underwent surgery within 7 days of initial diagnosis of COVID-19 infection at an academic quaternary care center, an academic community hospital, and a university-affiliated county hospital between March 1, 2020 and February 1, 2021. Patients were identified retrospectively through (1) review of all operating room cases that used advanced precautions for COVID-19 for unknown or confirmed COVID-19 status and (2) all patients from an existing internal database of all inpatients with COVID-19 who underwent an operation within 7 days of COVID-19 diagnosis. Patients with COVID-19 diagnosis >7 days before surgery were excluded, as were patients determined to have false positive testing by an infectious disease consultation.

Medical records were reviewed to determine disease severity using the definitions set by the Chinese Center for Disease Control criteria.¹³ We included only patients who met criteria for mild or asymptomatic disease. Asymptomatic patients were defined as having no respiratory symptoms, anosmia, fever, or any other attributable symptom of COVID-19 infection. Mild cases were defined as patients with upper respiratory symptoms not requiring the use of supplemental oxygen, anosmia, or other symptoms without radiographic features of pneumonia.¹⁴ Based on previous studies documenting high risk of COVID-19 associated thromboembolic disease, we defined COVID-19 associated complications as pneumonia, acute respiratory distress syndrome, respiratory failure, deep vein thrombosis (DVT), pulmonary embolism (PE), or any respiratory complications.^{7,15} We acknowledge that these complications are certainly possible to be not explicitly due to COVID-19 infection in these patients; unfortunately, exact determination of causality is not possible in this cohort.

Patient demographics, operative reports, and postoperative events were all abstracted from the electronic medical record. Data were collected and stored in a secure, Health Insurance Portability and Accountability Act (HIPAA)–compliant REDCap database. We analyzed patients' medical records for postoperative complications occurring within 30 days of discharge, including reoperations, DVT/PE, unplanned reintubations, renal failure, pneumonia, and unplanned readmissions.

COVID-19 testing algorithms and procedures

In our participating institutions, all patients requiring urgent surgical intervention were preoperatively screened for COVID-19 except for emergency “red line” cases. In patients with unknown COVID-19 status, COVID-19 precautions were employed until test results were obtained. In the quaternary and community settings, testing was performed at the system's Clinical Microbiology Laboratory on the Food and Drug Administration (FDA) Emergency Use Authorization approved Thermo TaqPath COVID-19 Combo Kit (ThermoFisher Scientific, Waltham, MA) on samples obtained via nasopharyngeal swab. Institutional testing demonstrated a clinical sensitivity of 98.3%, a specificity of 99%, and a negative predictive value of 99.99%.¹⁶ For tests performed in the county hospital setting, a variety of COVID-19 real-time polymerase chain reaction (RT-PCR) testing sites were used, with different COVID-19 RT-PCR assays. Samples were obtained either via nasopharyngeal or nasal swab. All preoperative testing samples

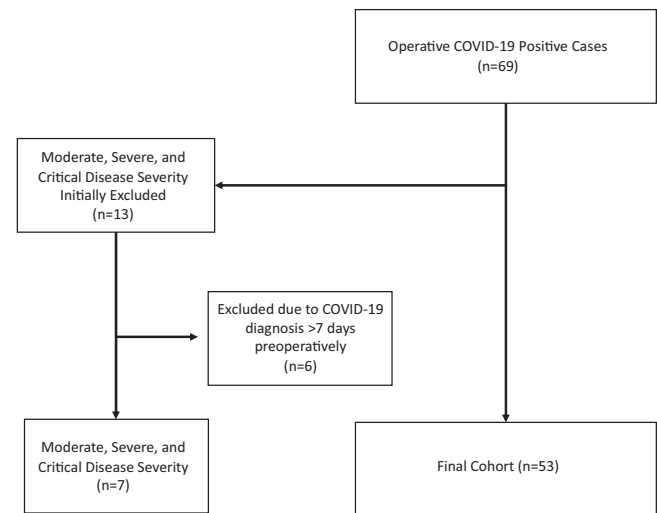


Figure 1. Flow chart of cohort inclusion. Description of creation of final study cohort. Patients were excluded either due to initial COVID-19 diagnosis greater than 7 days preoperatively or due to moderate, severe, or critical disease severity.

were processed via RT-PCR; antigen tests were not accepted at these sites for preoperative screening.

Postoperatively, COVID-19 testing was also conducted with the same PCR assays. Indications for COVID-19 testing in the postoperative period were not standardized and were based on clinical judgment and suspicion of COVID-19 infection. This was often after consultation with infectious disease specialists, but consultation was not required for repeat testing.

Our institutions did not standardize recommendations for surgical management of patients with COVID-19 infection. However, per societal guidelines, nonoperative management was encouraged in cases when deemed of acceptable surgical risk by shared decision-making between surgeon and patient. If COVID-19 was diagnosed preoperatively, a decision was made by the operating surgeon in conjunction with discussion of risk with patients regarding choosing operative or nonoperative management.

Study outcomes

The primary outcome was 30-day postoperative mortality in identified patients with asymptomatic or mild COVID-19 infection. Secondary outcome was perioperative morbidity, which included reoperations, DVT/PE, unplanned reintubations, renal failure, pneumonia, and unplanned readmissions.

Statistical analysis

Descriptive data were analyzed for all study patients. We compared patient and disease characteristics between patients who experienced postoperative complications versus those who did not. For continuous data, Student's *t* test was performed, and for categorical variables, either Pearson χ^2 or Fisher exact tests were performed. Data were presented in number of patients (*n*) with percentage (%) and either median with interquartile range (IQR) or mean plus minus standard deviation (SD) according to data distribution. Data transformation and analysis were performed using SPSS Statistics software version 27.0 (IBM Corp., IBM SPSS Statistics for Mac OS, version 27.0, Armonk, NY).

Ethical approval

This study design was independently reviewed by the University of California, Los Angeles Institutional Review Board (IRB) before

Table I
Patient demographics and case information

	Overall (N = 53)
Sex no. (%)	
Male	35 (66%)
Female	18 (34%)
Age	43.8 ± 14.8
Race/Ethnicity, no. (%)	
Black or African American	4 (7.5%)
Asian	1 (1.9%)
Hispanic or Latino	33 (62.3%)
White	13 (24.5%)
Other/Unknown	2 (3.8%)
BMI, mean ± SD	28.0 ± 6.4
Underweight BMI <18.5 no. (%)	1 (1.9%)
Obese BMI >30 no. (%)	19 (35.8%)
Comorbidities no. (%)	
None	17 (32.1%)
Diabetes mellitus	10 (18.8%)
Chronic kidney disease	2 (3.8%)
Hypertension	9 (17%)
Heart disease	4 (7.5%)
Chronic pulmonary disease, not asthma	1 (1.9%)
Asthma	3 (5.7%)
Chronic liver disease	2 (3.8%)
Malignancy	6 (11.3%)
Chronic neurologic disease	4 (7.5%)
HIV/AIDS	2 (3.8%)
Organ transplant recipient	1 (1.9%)
Immunocompromised	4 (7.6%)
Smoking status no. (%)	
Current smoker	12 (22.6%)
Former smoker	9 (17%)
Never smoked	32 (60.4%)

BMI, body mass index; HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; SD, standard deviation.

initiation. This study was deemed exempt from the university IRB due to secure data storage and minimal risk to patients.

Results

Between March 1, 2020, and February 1, 2021, 69 patients were identified. Of these patients, 3 were excluded due to moderate disease severity, 4 were excluded due to severe disease severity, and 6 due to critical disease severity. An additional 2 patients were of unknown disease severity at presentation due to obtundation, either in the setting of trauma or critical illness and died before disease severity could be ascertained. The final study cohort consisted of 53 patients (Figure 1). Description of patients excluded due to moderate to critical COVID-19 disease severity is included in Supplementary Table S1. Seven patients were excluded due to COVID-19 severity.

The majority of patients (90.4% [$n = 47$]), were asymptomatic upon initial presentation with surgical disease, and 7.7% ($n = 4$) presented with mild COVID-19 symptoms. Patient characteristics are presented in Table I. Common comorbidities among this cohort included obesity (35.8%), diabetes (18.8%), hypertension (17.0%), and malignancy (11.3%). More than half the population were never smokers, with 22.6% reporting active smoking status at the time of diagnosis.

The majority of patients underwent general surgical procedures (35.8%) followed by orthopedic procedures (18.9%). General anesthesia was used in 86.8% of cases, with 81.1% of patients requiring endotracheal intubation. Laparoscopy was performed in 26.4% of cases. The majority of patients were diagnosed with COVID-19 preoperatively, with only 7 postoperative diagnoses after initial negative testing. Surgical disease and COVID-19 presentation are listed in Table II.

Table II
Disease and surgery characteristics

Surgical service, no. (%)	
Cardiac surgery	2 (3.8%)
General surgery	19 (35.8%)
Neurological surgery	2 (3.8%)
Obstetrics/Gynecology	4 (7.6%)
Ophthalmology	2 (3.8%)
Otolaryngology/oral maxillofacial surgery	7 (13.2%)
Orthopedic surgery	10 (18.9%)
Plastic surgery	1 (1.9%)
Podiatric surgery	2 (3.8%)
Urology	2 (3.8%)
Vascular surgery	2 (3.8%)
Case urgency, no. (%)	
Elective	2 (3.8%)
Urgent/Emergency	51 (96.2%)
Method of anesthesia, no. (%)	
Local/monitored anesthesia care	7 (13.2%)
General with LMA	3 (5.7%)
General with endotracheal intubation	43 (81.1%)
Laparoscopy with insufflation, no. (%)	14 (26.4%)
COVID-19 presentation severity, no. (%)	
Asymptomatic preoperatively	48 (90.6%)
Mild COVID-19 preoperatively	4 (7.5%)
Unknown COVID-19 severity preoperatively	1 (1.9%)
O ₂ requirements at presentation, no. (%)	
Room air	51 (96.2%)
Intubated	2 (3.8%)
Preop COVID-19 NP swab negative, no. (%)	6 (11.3%)

O₂, oxygen; NP, nasopharyngeal; LMA, laryngeal mask airway; COVID-19, SARS-CoV-2.

Table III
Postoperative morbidity and mortality

Mortality, no. (%)	0 (0.0%)
Complications, no. (%)	
Overall	13 (24.5%)
Neurological	3 (5.7%)
Stroke	1 (1.9%)
Neurological infection of surgical space	2 (3.8%)
Pulmonary	6 (11.3%)
Postoperative ventilator dependence	2 (3.8%)
Reintubation	2 (3.8%)
Postoperative pneumonia	3 (5.7%)
ARDS	0 (0%)
Other pulmonary complications	2 (3.8%)
Cardiac	1 (1.9%)
Myocardial infarction	1 (1.9%)
Renal	2 (2.8%)
Acute kidney injury	2 (3.8%)
Hemodialysis	1 (1.9%)
Pulmonary embolism/deep vein thrombosis	1 (1.9%)
PE	0 (0%)
Lower extremity DVT	0 (0%)
Upper extremity DVT	1 (1.9%)
Infection, wound complication, bleeding	8 (15.1%)
Urinary tract infection	0 (0%)
Superficial surgical site infection	3 (5.7%)
Deep space surgical site infection	4 (7.5%)
Septic shock	2 (3.8%)
Central line associated bloodstream infection	1 (1.9%)
Postoperative hemorrhage	2 (3.8%)
COVID-19 complications (respiratory or thromboembolic)	7 (13.2%)
Reoperation	1 (1.9%)
Readmission <30 days	3 (5.7%)
Readmission for respiratory distress	1 (1.9%)

ARDS, acute respiratory distress syndrome; DVT, deep vein thrombosis; COVID-19, SARS-CoV-2; PE, pulmonary embolus.

Postoperative surgical and respiratory complication rates are presented in Table III. The overall 30-day mortality was 0%. The overall complication rate was 24.5%, with infection, wound complications, and bleeding being the most frequent category of

complication at 15.1%. Of our cohort, only 20.8% of patients developed new symptoms of COVID-19 infections postoperatively. Two patients (3.8%) were reintubated after postprocedural extubation, one after experiencing laryngospasm and another with residual muscle weakness after postoperative extubation requiring reintubation. No cases of reintubation were due to symptomatic COVID-19. Postoperatively, pneumonia developed in only 5.7% of patients. Cardiac complications and renal failure remained rare in this series, with an incidence of 1.9% ($n = 1$) for myocardial infarction and 3.8% ($n = 2$) for acute kidney injury. One case of thromboembolic disease was seen (1.9%), consisting of an upper extremity DVT after placement of central venous access catheter. Only 3 patients required readmission within 30 days (5.7%), and 1 patient ultimately required reoperation (1.9%).

The only predictive factor for an increased overall complication rate was a postoperative COVID-19 diagnosis ($P = .0001$, OR 70.2, CI [3.57–1382.29]). In subgroup analysis, predictor factors for COVID-19 associated complications were (1) pre-existing cancer diagnosis or immunosuppression ($P = .0183$, OR 6.15, 95% CI [1.06–35.8]); (2) length of operation ($P = .0394$); and (3) postoperative diagnosis of COVID-19 after negative initial testing ($P = .0013$, OR 29.33, 95% CI [3.37–230.45]) (Table IV).

Seven patients were excluded due to moderate to critical COVID severity. The overall mortality rate was 28.6%, and overall complication rate was 85.7%. The group excluded due to COVID severity was older (mean 49.9 years), weighed more (mean body mass index 31.1 kg/m²), and was more likely to be pregnant (28.6%) than the 53 patients in the study cohort. However, there is no statistical significance between the groups due to the small sample size.

Discussion

In this retrospective multicenter study, we observed a 0% mortality rate and a 24.5% overall complication rate in patients with asymptomatic or mild COVID-19 disease diagnosed within 7 days of surgery. The most common complications were pneumonia (5.7%)

and wound infection (13.2%), whereas 13.2% of patients developed complications possibly attributable to COVID-19 infection such as pneumonia, respiratory failure, and thromboembolic disease. To our knowledge, our series is the first study to date to specifically examine postoperative morbidity and mortality in patients with asymptomatic and mild COVID-19. The results of our study suggest that complication rates associated with operative intervention in patients with asymptomatic to mild COVID-19 infection is likely lower than previously described for patients with all degrees of disease severity of COVID-19. The low rates of perioperative morbidity and 0% mortality we observed among patients with asymptomatic and mild COVID-19 infection indicate there is equipoise between the risk of COVID-19 complications after surgery and risk of nonoperative management when surgery is the standard of care.

The postoperative mortality rate in our study was markedly lower than in rates from previous studies. Jonker et al⁷ reported a 16% 30-day perioperative mortality for patients testing positive for COVID-19, whereas the COVIDSurg collaborative reported a 23.8% mortality rate. In subgroup analysis of patients with asymptomatic COVID-19 infections, the 30-day mortality rates were 7.7%, 10.5%, and 22.4%.^{1,2,7} The Dutch study found no association between symptom severity, asymptomatic versus symptomatic, and overall mortality ($P = 1.0$).⁷

When patients test positive for COVID-19 and are asymptomatic preoperatively, it is unclear whether postoperative pulmonary complications are simply the natural history of the COVID-19 infection or if undergoing an operation increases the rate of pulmonary complications. We observed a lower rate of postoperative pulmonary complications relative to previous studies. Overall, 11.3% developed postoperative pulmonary complications, and only 14.6% of initially asymptomatic patients developed COVID-19 symptoms postoperatively. In comparison, the COVIDSurg Collaborative reported an overall pulmonary complication rate of 51.3% and 52.5% for patients undergoing emergency and elective surgery, respectively.²

Table IV
Characteristics by COVID-19 complication status

	No COVID-19 complications (no thromboembolic or respiratory, $n = 46$)	COVID-19 associated complications (thromboembolic or respiratory, $n = 7$)	<i>P</i> value
Sex, no. (%)			.6778
Male	31 (67.4%)	4 (57.1%)	
Female	15 (32.6%)	3 (42.9%)	
Age, mean \pm SD	43.0 \pm 14.3	49 \pm 18.3	.3232
BMI, mean \pm SD	27.8 \pm 6.5	29.2 \pm 5.4	.5910
Underweight BMI <18.5, no. (%)	1 (2.2%)	0	1
Obese BMI >30, no. (%)	15 (32.6%)	4 (57.1%)	.234
Comorbidities, no. (%)			
None	16 (34.8%)	1 (14.3%)	.4075
Diabetes mellitus	8 (17.4%)	2 (28.6%)	.6045
Cardiovascular disease	8 (17.4%)	2 (28.6%)	.6045
Chronic pulmonary disease	4 (6.7%)	0	1
Malignancy or immunosuppression	5 (10.9%)	3 (42.9%)	.0183
Smoking status, no. (%)			1
Current or former smoker	18 (39.1%)	3 (42.9%)	
Never smoked	28 (60.9%)	4 (57.1%)	
General endotracheal anesthesia	36 (78.3%)	7 (100%)	.3235
Laryngeal mask airway or monitored anesthesia care	10 (21.7%)	0	
Preop COVID-19 Dx	44 (95.7%)	3 (42.9%)	
Postop COVID-19 Dx	2 (4.3%)	4 (57.1%)	.0013
CXR or CT findings C/W COVID-19 preop	8 (17.4%)	3 (42.9%)	.1471
Preop COVID-19 severity			
Asymptomatic	41 (89.1%)	7 (100%)	
Mild	4 (8.7%)	0	
Unknown	1 (2.2%)	0	
Laparoscopic surgery	11 (23.9%)	3 (42.9%)	.3638
Open surgery	35 (76.1%)	4 (57.1%)	
Length of surgery, min (mean \pm SD)	124.5 \pm 85	202.6 \pm 127.6	.0394

BMI, body mass index; COVID-19, SARS-CoV-2; SD, standard deviation; CXR, chest x-ray; CT, computed tomography; Dx, diagnosis.

Patients who tested negative preoperatively but were postoperatively diagnosed with COVID-19 infection had a much higher likelihood of developing COVID-19 complications (4 of 6, 66.7%). Postoperative COVID-19 diagnoses may have been the result of false negative tests in the preoperative period, false positive testing in the postoperative period, seroconversion during the perioperative period, or in-hospital exposure. The most likely scenario would be patients who were admitted during the incubation period and seroconverted in the perioperative period. In-hospital exposures are unlikely given the incubation period of the virus, and we included only patients who tested positive within 7 days of surgery. A retrospective study of patients at 27 Dutch hospitals found that timing of diagnosis was strongly associated with survival in positive patients, with 92.3% of mortalities occurring in patients who were diagnosed in the postoperative period ($P = .001$).⁷ The higher rate of complications among patients with a postoperative COVID-19 diagnosis likely reflects a selection bias; postoperative COVID-19 testing is only performed on patients with development of new symptoms or a tumultuous postoperative course.

We acknowledge several limitations to our study. First, we are limited by our retrospective study design, which is subject to selection bias. As described earlier, our current testing protocol screens all patients preoperatively, but patients are repeatedly screened in the postoperative phase only if they demonstrate symptoms, need additional procedures, or if clinically indicated by provider evaluation. Patients with postoperative complications and unfavorable outcomes are more likely to undergo postoperative testing, especially with COVID-19 PCR testing in patients with unexplained fever or clinical deterioration. In these patients, the detection of asymptomatic to mild COVID-19 infection is certainly more likely than in patients without postoperative complications. Second, there was no appropriate group to serve as matched control cases. We considered using COVID-19 positive patients who underwent interventional radiology and endoscopic cases as matched control cases, but the sample size at our institution was insufficient. We additionally considered spontaneous vaginal deliveries as a comparison but deemed it biased due to the physiologic changes of pregnancy and lack of male comparison. We could not use in-patients with COVID-19 as matched control cases since patients with asymptomatic or mild disease would not require hospitalization. Another important limitation is that studies conducted reviewing patients in different locations during different periods of the COVID-19 pandemic are likely to have multifactorial differences in COVID-19 outcomes. This could be due to differing amounts of strain on health care systems, evolution of knowledge of how to manage COVID-19 patients, different proportions of COVID-19 strains, and other more subtle factors. Additionally, our study is limited by a small sample size of patients with moderate to critical COVID-19 infection. During the study period, only 7 patients with moderate to critical COVID-19 infection underwent surgical intervention within 7 days of diagnosis. Drawing conclusions from this small population is of limited use, and comparison is also limited by the differences in surgical disease severity.

Additionally, these data was collected before widespread vaccination efforts. Elderly patients and health care providers were eligible for vaccination only in the last 2 months of the study period, so the likelihood of capturing fully vaccinated patients is low. Additionally, history and physical exam notes were reviewed during patient assessment, and no patients were reported to have been partially or fully vaccinated either through study participation or early eligibility.

In conclusion, our study demonstrates 0% mortality, a 24.5% overall complication rate, and a 13.2% COVID-19 associated complication rate in patients with asymptomatic or mild COVID-19 infection diagnosed within 7 days before or after surgical intervention. Although more investigation into the safety of operative

intervention in patients with asymptomatic to mild COVID-19 infection is required, our data suggest that initial reports of high morbidity and mortality in patients with COVID-19 infections who undergo surgery may not be uniformly distributed across all degrees of COVID-19 severity. Preoperative assessment of COVID-19 disease severity should likely influence patient counseling and surgeon decision-making when considering surgical intervention in patients with positive preoperative COVID-19 tests.

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Conflict of interest/Disclosure

None declared.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [<https://doi.org/10.1016/j.surg.2021.12.024>].

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