Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company’s public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Periprocedural complications in patients with SARS-CoV-2 infection compared to those without infection: A nationwide propensity-matched analysis

Brajesh K. Lal, a,b,* Nikhil K. Prasad a,b, Brian R. Englum a, Douglas J. Turner a,b, Tariq Siddiqui b, Minerva Mayorga Carlin a,b, Rachel Lake a,b, John D. Sorkin c,d

a Department of Surgery, University of Maryland School of Medicine, Baltimore, MD, USA
b Surgery Service, Veterans Affairs Medical Center, Baltimore, MD, USA
c Geriatrics Research, Education, and Clinical Center, Veterans Affairs Medical Center, Baltimore, MD, USA
d Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA

Abstract

Background: Reports on emergency surgery performed soon after a COVID-19 infection that are not controlled for premorbid risk-factors show increased 30-day mortality and pulmonary complications. This contributed to a virtual cessation of elective surgery during the pandemic surge. To inform evidence-based guidance on the decisions for surgery during the recovery phase of the pandemic, we compare 30-day outcomes in patients testing positive for COVID-19 before their operation, to contemporary propensity-matched COVID-19 negative patients undergoing the same procedures.

Methods: This prospective multicentre study included all patients undergoing surgery at 170 Veterans Health Administration (VA) hospitals across the United States. COVID-19 positive patients were propensity matched to COVID-19 negative patients on demographic and procedural factors. We compared 30-day outcomes between COVID-19 positive and negative patients, and the effect of time from testing positive to the date of procedure (≤10 days, 11–30 days and >30 days) on outcomes.

Results: Between March 1 and August 15, 2020, 449 COVID-19 positive and 51,238 negative patients met inclusion criteria. Propensity matching yielded 432 COVID-19 positive and 1256 negative patients among whom half underwent elective surgery. Infected patients had longer hospital stays (median seven days), higher rates of pneumonia (20.6%), ventilator requirement (7.6%), acute respiratory distress syndrome (ARDS, 17.1%), septic shock (13.7%), and ischemic stroke (5.8%), while mortality, reoperations and readmissions were not significantly different. Higher odds for ventilation and stroke persisted even when surgery was delayed 11–30 days, and for pneumonia, ARDS, and septic shock >30 days after a positive test.

Discussion: 30-day pulmonary, septic, and ischaemic complications are increased in COVID-19 positive, compared to propensity score matched negative patients. Odds for several complications persist despite a delay beyond ten days after testing positive. Individualized risk-stratification by pulmonary and atherosclerotic comorbidities should be considered when making decisions for delaying surgery in infected patients.

Introduction

Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a pandemic by the World Health Organization on March 11, 2020. Reports indicate high rates of mortality and pulmonary complications after surgical procedures performed on COVID-19 positive patients. A report of 1128 surgical procedures (74% emergency procedures) performed in 52 hospitals...
procedures) conducted in 24 countries, during a COVID surge demonstrated 30-day mortality in 23.8%, postoperative pneumonia in 40.4%, and need for unexpected mechanical ventilation in 14.4.5 These data are similar to other studies on periprocedural risks for COVID-19 positive patients.1-5 Given the extraordinary circumstances surrounding COVID-19, including decreased healthcare capacity,6 delay in seeking or obtaining care,6 and unique factors selecting for surgery, a contemporary control group of COVID-19 negative patients undergoing similar procedures is necessary to make inferences about the risk attributable to the infection. The Veterans Health Administration (VA), one of the largest healthcare systems in the United States (US), provides care to over nine million individuals.7 Starting March 17, 2020, the VA deferred elective surgery nationwide to prevent the spread of COVID-19, preserve emergency surgery capabilities, and avoid adverse outcomes in non-emergency surgery. This deferral followed guidelines issued by the Centers for Medicare and Medicaid Services8 and the American College of Surgeons.9 As COVID-19 cases decreased across the country, VA facilities selectively restarted elective procedures. The current approach involves delaying elective surgery for at least ten days after a positive test in asymptomatic patients or ten days after the resolution of symptoms in symptomatic patients.10 Emergency surgery is performed without delay.

There are limited data describing the contribution of a COVID-19 infection to postoperative outcomes or the optimal delay in surgery after infection. With a national database containing electronic medical records (EMR) from serving nine million veterans across the US, the VA provides an opportunity to study the impact of SARS-CoV-2 on surgical patients. To help establish evidence-based guidance on the risk of surgery during the COVID-19 pandemic, we compared COVID-19 positive to contemporary COVID-19 negative patients undergoing a broad range of surgeries, after a propensity match that included identical procedure and case urgency.

Methods

Study design

We conducted a nationwide, multicenter, prospective study comparing COVID-19 positive and negative patients undergoing identical surgical procedures with identical urgency classifications. The COVID-19 patients were propensity score matched to patients who did not have COVID-19. Study participants were obtained from all 170 VA hospitals and 1255 VA health care centers across the US. The protocol was reviewed and approved by the University of Maryland Institutional Review Board and the Baltimore VA Medical Center Research and Development Committee.

Participants

We identified patients who underwent a surgical procedure between March 1 and August 15, 2020 and collected data on demographic, medical, and surgical characteristics. Our exposure was a positive SARS-CoV-2 quantitative RT-PCR test. Laboratory testing for SARS-CoV-2 infection was uniform across VA facilities.

All included patients had a test for SARS-CoV-2 prior to or on the date of surgery. Patients who were positive by PCR before or on the date of surgery were classified COVID-19 positive. Patients who were tested and never found to be positive at any time during the study period were classified COVID-19 negative. Patients who were not tested were excluded. If multiple procedures were performed during the study period in a COVID-19 positive patient, the procedure performed nearest to the date of the first positive test was defined as the index procedure. Similarly, in the COVID-19 negative group, the first procedure was considered the index procedure.

Data collection

Study data were obtained from the Department of Veterans Affairs Informatics and Computing Infrastructure (VINCI) database which stores data from the VA’s EMR (Computerized Patient Record System, CPRS).11

Data on age, sex, race and ethnicity, body mass index (BMI), and American Society of Anesthesiologists (ASA) physical status classification were obtained.12 The Charlson Comorbidity Index (CCI) was computed from a composite of 17 comorbidities using International Classification of Diseases–10 (ICD-10) codes for the 2 years prior to the date of surgery.13 The Current Procedural Terminology (CPT) code, case urgency (elective, urgent, or emergency), and anesthesia used for each procedure were obtained. Anesthesia was classified as general or other (a composite of sedation, spinal, epidural and local).

Outcomes

Patient outcomes up to 30-days after the index procedure were recorded. We studied four primary outcome measures: mortality, readmission, reoperation, and hospital length of stay (LOS). Secondary outcome measures (related to pulmonary complications) included postoperative pneumonia, need for mechanical ventilation, and acute respiratory distress syndrome (ARDS). Secondary outcomes (related to inflammatory, thrombotic, and ischemic syndromes) including septic shock, myocardial infarction (MI), ischemic stroke, and acute pulmonary embolism (PE). ICD-10 diagnosis codes were used to identify the outcome measures; ICD-10 and CPT codes were used to identify mechanical ventilation.

Statistical analysis

Summary statistics comparing COVID-19 positive and negative patients are presented as frequencies and percentages; means and standard deviations (SD); or medians and interquartile ranges (IQR). Comparisons of the two groups were performed using Pearson’s Chi² test and Fisher’s Exact test for categorical data. Student’s t-test was used for normally distributed continuous data, and the Mann-Whitney-U test was used for non-normally distributed continuous data. Outcomes were first compared between unmatched COVID-19 positive and negative patients.

COVID-19 positive patients were propensity score matched to COVID-19 negative patients (propensity to be COVID-19 positive, matching ratio 3:1, control to case). The match started with an exact match on all digits of the CPT code for the index procedure and an exact match on case urgency (elective, urgent or emergency). This was followed by a nearest neighbor match on age, sex, race, ethnicity, BMI, smoking status, CCI, ASA class, type of anesthesia, and history of cancer. For each outcome measure, we performed two analyses. The first compared outcomes in the matched COVID-19 positive and negative patients. The second analysis used a simple logistic regression with a 4-level independent variable for time from positive test to surgery: 1) COVID-19 negative, 2) <10 days from positive test to surgery, 3) 11–30 days, and 4) >30 days. The rationale for these strata are as follows: 1) According to CDC guidelines, the isolation period after onset of COVID-19 symptoms is ten days.14 2) It has been reported that 98% of patients with COVID-19 exposure develop symptoms within 11.5 days of infection.15 3) Little is known about the risk for adverse events up to and greater than one month after testing positive. Odds ratios (OR) and 95% confidence intervals (CI) for clinical outcome measures were calculated for each time strata relative to COVID-19 negative patients. A two-sided p of ≤0.05 was considered statistically significant. Statistical analyses were performed using R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).
Role of the funding source

The VA and the funding agencies had no role in the study design, analysis, interpretation, or manuscript.

Results

At the time of analysis (September 25, 2020), 30-day follow-up was complete on all patients undergoing surgery between March 1 and August 15, 2020. 93,031 surgical procedures were performed on 78,972 patients, with 53,697 patients meeting inclusion criteria. A total of 470 patients tested positive for SARS-CoV-2 infection, and 53,227 never tested positive before or on the date of their procedure. After excluding patients with missing data, we had 449 patients in the COVID-19 positive group and 51,238 patients in the negative group. Matching on propensity for being in the COVID-19 positive group resulted in a final cohort of 432 COVID-19 positive and 1256 negative patients (Fig. 1).

In the unmatched cohort, the COVID-19 positive group included more black patients (43% vs 19%; p < 0.001), greater comorbidity burden (3.6 vs 3.1; p < 0.001), more patients with ASA class four or five (25.2% vs 12.7%; P < 0.001), and more urgent or emergency procedures (55.3% vs 36.5%, p < 0.001) compared to the COVID-19 negative group (Supplemental Table 1). In unadjusted 30-day outcomes, COVID-19 positive patients had higher mortality rates (3.3% vs. 0.8%, p < 0.001) and longer median LOS (7 vs 3 days, p < 0.001) but no differences in readmission (8.9% vs. 7.1%, p = 0.17) or reoperation (8.7% vs. 6.9%, p = 0.16). COVID-19 positive patients had higher rates of pneumonia (21.4% vs. 3.3%, p < 0.001), postoperative mechanical ventilation (7.6% vs. 1.9%, p < 0.001), ARDS (16.9% vs. 2.8%, p < 0.001), septic shock (14.3% vs. 3.4%, p < 0.001), MI (4.7% vs. 1.5%, p < 0.001), ischemic stroke (6.0% vs. 1.9%, p < 0.001) and PE (3.8% vs. 1.8%, p = 0.01).

After propensity score matching, the standardized mean differences of the propensity scores comparing COVID-19 positive and negative patients were zero for their full 5-digit CPT codes, levels of procedural urgency, ethnicity, and comorbidity burden (CCI), and close to zero for all other variables included in the matching.
algorithm (Fig. 2). Demographic, clinical, and procedural characteristics including levels of urgency were similar in the matched cohort (Table 1).

After matching, COVID-19 positive patients demonstrated longer median LOS (7 vs 5 days, $p < 0.001$). Infected patients had higher 30-day rates of pneumonia (20.6% vs. 6.0%, $p < 0.001$), postoperative mechanical ventilation (7.6% vs. 4.1%, $p = 0.01$) and ARDS (17.1% vs 6.8%, $p < 0.001$). Mortality, reoperations, and readmissions were not different between the groups (Table 2). Among COVID-19 positive patients, 24.3% (105/432) had at least one pulmonary complication and 12.4% (13/105) of those died. Among COVID negative patients, 10.7% (134/1256) had at least one pulmonary complication and 14.9% (20/134) of those died. Infected patients had higher rates of septic shock (13.7% vs. 6.8%, $p < 0.001$) and ischemic stroke (5.8% vs. 2.9%, $p = 0.01$). Rates of PE were similar and rates of MI were nominally higher among COVID-19 positive patients but did not reach statistical significance (4.6% vs. 2.7%, $p = 0.07$).

The median time interval between the COVID-19 positive test and index procedure 42 days (IQR 21, 73). COVID-19 negative patients had a negative test 2 days prior to their procedure (IQR 1, 3). SARS-CoV-2 infection was diagnosed within ten days prior to surgery in 70 patients (16.2%), between 11 and 30 days prior in 96 patients (22.2%), and between 30 and 150 days prior in 266 patients (61.6%; Supplemental Fig. 1). The greatest odds of pneumonia and septic shock occurred in procedures within ten days of a positive test; however, higher odds of pneumonia, ARDS, and septic shock persisted even when a procedure was performed 11–30 days or more than 30 days after a positive test (Table 3). Odds for mechanical ventilation and ischemic stroke were elevated up to 30 days after a positive test. Frequency and percentage of postoperative complications by time interval from test to surgery is presented in Supplemental Table 2.

Discussion

Postprocedural pulmonary and septic complications are higher in patients with preprocedural SARS-CoV-2 infection compared to similar patients without infection. The rates for these complications are lower than earlier reports based largely on uncontrolled studies with large proportions of high-risk emergency procedures performed early (within ten days) after COVID-19 diagnosis. The propensity matched controls in this study allowed for a better estimation of the true impact of COVID-19 on outcomes. Peri-procedural ischemic stroke occurs more frequently in COVID-19 positive compared to negative patients, and MI rates trend this direction. This finding argues for careful cardiac and cerebrovascular risk-stratification of infected patients being considered for surgery. The risk for pulmonary complications and septic shock persists even in patients undergoing procedures delayed more than 30 days after positive COVID-19 testing. The odds for stroke are elevated up to 30 days after a positive test. These findings have important implications for clinical decision making since persistent COVID-related risks must be weighed against the risk for prolonged delays in offering surgery.

Early in the pandemic, high peri-procedural pulmonary complications, systemic sepsis and mortality resulted in a virtual cessation of elective surgery across the world. Available outcomes data present challenges, as they derive primarily from emergency procedures performed soon after a COVID-19 infection and lack adjustment for premorbid risk-factors known to contribute to complications. In 9 COVID-19 positive patients undergoing emergency surgery for hip fractures, the mortality was 56%.16 COVID-19 positive transplant recipients also demonstrated high rates of postoperative infections and mortality.1 Procedures performed early after a COVID-19 infection also result in high complication rates. In 34 patients undergoing an operation within 2.5 days of being diagnosed with the infection, 100% developed pneumonia,
Table 1
Description of patients by COVID-19 status after propensity score matching.

| DEMOGRAPHICS                      | COVID-19 Negative | COVID-19 Positive | p     |
|-----------------------------------|-------------------|-------------------|-------|
| N = 1256                          | N = 432           |                   |       |
| Age, years (SD)                   | 64.8 (12.3)       | 65.1 (12.7)       | 0.69  |
| Sex, male                         | 1171 (93.2)       | 398 (92.1)        | 0.51  |
| Race                              |                   |                   | 0.14  |
| Black                             | 478 (38.1)        | 187 (43.3)        |       |
| White                             | 96 (7.6)          | 27 (6.2)          |       |
| Other                             | 682 (54.3)        | 218 (50.5)        |       |
| Hispanic                          | 1160 (92.4)       | 398 (92.1)        | 0.96  |
| BMI, kg/m² (SD)                   | 29.8 (6.9)        | 30.0 (6.9)        | 0.71  |
| CLINICAL RISK FACTORS             |                   |                   |       |
| Smoking Status                    |                   |                   | 0.18  |
| Current                           | 237 (18.9)        | 62 (14.4)         |       |
| Former                            | 549 (41.7)        | 201 (46.5)        |       |
| Never                             | 406 (32.3)        | 143 (33.1)        |       |
| Unknown                           | 64 (5.1)          | 26 (6.0)          |       |
| Comorbidity index, CCI (SD)       | 3.6 (3.4)         | 3.6 (3.3)         | 0.91  |
| Heart failure                     | 16 (1.3)          | 10 (2.3)          | 0.20  |
| COPD                              | 305 (24.3)        | 101 (23.4)        | 0.75  |
| Cirrhosis                         | 49 (3.9)          | 18 (4.2)          | 0.92  |
| HIV                               | 16 (1.3)          | 10 (2.3)          | 0.20  |
| Dialysis dependent renal failure  | 119 (9.5)         | 33 (7.6)          | 0.30  |
| PROCEDURAL RISK FACTORS           |                   |                   |       |
| ASA Class                          |                   |                   | 0.06  |
| 1                                 | 3 (0.2)           | 3 (0.7)           |       |
| 2                                 | 195 (15.5)        | 58 (13.4)         |       |
| 3                                 | 778 (61.9)        | 260 (60.2)        |       |
| 4                                 | 279 (22.2)        | 108 (25.0)        |       |
| 5                                 | 1 (0.1)           | 3 (0.7)           |       |
| General anesthesia                | 737 (58.7)        | 269 (62.3)        | 0.21  |
| Organ system of surgery           |                   |                   | 1.00  |
| Musculoskeletal                   | 263 (20.9)        | 89 (20.6)         |       |
| Urological                        | 250 (19.9)        | 85 (19.7)         |       |
| Gastrointestinal                  | 194 (15.4)        | 68 (15.7)         |       |
| Cardiovascular                    | 163 (13.0)        | 57 (13.2)         |       |
| Ophthalmological                  | 111 (8.8)         | 37 (8.6)          |       |
| Respiratory                       | 105 (8.4)         | 35 (8.1)          |       |
| Integumentary                     | 74 (5.9)          | 27 (6.2)          |       |
| Neurological                      | 69 (5.5)          | 25 (5.8)          |       |
| Endocrine                         | 9 (0.7)           | 3 (0.7)           |       |
| Gynecological                     | 6 (0.5)           | 2 (0.5)           |       |
| Lymphatic                         | 6 (0.5)           | 2 (0.5)           |       |
| Auditory                          | 3 (0.2)           | 1 (0.2)           |       |
| Mediastinum/Diaphragm             | 3 (0.2)           | 1 (0.2)           |       |
| Urgency level                     |                   |                   | 0.92  |
| Elective                          | 580 (46.2)        | 196 (45.4)        |       |
| Urgent                            | 544 (43.3)        | 188 (43.5)        |       |
| Emergency                         | 132 (10.5)        | 48 (11.1)         |       |

Data represents frequency (%) unless indicated. Averages presented as means. SD, standard deviation; BMI, body mass index; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; ASA, American Society of Anesthesiologists.

Table 2
30-day postoperative outcomes COVID-19 status after propensity score matching.

| COVID-19 Negative | COVID-19 Positive | p-value |
|-------------------|-------------------|---------|
| N = 1256          | N = 432           |         |
| Mortality          | 28 (2.2)          | 15 (3.5) | 0.22 |
| Reoperation        | 131 (10.4)        | 36 (8.3) | 0.24 |
| Readmission        | 113 (9.0)         | 33 (7.6) | 0.44 |
| Length of stay, days* | 5 [2, 10]   | 7 [2, 23]  | <0.001 |
| Pneumonia          | 75 (6.0)          | 89 (20.6) | <0.001 |
| Postoperative mechanical ventilation | 51 (4.1) | 33 (7.6) | 0.01 |
| ARDS               | 86 (6.8)          | 74 (17.1) | <0.001 |
| Septic shock       | 86 (6.8)          | 59 (13.7) | <0.001 |
| Pulmonary embolism  | 27 (2.1)          | 15 (3.5) | 0.18 |
| Myocardial infarction | 34 (2.7)  | 20 (4.6) | 0.07 |
| Ischemic stroke    | 37 (2.9)          | 25 (5.8) | 0.01 |

The data is expressed as number (percentage) unless specified otherwise. *Median [interquartile range]. ARDS, Acute respiratory distress syndrome.
ARDS: Acute respiratory distress syndrome.

There are limited studies on the risk of postprocedural adverse events attributable to COVID-19 after adjusting for important covariates. Available reports have three main limitations: 1) They compare COVID-19 positive patients to pre-pandemic patients;2,22,25 2) they do not include elective surgery;16,21,23 or 3) they do not adjust for comorbidity burden.2,6,22,25 Propensity score-matching offers an opportunity to compare outcomes between COVID-19 positive and negative patients with similar demographic features and comorbidities undergoing similar operations (emergency or elective). Given sample size limitations, it is difficult to achieve this analysis using data from a single center. One group reported a propensity score matched analysis but was limited to 25 COVID-19 patients undergoing emergency surgery within 2.12 ± 0.93 days of testing positive.18 The VINCI database provides the breadth and volume of data needed to match individuals on the specific procedure, level of urgency, demographics, and risk factors. After propensity score-matching, we found that COVID-19 positive patients demonstrated elevated rates of post-procedural pneumonia, ARDS, postoperative mechanical ventilation, and septic shock compared to uninfected controls. These translated into a prolonged LOS. The observed rates for complications were lower than in previous reports and likely reflect the use of appropriate controls, our COVID-19 positive case mix (54.6% urgent/emergency procedures, 62.3% with general anesthesia), and lead time from test to surgery (16.2% of COVID-19 positive patients had surgery within ten days of testing). Infected patients had similar rates of mortality, reoperation, readmission, and acute PE compared to uninfected patients. These findings may reflect increased collective knowledge driving improved anticipation, prevention, detection, and management of COVID-related complications.

It is reassuring that a delay in surgery by ten days after a positive test for COVID-19 reduces postprocedural complications. However, not all complications returned to non-COVID-19 levels. The odds for pneumonia, ARDS and septic shock were high when a procedure was performed within ten days of a positive test and remained elevated even when procedures were delayed by >30 days. The odds of postoperative mechanical ventilation were elevated up to 30 days after a positive test. Scattered reports have suggested the possibility of persistent pulmonary risks when procedures are performed 2–4 weeks after a test is positive.20,24 Our findings argue for consideration of delaying elective surgery for 30 or more days, particularly in patients with pre-existing pulmonary risk factors such as smoking, chronic obstructive pulmonary disease and severe cardiac disease, which have all been associated with COVID-19 pneumonia.

There are limited studies on the risk of postprocedural adverse events attributable to COVID-19 after adjusting for important covariates. Available reports have three main limitations: 1) They compare COVID-19 positive patients to pre-pandemic patients; 2) they do not include elective surgery; or 3) they do not adjust for comorbidity burden. Propensity score-matching offers an opportunity to compare outcomes between COVID-19 positive and negative patients with similar demographic features and comorbidities undergoing similar operations (emergency or elective). Given sample size limitations, it is difficult to achieve this analysis using data from a single center. One group reported a propensity score matched analysis but was limited to 25 COVID-19 patients undergoing emergency surgery within 2.12 ± 0.93 days of testing positive. The VINCI database provides the breadth and volume of data needed to match individuals on the specific procedure, level of urgency, demographics, and risk factors. After propensity score-matching, we found that COVID-19 positive patients demonstrated elevated rates of post-procedural pneumonia, ARDS, postoperative mechanical ventilation, and septic shock compared to uninfected controls. These translated into a prolonged LOS. The observed rates for complications were lower than in previous reports and likely reflect the use of appropriate controls, our COVID-19 positive case mix (54.6% urgent/emergency procedures, 62.3% with general anesthesia), and lead time from test to surgery (16.2% of COVID-19 positive patients had surgery within ten days of testing). Infected patients had similar rates of mortality, reoperation, readmission, and acute PE compared to uninfected patients. These findings may reflect increased collective knowledge driving improved anticipation, prevention, detection, and management of COVID-related complications.

It is reassuring that a delay in surgery by ten days after a positive test for COVID-19 reduces postprocedural complications. However, not all complications returned to non-COVID-19 levels. The odds for pneumonia, ARDS and septic shock were high when a procedure was performed within ten days of a positive test and remained elevated even when procedures were delayed by >30 days. The odds of postoperative mechanical ventilation were elevated up to 30 days after a positive test. Scattered reports have suggested the possibility of persistent pulmonary risks when procedures are performed 2–4 weeks after a test is positive.20,24 Our findings argue for consideration of delaying elective surgery for 30 or more days, particularly in patients with pre-existing pulmonary risk factors such as smoking, chronic obstructive pulmonary disease and severe cardiac disease, which have all been associated with COVID-19 pneumonia.

There are limited studies on the risk of postprocedural adverse events attributable to COVID-19 after adjusting for important covariates. Available reports have three main limitations: 1) They compare COVID-19 positive patients to pre-pandemic patients; 2) they do not include elective surgery; or 3) they do not adjust for comorbidity burden. Propensity score-matching offers an opportunity to compare outcomes between COVID-19 positive and negative patients with similar demographic features and comorbidities undergoing similar operations (emergency or elective). Given sample size limitations, it is difficult to achieve this analysis using data from a single center. One group reported a propensity score matched analysis but was limited to 25 COVID-19 patients undergoing emergency surgery within 2.12 ± 0.93 days of testing positive. The VINCI database provides the breadth and volume of data needed to match individuals on the specific procedure, level of urgency, demographics, and risk factors. After propensity score-matching, we found that COVID-19 positive patients demonstrated elevated rates of post-procedural pneumonia, ARDS, postoperative mechanical ventilation, and septic shock compared to uninfected controls. These translated into a prolonged LOS. The observed rates for complications were lower than in previous reports and likely reflect the use of appropriate controls, our COVID-19 positive case mix (54.6% urgent/emergency procedures, 62.3% with general anesthesia), and lead time from test to surgery (16.2% of COVID-19 positive patients had surgery within ten days of testing). Infected patients had similar rates of mortality, reoperation, readmission, and acute PE compared to uninfected patients. These findings may reflect increased collective knowledge driving improved anticipation, prevention, detection, and management of COVID-related complications.

It is reassuring that a delay in surgery by ten days after a positive test for COVID-19 reduces postprocedural complications. However, not all complications returned to non-COVID-19 levels. The odds for pneumonia, ARDS and septic shock were high when a procedure was performed within ten days of a positive test and remained elevated even when procedures were delayed by >30 days. The odds of postoperative mechanical ventilation were elevated up to 30 days after a positive test. Scattered reports have suggested the possibility of persistent pulmonary risks when procedures are performed 2–4 weeks after a test is positive.20,24 Our findings argue for consideration of delaying elective surgery for 30 or more days, particularly in patients with pre-existing pulmonary risk factors such as smoking, chronic obstructive pulmonary disease and severe cardiac disease, which have all been associated with COVID-19 pneumonia.

Table 3

| COVID-19 Negative (n = 1256) | COVID-19 Positive | Interval between testing and date of procedure |
|---------------------------------|------------------|-------------------------------------------|
| Pneumonia Reference 7.7 (4.4–13.3) | Reference 6.2 (3.7–10.1) | Reference 2.7 (1.8–4.1) |
| Postoperative mechanical ventilation Reference 3.1 (1.3–6.4) | Reference 3.1 (1.5–5.9) | Reference 1.3 (0.7–2.3) |
| ARDS Reference 4.0 (2.2–7.2) | Reference 4.5 (2.7–7.5) | Reference 2.0 (1.3–3.0) |
| Septic shock Reference 3.4 (1.8–6.2) | Reference 2.7 (1.5–4.8) | Reference 1.7 (1.1–2.6) |
| Myocardial infarction Reference 2.2 (0.6–5.7) | Reference 1.6 (0.9–4.0) | Reference 1.7 (0.8–3.2) |
| Ischaemic stroke Reference 1.0 (0.2–3.3) | Reference 3.4 (1.5–7.0) | Reference 1.8 (0.9–3.4) |

ARDS: Acute respiratory distress syndrome.
Conclusions

We did not find higher rates of postprocedural mortality, reoperation, or readmission in patients with prior COVID-19 infection, potentially due to increased elective cases and improved care for COVID-19 in our cohort. COVID-19 positive patients did have higher risks of pulmonary, septic, and ischemic complications, which persisted for 30 days or longer after a positive test. These findings underscore the importance of preoperative screening for SARS-CoV-2 infection and consideration for deferring elective surgery up to or beyond 30 days, particularly in those with pulmonary or atherosclerotic risk factors. Strategies for targeted prophylaxis, reduced thresholds for testing, and aggressive treatments for these complications need to be evaluated.

Contributors

The co-authors contributed to study conception, protocol development, data collection, data interpretation, and critical revision of the manuscript. BKL is the guarantor.

Data sharing

Data sharing requests will be considered upon written request to the corresponding author. Deidentified participant data or other prespecified data will be available subject to a written proposal and a signed data sharing agreement with the Veterans Affairs Informatics and Computing Infrastructure.

Funding sources

This study was funded by Veterans Affairs awards HSRD C19-20-407, RRD RX000995 and CSRD CX001621, and NIH awards NS080168, NS097876 and AG000513 (BKL); National Institutes of Health awards AG028747, DK072488, and Baltimore VA Medical Center GRECC (JDS); National Institutes of Health T32 AG002622 (NKP).

The views expressed are those of the authors and not necessarily those of the Veterans Affairs or the National Institutes of Health.

Declaration of competing interest

We declare no competing interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2020.12.024.

References

1. Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine. 2020;21. https://doi.org/10.1016/j.eclinm.2020.100331.
2. Egol KA, Konda SR, Bird ML, et al. Increased mortality and major complications in hip fracture care during the COVID-19 pandemic: A New York city perspective. J Orthop Trauma. 2020;34(8):395—402. https://doi.org/10.1097/BOT.0000000000001845.
3. Michaels MG, La Hoz RM, Danziger-Isakov L, et al. Coronavirus disease 2019: implications of emerging infections for transplantation. Am J Transplant. 2020;20(7):1768—1772. https://doi.org/10.1111/ajt.15832.
4. Rocco B, Sighinolfi MC, Sandri M, et al. The dramatic COVID-19 outbreak in Italy is responsible of a huge drop in orthopaedic surgical activity: a multicenter observational study. BJU Int. 2020. https://doi.org/10.1111/bju.15149. Published online.
5. Rocco B, Sighinolfi MC, Sandri M, et al. The dramatic COVID-19 outbreak in Italy is responsible of a huge drop in orthopaedic surgical activity: a multicenter observational study. BJU Int. 2020. https://doi.org/10.1111/bju.15149. Published online.
6. Wong Laura E, Hawkins Jessica E, Langness Simone, Murrell Karen L, Irwin A, Sammann Amanda. Where are the patients? Addressing COVID-19 fear to encourage sick patients to seek emergency care. NEJM Catalyst; 2020. Published online https://catalyst.nejm.org/docs/doi/10.1056/CAT.20.0193.
7. Veterans Affairs Health Administration. U.S. Department of veterans Affairs. Published https://www.va.gov/health/. 2020 Accessed September 15, 2020.
8. Centers for Medicare and Medicaid Services. Non-emergent, elective medical services, and treatment recommendations. Published https://www.cms.gov/files/document/31820-Cino-Adult- Elective-Surgery-and-Procedures- Recommendations.pdf. 2020. Accessed September 28, 2020.
9. American College of Surgeons. COVID-19: guidance for triage of non-emergent surgical procedures. https://www.facs.org/covid-19/clinical-guidance/triage. https://www.facs.org/about-acs/covid-19/information-for-surgeons/triage. https://www.facs.org/covid-19/clinical-guidance/triage. Accessed September 28, 2020.
10. Centers for Disease Control and Prevention. Interim guidance for rapid antigen testing for SARS-CoV-2 CDC. Published https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html. 2020. Accessed September 28, 2020.
11. U.S. Department of Veterans Affairs. VA Informatics and computing infrastructure (VINCI) homepage. https://www.hsrda.hrsa.gov/researchers/vinci. 2018. Accessed September 28, 2020.
12. Mayhew D, Mendonca V, Murthy BVS. A review of ASA physical status — historical perspectives and modern developments. Anaesthesia. 2019;74(3):373—379. https://doi.org/10.1111/anae.14560.
13. Quan H, Sundararajan V, Halfon P, et al. Coding_Algorithms_for_Defining_Comorbidities_in.10. Med Care. 2005;43(11):1130—1139.
14. Wölfl F, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020;581(7809):465—469. https://doi.org/10.1038/s41586-020-2196-x.
15. Lauer SA, Grantz KH, Bi Q, et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported cases: estimation and application. Ann Intern Med. 2020;172(9):577—582. https://doi.org/10.1322/260-0504.
16. LeBrun DG, Konaris MA, Ghahramani CM, et al. Hip fracture outcomes during the COVID-19 pandemic: early results from New York. J Orthop Trauma. 2020;34(8):403—410. https://doi.org/10.1097/BOT.0000000000001849.
17. Wu Z, MaGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for disease control and prevention. JAMA - J Am Med Assoc. 2020. https://doi.org/10.1001/jama.2020.2648. Published online.
18. Yang J, Zheng Y, Guo X, et al. Prevalence of comorbidities and its effects in coronavirus disease 2019 patients: a systematic review and meta-analysis. Int J Infect Dis. 2020;94:91—95. https://doi.org/10.1016/j.ijid.2020.03.017.
19. Barkhordari K, Khajavi MR, Bagheri J, et al. Early respiratory outcomes following cardiac surgery in patients with COVID-19. J Card Surg. 2020. https://doi.org/10.1111/jocs.14915. Published online August 13, jocs.14915.
20. Glaseby JC, Nepogodiev D, Omar O, et al. Delaying surgery for patients with a previous SARS-CoV-2 infection. Br J Surg. 2020. https://doi.org/10.1002/bjs.12050. Published online.
21. Konda SR, Ranson RA, Solasz SJ, et al. Modicification of a validated risk stratification tool to characterize geriatric hip fracture outcomes and optimize care in a post-COVID19 World. J Orthop Trauma. 2020. https://doi.org/10.1097/BOT.0000000000001895. Published online.
22. Ghirmandi R, Pipola V, Terzi S, et al. The impact of SARS-CoV-2 pandemic on oncologic and degenerative spine surgery department activity: the experience of nizzoli orthopedic institute under COVID-19 lockdown. Eur Rev Med Pharmacol Sci. 2020. https://doi.org/10.26355/eurrev_202007_21926. Published online.
23. Kayani B, Onochie E, Patil V, et al. The effects of COVID-19 on perioperative morbidity and mortality in patients with hip fractures: a multicentre cohort study. Bone Joint Lett J. 2020;102(9):1—10.
24. Stevenson JD, Evans S, Moritz G, et al. Mortality of high-risk orthopaedic oncology patients during the COVID-19 pandemic: a prospective cohort study. J Surg Oncol. 2020. https://doi.org/10.1002/jso.26127. Published online.
25. Madjed M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system. JAMA Cardiol. 2020;5(7):831. https://doi.org/10.1001/jamacardio.2020.1286.
26. Lee KR, Bae JH, Hwang IC, Kim KK, Suh HS, Ko KD. Effect of influenza vaccination on risk of stroke: a systematic review and meta-analysis. Neuroepidemiology. 2017;48(3):110—119. https://doi.org/10.1159/000487080.
27. Merkle AE, Parikh NS, Mir S, et al. Risk of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) vs patients with influenza. JAMA Neurol. 2020. https://doi.org/10.1001/jamaneurol.2020.2730. Published online.