World J Surg (2023) 47:573–577
https://doi.org/10.1007/s00268-023-06891-z

ORIGINAL SCIENTIFIC REPORT

Safety of Surgery Among Asymptomatic SARS-CoV-2 PCR-Positive Patients: A Single-Center Retrospective Cohort Study

Ozlem Aydın[1] · Pınar Ergen[1] · Haluk Vahaboglu[1]

Accepted: 25 December 2022 / Published online: 13 January 2023

Abstract

Background Screening with SARS-CoV-2 PCR tests is recommended for all patients undergoing surgery under general anesthesia, and elective surgery is deferred for positive patients. This study evaluated the outcomes of asymptomatic PCR-positive patients who underwent general anesthesia and surgery.

Methods Patient data were collected from the hospital records of patients who underwent surgery between January 2021 and May 2022. Asymptomatic patients with a positive PCR test between 7 days before and 5 days after surgery were compared with controls. The cases were propensity score-matched with a 1:2 ratio to the controls. All-cause in-hospital mortality was the primary outcome of the study.

Results A total of 217 asymptomatic PCR-positive patients were matched to 434 controls. In multivariate analysis, PCR-positive test results were not associated with mortality (log(OR) (95%CIs), p; 0.86 (− 0.13, 1.9), 0.09). Age and ASA score (>3) were the most significant risk factors associated with mortality.

Conclusion This study found that surgery among asymptomatic PCR-positive patients was not associated with increased mortality.

Introduction

SARS-CoV-2 (SARS2) infects and eventually disrupts ACE2 plus TMPRSS2 expressing cells of the lower respiratory tract, causing severe complications such as diffuse alveolar damage and bacterial or fungal bronchopneumonia [1, 2]. Intubation under general anesthesia poses a significant risk of postoperative pulmonary complications [3]. Surgical operations requiring general anesthesia have the potential to cause severe outcomes in patients with perioperative SARS2 infection.

Although some studies did not find significant associations between surgery and adverse outcomes among perioperative SARS2 PCR-positive patients [4], other studies have also shown significant associations [5]. One study found that surgery <7 weeks after recovering from COVID-19 was significantly associated with mortality [6]. The American Society of Anesthesiologists recommends waiting 4–12 weeks after a confirmed COVID-19 infection (COVID-19 and elective surgery (asahq.org)). These recommendations resulted in screening all patients with respiratory PCR testing, even for patients without symptoms, and deferring elective surgery for PCR-positive patients.

The burden of screening all patients with PCR tests and the medical consequences of deferring surgery for asymptomatic PCR-positive patients is a significant health

✉ Haluk Vahaboglu
vahabo@hotmail.com

Ozlem Aydın
ozlemsenaydin@hotmail.com

Pınar Ergen
pergen71@hotmail.com

1 Tıp Fakültesi, Istanbul Medeniyet Universitesi, Istanbul, Turkey

issue. The outcomes of screening surgical patients are of medical interest, but the data are sparse.

We evaluated the outcomes of PCR-positive patients who underwent surgery under general anesthesia.

Material and methods

Study design and data collection

We conducted a single-center retrospective cohort study among surgical patients who underwent mechanical ventilation for general anesthesia, and compared perioperative SARS2 PCR-positive patients with controls. Symptomatic patients underwent deferred surgery unless they had a life-threatening surgical condition and were thus not included in the cohort. Symptomatic patients were defined using WHO clinical criteria (https://apps.who.int/iris/bitstream/handle/10665/360579/WHO-2019-nCoV-Surveillance-Case-Definition-2022.1-eng.pdf). We analyzed a propensity score-matched (1:2) subgroup.

We obtained data from the hospital's electronic records by filtering the hospitalized surgical patients from January 2021 to May 2022. We excluded patients with SARS2 multiplex PCR-positive results before 7 days and 5 days after surgery. Thus, we kept patients with PCR-positive test results between 7 days before and 5 days after surgery and patients with negative PCR test results as controls.

The outcome was all-cause in-hospital mortality.

We compared age, sex, and underlying diseases, such as diabetes, hypertension, cardiovascular disease, chronic renal disease, and malignant disease, between patients who survived and those who died. We also compared the American Society of Anesthesiologists (ASA) scores recorded by an anesthesiologist before surgery.

The ASA scores were as follows: (1) The patient was entirely healthy and fit, (2) the patient had a mild systemic disease, (3) the patient had a severe systemic disease but was not incapacitated, (4) the patient had an incapacitating illness that constantly threatens life, and (5) a moribund patient not expected to live 24 h with or without surgery [7].

This study was approved institute ethical committee with the number of 2022/0587.

Statistics

Continuous variables were presented as the median and interquartile range (IQR; 0.25–0.75) and compared using the Wilcoxon rank sum test. Count data were presented as numbers and percentages and compared using Pearson's Chi-squared test or, where required, Fisher's exact test.

Propensity scores were estimated using a logistic model with independent variables, including age, sex, ASA score, emergency surgery, diabetes, hypertension, cardiovascular disease, chronic renal disease, and malignant disease. We matched PCR-positive surgical patients in a 1:2 ratio to PCR-negative surgical patients using the "matchit" package using the nearest neighbor method with replacement. The balance between the before and after matching variables was estimated using mean differences and Kolmogorov–Smirnov tests.

We constructed an initial model by including variables that were found to be significant ($p < 0.05$) in the univariate comparisons. However, ASA score was included in the model as a categorical variable (score >3). Underlying disease was dichotomized as having one or more of the following: diabetes, hypertension, cardiovascular disease, chronic renal disease, and malignant disease. The final model was created using backward elimination of non-

Table 1 Characteristics of the cohort

Variables	Died		*p* value[2]
	No *N* = 17375[1]	Yes *N* = 194[1]	
PCR (+)ive[3]	206 (1.2%)	11 (5.7%)	**<0.001**
ASA score[4]			**<0.001**
1	6,680 (38%)	12 (6.2%)	
2	8,856 (51%)	39 (20%)	
3	1,731 (10.0%)	93 (48%)	
4	105 (0.6%)	48 (25%)	
5	3 (<0.1%)	2 (1.0%)	
Surgical emergency	2,994 (17%)	128 (66%)	**<0.001**
Age	47 (27, 63)	68 (50, 78)	**<0.001**
Sex			0.7
Female	8,947 (51%)	97 (50%)	
Male	8,428 (49%)	97 (50%)	
Diabetes	592 (3.4%)	27 (14%)	**<0.001**
Hypertension	136 (0.8%)	9 (4.6%)	**<0.001**
Cardiovascular disease	63 (0.4%)	15 (7.7%)	**<0.001**
Chronic renal disease	675 (3.9%)	24 (12%)	**<0.001**
Malign disease	764 (4.4%)	21 (11%)	**<0.001**

Significant comparisons with a *p*-value ≤ 0.05 are given in bold

[1]*n* (%); Median (IQR)

[2]Fisher's exact test; Fisher's exact test for count data with simulated *p* value (based on 2000 replicates); Pearson's Chi-squared test; Wilcoxon rank sum test

[3]SARS-CoV-2 rtPCR

[4]1, Patient is a completely healthy fit patient; 2, patient has mild systemic disease; 3, patient has severe systemic disease that is not incapacitating; 4, patient has incapacitating disease that is a constant threat to life; 5, a moribund patient who is not expected to live 24 h with or without surgery

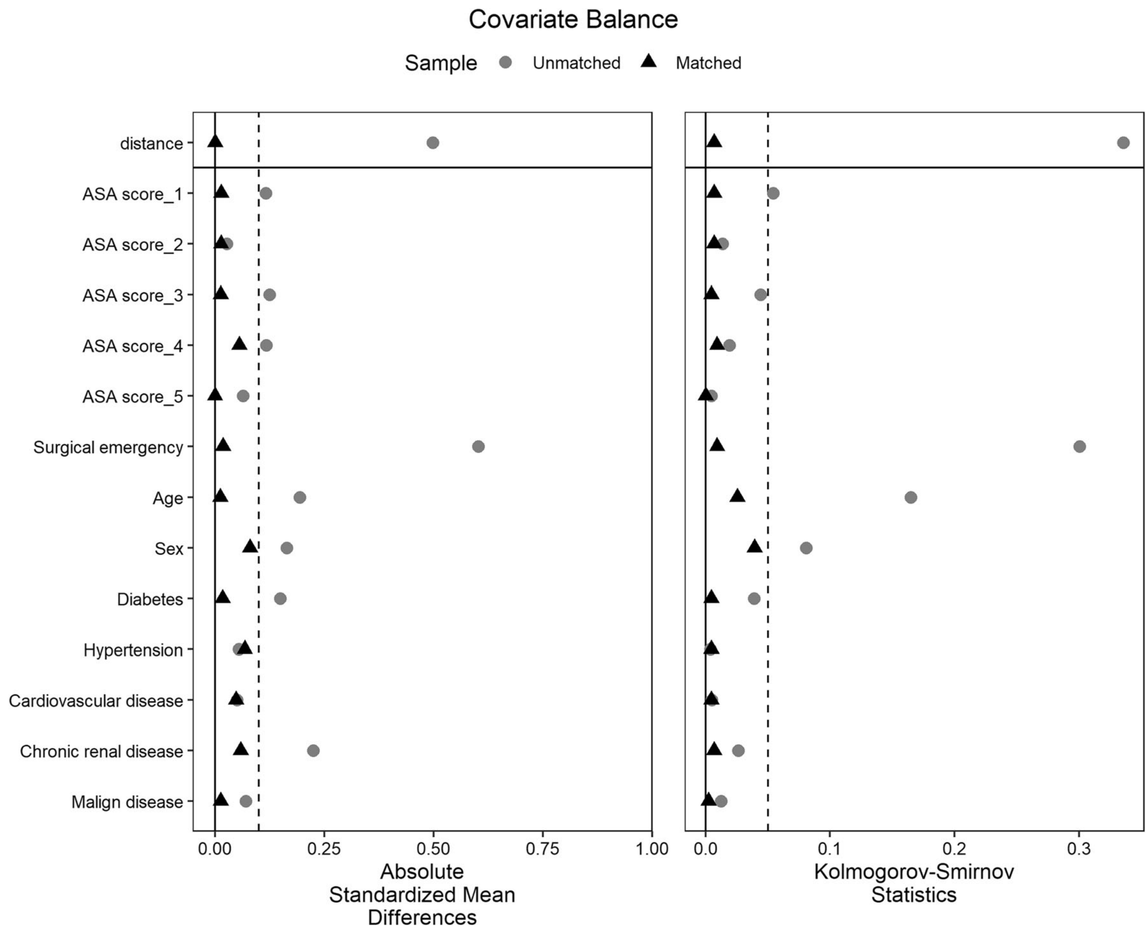


Fig. 1 Covariate balance before and after adjusting. The dotted lines represent threshold values for balance used in absolute mean differences and Kolmogorov–Smirnow statistics

significant variables. Multicollinearity and interactions were tested.

We also constructed a nomogram from the final model using the predictive performance of variables using the rms package.

Statistical analyses were conducted using the open-source R version R-4.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

During the study period, 17,569 patients underwent surgery under general anesthesia. The characteristics of the cohort are summarized in Table 1. Briefly, of the 194 patients who died in hospital, 11 (5.7%, $p < 0.001$) were SARS2 PCR positive. ASA scores were higher among patients who died, and emergency surgery was more frequent (n (%), 128 (0.66); $p < 0.001$). Patients who died were older than those who survived (median (IQR), 68 years (50, 78); <0.001) and had more underlying diseases. A total of 217 patients were PCR positive; among these, 52 had stayed in the COVID-19 wards and received oxygen support of varying intensity. Of the 52 patients, 21 were treated in COVID-19 wards after surgery (median (days), IQR: 6 (2, 10)), while 31 were treated in COVID-19 wards before surgery (median (days), IQR: 6 (2, 9)), and among these, five and three patients died, respectively ($p = 0.321$).

Due to the imbalance between PCR-positive and PCR-negative patients (PCR-positive *n* (%); 217 (0.1%)), we conducted comparisons on a propensity score-matched subgroup. We generated propensity scores and matched SARS2 PCR-positive patients at a ratio of 1:2 to the controls. Figure 1 displays the before and after balance between matching variables compared with the mean differences and Kolmogorov–Smirnov statistics [8]. The variables were balanced after matching. We first applied a full model and then backward-eliminated variables to obtain sufficient discriminative power and shrinkage values. Table 2 presents the point estimates for the full and

Table 2 Point estimates from the final logistic model

Characteristic	Full model			Final model		
	log(OR)[1]	95% CI[1]	*p* value	log(OR)[1]	95% CI[1]	*p* value
PCR (+)ive[2]	0.78	− 0.23, 1.8	0.13	0.86	− 0.13, 1.9	0.086
ASA score >3	3.1	1.8, 4.5	**<0.001**	3.1	1.7, 4.4	**<0.001**
Surgical emergency	1.2	0.17, 2.5	**0.029**	1.3	0.23, 2.5	**0.022**
Age	0.04	0.02, 0.07	**<0.001**	0.05	0.02, 0.07	**<0.001**
Sex	0.38	− 0.66, 1.4	0.5			
Underlying disease[3]	0.87	− 0.36, 2.0	0.14			

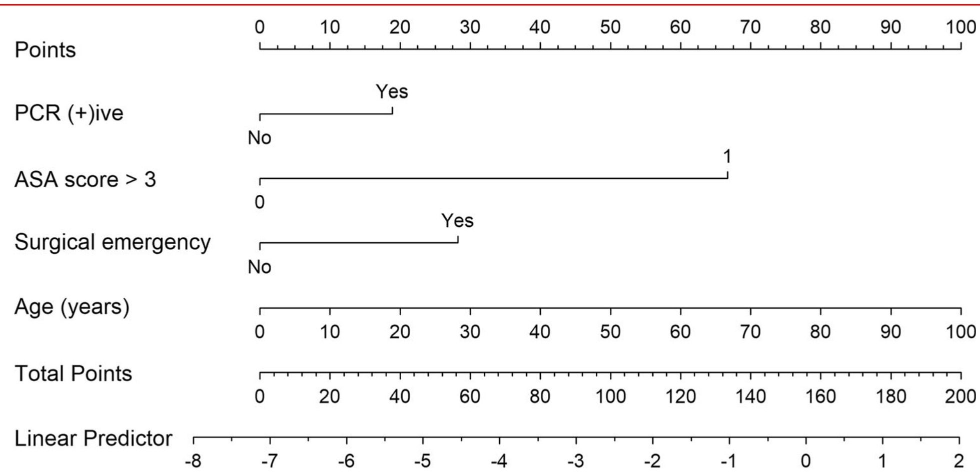
Significant comparisons with a *p*-value $\leq$ 0.05 are given in bold

[1]OR = odds ratio, CI = confidence interval

[2]PCR(+)ive, SARS-CoV-2 rtPCR positive

[3]Underlying disease, any of diabetes, hypertension, chronic renal disease, chronic cardiovascular disease or malign disease

Fig. 2 Nomogram constructed from the predictions of the final logistic model



final models. In the final model, the point estimate for PCR-positives was not significant (log(OR) (95%CIs), *p*; 0.86 (− 0.13, 1.9), 0.086). However, an ASA score >3, older age, and surgical emergency were associated with all-cause in-hospital mortality. The discriminative power of the final model was 0.85 (C-index = 0.85), and the shrinkage factor was 0.94 ([model x^2 − (d.f. − 1)]/model x^2) [9, 10].

Figure 2 shows the nomogram constructed from the predictive performance of the variables in the final model. Older age and ASA score >3 significantly impacted the outcome, while the SARS2 PCR test was only marginally associated with mortality.

Discussion

This study failed to show a significant difference between PCR-positive and PCR-negative surgical patients regarding all-cause in-hospital mortality. In other words, this study does not support the preoperative screening of asymptomatic patients using the SARS2 PCR test. In our hospital, all symptomatic patients defer surgery, unless a life-threatening emergency occurs. We studied perioperatively PCR-positive asymptomatic patients and compared them to PCR-negative controls. One study reported a 20.5% mortality rate among postoperative patients who developed COVID-19 [11]. Another study reported the significance of the timing between PCR-positive testing and surgery [6]. Some studies failed to identify significant outcome differences [4, 12]. However, neither of these studies compared perioperative asymptomatic PCR-positive patients to PCR-negative controls and thus did not explicitly address the outcomes of screening all asymptomatic preoperative patients.

We found that age and an ASA score >3 were significant risk variables associated with mortality. However, emergency surgery and a positive SARS2 PCR test only marginally affected adverse outcomes. One study found that age and being SARS2 PCR positive had a significant prognostic value in cardiac surgery [13]. However, in this study, most patients were symptomatic, and a history of heart failure was more common among PCR-positive patients. Preoperative risk stratification for asymptomatic SARS2 PCR-positive patients is of scientific interest [14].

There are some limitations to our study. First, this was a retrospective study; therefore, we could not extract the detailed baseline characteristics of the patients. Second, this was a single-center study, which limits the generalization of the findings. Third, this study did not analyze all postoperative pulmonary complications. Lastly, since we have no gold standard test to identify true positives, we must consider that false positive PCR test results might exist and negatively affect statistical inferences.

Finally, our study found that surgery among asymptomatic PCR-positive patients was not associated with increased mortality. Further studies are required to provide more robust results.

Acknowledgements We thank Editage™ for English editing the manuscript.

Declarations

Conflict of interest Authors have no conflict of interest.

Informed consent Waived by the Ethical Committee.

References

1. Lukassen S, Chua RL, Trefzer T et al (2020) SARS-CoV-2 receptor ACE 2 and TMPRSS 2 are primarily expressed in bronchial transient secretory cells. EMBO J 39:1–15
2. Borczuk AC, Salvatore SP, Seshan SV et al (2020) COVID-19 pulmonary pathology: a multi-institutional autopsy cohort from Italy and New York City. Mod Pathol 33:2156–2168
3. Neto AS, Hemmes SNT, Barbas CSV et al (2016) Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: a meta-analysis of individual patient data. Lancet Respir Med 4:272–280
4. Mavrothalassitis O, Pirracchio R, Fong N et al (2022) Outcome of surgical patients during the first wave of the COVID-19 pandemic in US hospitals. Br J Anaesth 128:e35–e37
5. Bhangu A, Nepogodiev D, Glasbey JC et al (2020) Mortality and pulmonary complications in patients undergoing surgery with perioperative sars-cov-2 infection: an international cohort study. Lancet 396:27–38. https://doi.org/10.1016/S0140-6736(20)31182-X
6. Collaborative C, Collaborative G (2021) Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. Anaesthesia 76:748–758
7. Sutton R, Bann S, Brooks M, Sarin S (2002) The Surgical Risk Scale as an improved tool for risk-adjusted analysis in comparative surgical audit. Br J Surg 89:763–768
8. Austin PC, Stuart EA (2015) Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. Stat Med 34:3661–3679
9. Harrell FE Jr, Lee KL, Mark DB (1996) Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med 15:361–387
10. Steyerberg EW, Eijkemans MJC, Harrell FE, Habbema JDF (2001) Prognostic modeling with logistic regression analysis: in search of a sensible strategy in small data sets. Med Decis Mak 21:45–56
11. Lei S, Jiang F, Su W et al (2020) Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine 21:100331
12. Kader N, Clement ND, Patel VR et al (2020) The theoretical mortality risk of an asymptomatic patient with a negative SARSCoV-2 test developing COVID-19 following elective orthopaedic surgery. Bone Jt J 102-B:1256–1260
13. Bonalumi G, Pilozzi Casado A, Barbone A et al (2022) Prognostic value of SARS-CoV-2 on patients undergoing cardiac surgery. J Card Surg 37:165–173
14. Silvapulle E, Johnson D, Darvall JN (2022) Risk stratification of individuals undergoing surgery after COVID-19 recovery. Br J Anaesth 128:e37–e39