Original Article

Perioperative outcomes in patients with symptomatic versus asymptomatic previous COVID-19 infection undergoing neurosurgical treatment (post–COVID-19 study)

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Abstract

Background and Aims: The long-term effects of coronavirus disease 2019 (COVID-19) infection (long-COVID) are being increasingly recognized. The long-COVID effects are more likely in individuals who were symptomatic than asymptomatic during their previous COVID-19 infection. The data on perioperative outcomes of patients undergoing elective neurosurgery long after their recovery from COVID-19 infection is lacking. The primary objective of this study was to compare the perioperative outcomes after elective neurosurgery between patients who were symptomatic and those who were asymptomatic during their previous COVID-19 infection. The secondary objectives were to compare the earlier COVID-19 characteristics and the perioperative pulmonary profile during current surgery between these groups.

Material and Methods: This prospective observational study was performed in adult patients undergoing elective neurosurgery with history of previous COVID-19 infection. Data was collected regarding previous COVID-19 infection (symptoms, hospitalization, treatment, complications, etc.) and current perioperative characteristics (pulmonary profile, perioperative complications, hospital stay, mortality, etc.).

Results: A total of 50 patients were recruited during the study period, of which 35 (73%) patients were symptomatic during previous COVID-19 infection (two patients were excluded). The mean duration between current surgery and previous COVID-19 infection was 7 months. Patients symptomatic during earlier COVID-19 infection were females, older, and had a lower oxygen level during current surgery. There was no difference between symptomatic and asymptomatic groups in adverse perioperative outcomes such as desaturation, pulmonary or extrapulmonary complications, or non-extubation.

Conclusion: The perioperative outcomes of patients undergoing elective neurosurgery with previous mild to moderate symptomatic COVID-19 infection may not be different from those of patients with asymptomatic COVID-19 infection.

Keywords: Complications, COVID-19, neurosurgery, perioperative outcomes

Key Message: This study explored perioperative outcomes in patients with previous COVID-19 infection undergoing elective neurosurgery at a later date. Outcomes were compared between patients who were symptomatic during their previous COVID-19 infection and those who were asymptomatic. Mild to moderately symptomatic patients may not be at a higher risk of major pulmonary or extrapulmonary complications.

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Introduction

Over the last 3 years, millions of people worldwide have been affected by coronavirus disease 2019 (COVID-19) infection. Some of these patients present for the management of their surgical pathologies long after their COVID-19 infection has clinically resolved. Surgeries performed in patients with active COVID-19 infection were associated with increased postoperative mortality and pulmonary complications.[1,2] Hence, delaying elective surgery for >7 weeks was recommended.[3] This strategy resulted in reduced 30-day mortality and morbidity. It is, therefore, likely that the outcomes after surgery (done at a later date) may also be dependent on whether the patients were symptomatic or asymptomatic during the previous COVID-19 infection. Reduced perioperative mortality was seen in COVID-19 patients if they were asymptomatic for infection at the time of surgery.[3] It is expected that a similar pattern is observed in patients who were asymptomatic during their earlier COVID-19 infection when they undergo a surgery long after COVID-19 infection. The pulmonary and extrapulmonary postoperative complications during surgery done long after COVID-19 infection may be different between patients who were symptomatic (who manifested with COVID-19 infection symptoms) and asymptomatic (diagnosed to be COVID-19 positive without actually manifesting symptoms of COVID-19) during their earlier COVID-19 infection.

Currently, data on perioperative outcomes of patients undergoing elective neurosurgery long after they have recovered from COVID-19 infection is absent. With a decrease in COVID-19 infections and an increase in the number of patients requiring elective neurosurgeries (especially because many elective surgeries were postponed due to COVID-19), many patients with previous COVID-19 infection are undergoing elective neurosurgery. It is unclear if the perioperative outcomes are dependent on their earlier COVID-19 clinical symptom status. The present study intends to examine this aspect to fill the knowledge gap. The findings are likely to help in planning and providing better perioperative care in these patients.

The primary objective of this study was to compare the perioperative outcomes in patients undergoing elective neurosurgery who were earlier diagnosed with COVID-19 infection but were different in terms of presence or absence of COVID-19 symptoms. The secondary objectives were to compare the symptomatic and asymptomatic patients with respect to their earlier COVID-19 characteristics and perioperative pulmonary profile during current surgery. We hypothesized that patients who were symptomatic for their earlier COVID-19 infection will be at increased risk of adverse perioperative outcomes when they undergo surgery later.

Material and Methods

This was a prospective observational study conducted at a tertiary care academic neurosciences hospital over a period of 12 months (from October 2021 to September 2022). The study participants included consecutive adult patients (age >18 years) with a previous history of COVID-19 infection diagnosed by either reverse transcriptase polymerase chain reaction (RT-PCR) or rapid antigen test (RAT) from nasopharyngeal samples and currently presenting for elective neurosurgical intervention. Children and patients undergoing emergency neurosurgeries were excluded. Written informed consent was obtained from all patients recruited into the study. The study was initiated after obtaining approval from the institute ethics committee and registration of the study with Clinical Trial Registry of India (CTRI/2021/10/037117).

Symptomatic patients in this study were defined as patients who had any symptom of COVID-19 infection, such as sore throat, cough, fever, breathlessness, fatigue, running nose, etc., during their COVID-19 infection, while asymptomatic patients were those who tested positive for COVID-19 infection without any symptoms when testing as a prerequisite for travel, routine community screening, or as part of contact tracing, etc.

During the current admission for undergoing neurosurgery, the following data was collected from patients recruited into the study. Preoperatively, age, gender, diagnosis, and neurosurgical procedure were noted. With respect to their previous COVID-19 infection, the following details were obtained: date of test positivity, duration between the current surgery and diagnosis of COVID-19 infection, the test used to diagnose COVID-19 infection, whether the patient was asymptomatic or symptomatic, the symptoms developed due to COVID-19 infection and the treatment given, whether the patient was hospitalized for the infection, intensive care unit (ICU) admission if any, number of days of oxygen supplementation, whether the patient was intubated and ventilated, and complications that developed following COVID-19 infection.

Intraoperatively, before induction of anesthesia, the baseline heart rate (HR), blood pressure (BP), and peripheral oxygen saturation (SpO_2) on room air (from pulse oximeter) were noted. An arterial blood gas analysis was also performed to obtain information on preoperative partial pressure of oxygen (PaO_2) and carbon dioxide ($PaCO_2$). After induction of anesthesia, data on desaturation events (defined as SpO_2 <94%) and the lowest intraoperative SpO_2 were collected. The highest end-tidal carbon dioxide ($EtCO_2$) and highest peak airway pressures (Paw) were also noted. Any interventions for managing desaturation and for treating increased airway pressures were also recorded. Data was also collected regarding extubation, reintubation, and transfer to ICU for elective ventilation after completion of the surgical procedure.

Our primary outcome measure was occurrence of perioperative complications as defined below. The patient was followed for the following complications till discharge from the hospital. Respiratory complications were defined as the need for mechanical ventilation or reintubation for any reason (oxygenation, ventilation, or airway protection) and the occurrence of new-onset pneumonia. Cardiac complications were defined as new-onset myocardial infarction or cardiac arrest during the hospital stay or the need of inotrope/vasopressor for hemodynamic stability or referral to an advanced cardiac center for expert management. Neurological complications were defined as deterioration in the level of consciousness, occurrence of a new stroke, development of new-onset deficits or seizure. Data was collected for hematological complications (including anemia defined as hemoglobin <9 g%, thrombocytopenia defined as platelet count <1 lakh/mm^3), thromboembolic complications (pulmonary embolism or deep vein thrombosis), and electrolyte/endocrine disturbances of sodium, potassium, chloride, calcium, and glucose. The durations of mechanical ventilation, ICU stay, and hospital stay, and in-hospital mortality were also recorded. For the conduct of this study, no changes were made in the usual patient care.

Statistical analysis

A formal sample size estimate was not done as this was an exploratory study. Data were collated offline on a Microsoft Excel version 2007 spread sheet and analyzed using Statistical Package for the Social Sciences (SPSS) version 28. Interval scale and ordinal data were described using median and interquartile range (IQR). Nominal variables were described as frequency and percentages. For comparison of normally distributed variables, *t*-test was used. Mann–Whitney U test was used to analyze the data that was not normally distributed. Factors significant on univariate analysis were entered into a multivariate logistic regression to compare symptomatic and asymptomatic patients. A P value < 0.05 was considered statistically significant.

Results

We recruited 50 consecutive patients during the study period. All patients had COVID-19 infection in the past, and the present admission was for a neurosurgical procedure. Postoperative data was incomplete for two patients, and therefore, analysis was performed for 48 patients [Figure 1, flow diagram].

Out of these 48 patients, 35 (73%) patients had been symptomatic for their earlier COVID-19 infection and 13 patients (27%) had been asymptomatic. Out of the 35 symptomatic patients, eight had breathlessness as a symptom. Nine patients had vascular lesions including cerebral aneurysms, arteriovenous malformations, arteriovenous fistulas, and Moya Moya disease; 20 patients had supratentorial lesions, seven patients had posterior fossa lesions or cerebellopontine angle lesions, seven had spine lesions, and another five had miscellaneous diagnosis like infection, epilepsy, trigeminal neuralgia, cerebrospinal fluid rhinorrhea, etc., Forty-one patients in the study cohort underwent cranial surgery (29 in the symptomatic group and 12 in the asymptomatic group), while seven underwent spine surgery (six symptomatic and one asymptomatic).

The mean age of patients in the symptomatic group was 46 years and in the asymptomatic group was 29 years. The time duration between COVID-19 infection and the date of the surgery was 272 (42–797) and 227 (2–595) days, respectively. In the entire cohort of 48 patients, three had hypertension, five had type 2 diabetes, one had bronchial asthma, four had both diabetes and hypertension, and one patient had hypertension, diabetes, bronchial asthma, and hypothyroidism.

Comparing the demographic profile between symptomatic and asymptomatic patients, the symptomatic patients were older, weighed more, and were more likely to belong to female gender on univariate analysis. More symptomatic patients had received treatment for COVID-19 infection for obvious reasons. Most of the patients received vitamin C, zinc, azithromycin, and paracetamol as the treatment regime. Three patients in the asymptomatic group were admitted to the hospital during COVID-19 infection. This is because in the first wave of the pandemic, the infected patients were being admitted to hospital for observation and isolation. However, on multivariate analysis, only age and gender were significantly different between the groups. There was no difference between the groups with respect to rates of hospitalization or ICU admissions for COVID-19 infection [Tables 1 and 2].

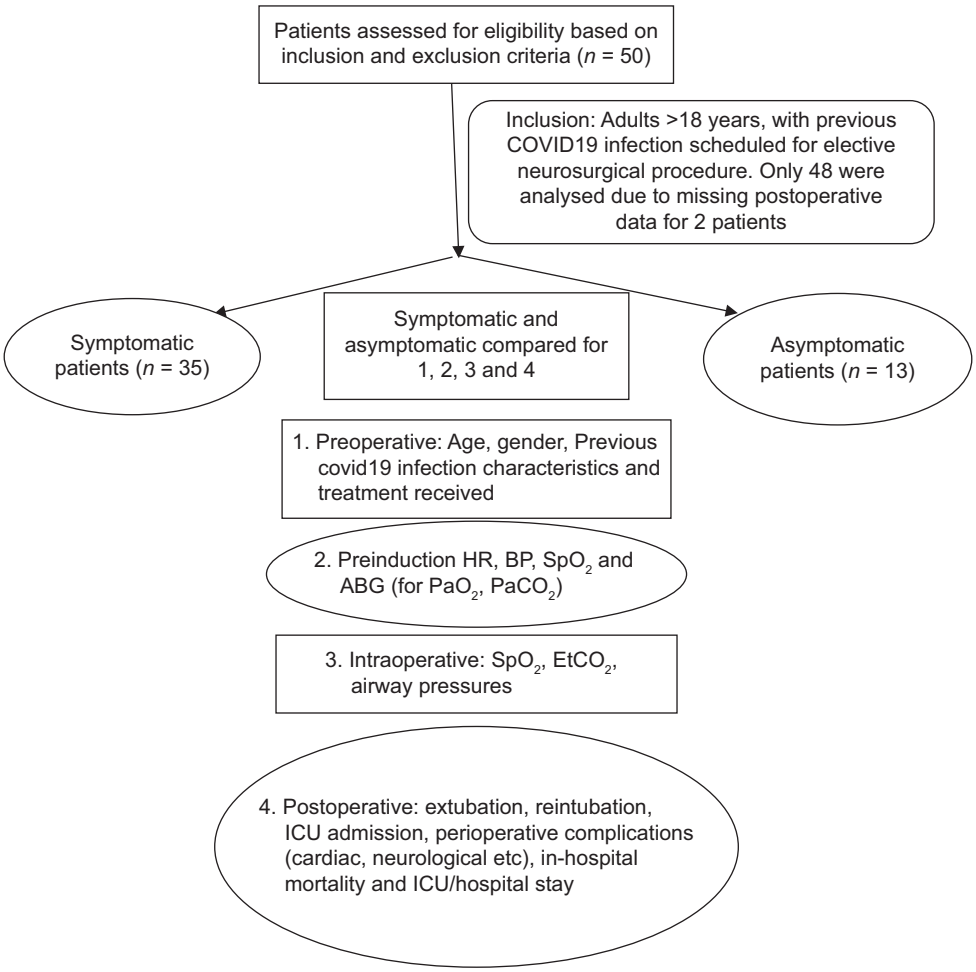

Figure 1: Flow diagram shows the steps of conduct of the study and number of patients at each stage of the study

Table 1: Comparison of demographic and COVID-19 variables between symptomatic and asymptomatic COVID-19 neurosurgical patients (univariate analysis)

Variables	Symptomatic COVID-19 (*n*=35)	Asymptomatic COVID-19 (*n*=13)	*P*
Age (years)	45.8±13.9	29.3±11.1	**<0.001**
Weight (kg)	65 (59-77)	60 (48.5-62.5)	**0.076**
Female gender	18/35	2/13	**0.046**
Duration between COVID-19 infection and surgery (days)	271.6±175.4	227.5±180.4	0.448
Patients who received treatment for earlier COVID-19 infection	28/30	9/13	**0.058**
Patients hospitalized for COVID-19	12/35	3/13	0.727
Patients admitted to ICU for COVID-19 infection	3/35	0/13	0.553

The data are expressed as mean±standard deviation or median and interquartile range or as numbers. COVID-19=coronavirus disease 2019, ICU=intensive care unit. The P values which are significant are given in bold

Comparing the pulmonary profile between symptomatic and asymptomatic patients, among the symptomatic COVID-19 patients, seven patients had received oxygen supplementation for COVID-19 infection and 26 had not (data was not available for two patients), while in the asymptomatic group, out of 13 patients, only one had received oxygen during the past COVID-19 infection. However, this was not statistically significant. In the entire cohort of COVID-19–infected patients, three had been admitted to ICU. One patient was admitted for observation, one received noninvasive ventilation, and another received high-flow oxygen therapy.

During the current admission for the neurosurgical procedure, preoperative PaO_2 (on room air, observed in the operating room before induction of anesthesia) was significantly higher in asymptomatic patients compared to symptomatic patients. All the patients in the study cohort had a preoperative chest X-ray, which was normal. Intraoperative desaturation occurred

Table 2: Results of logistic regression analysis between symptomatic and asymptomatic COVID-19 neurosurgical patients

Variables	B	SE	Wald	df	Sig.	Exp (B)	95% CI for Exponential (B)	
							Lower	Upper
Age	-0.113	0.048	5.617	1	**0.018**	0.89	0.81	0.981
Gender	2.896	1.279	5.127	1	**0.024**	18.10	1.48	221.98
Weight	-0.061	0.045	1.824	1	0.177	0.94	0.86	1.03
Patients who received treatment for earlier COVID-19 infection	-2.600	1.626	2.558	1	0.110	0.07	0.01	1.80

CI=confidence interval, COVID-19=coronavirus disease 2019EXP=Exponential. The P values which are significant are given in bold. SE=standard error

Table 3: Comparison of perioperative outcomes between symptomatic and asymptomatic COVID-19 neurosurgical patients

Variables	Symptomatic COVID-19	Asymptomatic COVID-19	*P*
Preoperative PaO_2 (mmHg)	99.9±34.4	134.6±81.4	**0.047**
Preoperative $PaCO_2$ (mmHg)	32.5±6.2	35.3±5.1	0.187
Lowest SpO_2% during anesthesia	96.4±2.2	97.3±1.9	0.376
Highest Paw (mmHg) during anesthesia	21.0±3.9	19.3±3.7	0.207
Perioperative hypotension	13/35	4/13	0.747
Extubation after surgery	31/35	9/12	0.350
Postoperative ICU care	5/33	3/13	0.669
Postoperative new deficits or stroke	4/35	3/13	0.370
Postoperative abnormal laboratory values	11/35	5/13	0.735
Postoperative hospital stay duration	5 (3–6)	5 (4–8)	0.348

The data are expressed as mean±standard deviation or median and interquartile range or as numbers. COVID-19=coronavirus disease 2019, ICU=intensive care unit, $PaCO_2$=partial pressure of carbon dioxide, PaO_2=partial pressure of oxygen, Paw=peak airway pressure, SpO_2=peripheral oxygen saturation. The P values which are significant are given in bold

in two out of 35 patients in the symptomatic group and none in the asymptomatic group, and this was not statistically significant. Also, there was no difference between the groups with respect to the lowest intraoperative SpO_2. There were no differences with regard to intraoperative highest $EtCO_2$ or Paw [Table 3].

Comparing the perioperative outcomes between symptomatic and asymptomatic patients, perioperative hypotension and incidences of new-onset stroke or new-onset neurological deficits were not different between the two groups. There were no significant differences between the groups with respect to derangement in biochemical parameters, namely, sodium, potassium, or glucose. Anemia was observed in four out of 35 patients in the symptomatic group and two out of 13 patients in the asymptomatic group. Blood glucose abnormalities were seen in five patients in the symptomatic group and none in the asymptomatic group.

There was no difference in immediate postoperative extubation rates between the groups. Five out of 33 in the symptomatic group and three out of 13 patients in the asymptomatic group required postoperative ICU care, which was not statistically different. The eight patients who required ICU care had the following diagnosis. In the symptomatic category, two patients had meningioma, one had parietal tumor, one had C4–C5 prolapsed intervertebral disc, and one had pituitary tumor. Among the asymptomatic patients, two had anterior communicating artery aneurysm and one had split cord malformation with tethered cord. The reasons for postoperative ICU admission were blood loss in patients with tumors and spine cases, leading to hypotension requiring vasopressor infusion, aneurysm rupture intraoperatively in aneurysm cases, and carotid artery injury in pituitary macroadenoma. Also, there was no difference in the duration of hospital stay between the two groups. There was only one death in the entire study cohort, which was due to a surgical complication.

Since the study cohort comprised both cranial and spine surgery patients, a subgroup analysis was also performed to compare the two groups with respect to their demographics and COVID-19 characteristics. There was no difference between the two groups with respect to any of the variables [Table 4].

Discussion

The current study specifically looked at the differences in perioperative outcomes between symptomatic and asymptomatic patients (of previous COVID-19 infection) presenting for elective neurosurgery at a later date. These COVID-19–recovered patients may have residual abnormalities, which can have bearing on the postoperative outcomes.

Table 4: Comparison of demographic and COVID-19 variables between cranial and spinal neurosurgical patients

Variables	Cranial surgery (*n*=41)	Spine surgery (*n*=7)	*P*
Male gender	24/41	4/7	1.000
Patients who received treatment for earlier COVID-19 infection	32/37*	5/6*	1.000
Age (years)	40.7±15.2	44.5±14.1	0.540
Weight (kg)	64±13.1	66.2±9.1	0.662
Duration between COVID-19 diagnosis and surgery (days)	252.4±161.2	298.8±257.1	0.526
Patients symptomatic for COVID-19	29/41	6/7	0.656
Patients hospitalized for COVID-19	11/41	4/7	0.183
Patients admitted to ICU for COVID-19 infection	2/41	1/7	0.384

*The data are expressed as mean±standard deviation or as numbers. *For some patients, data on treatment received for COVID-19 infection is not available. COVID-19=coronavirus disease 2019*

We found that a greater number of females and older age patients were symptomatic for COVID-19 infection. However, Gupta *et al.*[4] found that males are more likely to be symptomatic for COVID-19 infection than females. Literature supports our findings that asymptomatic patients are usually younger than symptomatic patients.[5]

We observed no difference between symptomatic and asymptomatic patients with respect to immediate postoperative extubation rates, admission to ICU, or duration of hospital stay after elective neurosurgical intervention. A previous retrospective study comparing COVID-19 and non–COVID-19 neurosurgical patients also did not observe differences in perioperative outcomes.[6] Hence, perioperative outcomes are less likely to be affected by COVID-19 status when patients undergo surgery long after COVID-19 infection. Outcomes are more likely to be determined by the severity of the neurological problem and the inherent risks associated with neurological patients undergoing surgery than COVID-19–related changes.[7] In our study, patients were admitted to ICU not because of pulmonary complications, but for intraoperative neurological complications like excessive blood loss or intraoperative brain bulge. We cannot comment on the differences in mortality rates as the incidence of in-hospital deaths in our study cohort was very low. Vosburg *et al.*analyzed the 30-day mortality and morbidity in 53 patients who underwent bariatric surgery after recovery from COVID-19 infection.[8] The authors did not observe mortality or any cardiovascular, respiratory, or thromboembolic events. The average duration between the diagnosis of COVID-19 and bariatric surgery was 82.5 days, and 38% of COVID-19 patients were asymptomatic.

We also did not find any differences with respect to perioperative complications such as hypotension or neurological complications. Piraee *et al.*[9] compared the outcomes of symptomatic and asymptomatic COVID-19 patients in 40,957 COVID-19–positive patients, of which 5.68% were asymptomatic. Symptomatic patients were found to have higher mortality. However, these are not postoperative outcomes, but general outcomes. Carrier *et al.* studied the postoperative outcomes in 44 COVID-19–positive patients, of which 26 were symptomatic at the time of surgery.[10] The rates of complications were higher in symptomatic patients. The mortality rates were also higher in symptomatic patients without statistical difference. These COVID-19–infected patients underwent surgery before or within 72 h of being detected as COVID-19 positive. The higher complication rates in symptomatic patients is expected as the patients were in the acute phase of the infection while undergoing surgery.

Postoperative respiratory complications were found to be higher in symptomatic COVID-19 children compared to asymptomatic children when the surgeries were performed within 10 days of COVID-19 positive diagnosis.[11] In our study, we did not find higher complication rates in symptomatic patients, probably because the study patients underwent surgery after >200 days of COVID-19 infection.

With respect to pulmonary complications, the only difference between the two groups was the preoperative PaO_2. Patients who recover from COVID-19 are known to have residual lung damage. Although there was an improvement in chest computed tomography (CT) scores after 3 months of recovery from COVID-19 infection, more than 50% of patients continued to have abnormalities in the chest CT in the form of ground-glass opacities, septal thickening, and fibrosis.[12] The pulmonary function tests also showed impairment in nearly 10% of the patients. In addition, the 6-min walk distances were considerably lower than in healthy controls. These abnormalities have been attributed to the cytokine storm and the resulting inflammation. We did not find any difference with respect to increased airway reactivity in the form of increased carbon dioxide or intraoperatively airway pressures. This is probably because there was no active infection in these patients

and there was a significant gap between COVID-19 infection and current neurosurgery.

There is a dearth of literature on patients with COVID-19 infection undergoing neurosurgery. Most of the existing literature discusses about the impact COVID-19 outbreak had on the neurosurgical practices worldwide and the recommendations made to reduce the transmission of infection. During the COVID-19 pandemic, elective surgeries were postponed to divert the limited hospital resources toward care of COVID-19–infected patients, especially those who might require postoperative ICU admission.[13,14]

The neurological patients infected with COVID-19 were also likely to have higher incidence of complications while undergoing an intervention. Patients with acute ischemic stroke with concurrent COVID-19 infection had higher rates of intracranial bleeding complications and subarachnoid hemorrhage and poorer clinical outcomes after revascularization compared to their non–COVID-19 counterparts.[15] There was increased incidence of thrombotic and hemorrhagic complications in neurosurgical patients undergoing interventions.[16]

While previous studies have focused on the effects of current or recent COVID-19 infection on postoperative outcomes, the novelty of our study is that this is the first study to explore the effects of previous COVID-19 infection, which was >6 months before the current date of the neurosurgical procedure. Our findings suggest that these patients are not at an increased risk of major postoperative complications.

Limitations of the study: The small sample size precludes any definitive conclusion and can only provide limited but important insight into the impact of symptoms of previous COVID-19 infection on perioperative outcomes during the subsequent neurosurgery. Only a small proportion of India's total population afflicted with previous COVID-19 infection underwent neurosurgical procedures since the pandemic, and we do not expect any significant increase in sample size by extending the study period beyond 1 year. Moreover, a longer period since COVID-19 pandemic will prejudice our study purpose, as the impact of COVID-19 on perioperative outcomes may be negligible with passage of time. Second, the low sample size precluded us from comparing complications with a low incidence, such as renal dysfunction, thromboembolism, mortality, etc., Third, our patient population had majority with mild to moderate infection and only three patients with severe infection. Hence, our findings may not be generalizable to neurosurgical patients with previous severe COVID-19. Lastly, comparing the perioperative outcomes after neurosurgery between patients with no previous COVID-19 infection and patients with previous COVID-19 infection would have provided better information about the actual contribution of COVID-19 on outcomes than comparing only asymptomatic and symptomatic previous COVID-19 infection.

Conclusions

Elective neurosurgery long after previous COVID-19 infection may not result in increased morbidity or mortality or adverse intraoperative airway-related problems even if the patient had been mild to moderately symptomatic during the earlier COVID-19 infection and the neurosurgery performed is beyond 6 months of COVID-19 infection. A decreased preoperative PaO_2 can be expected in symptomatic patients, but this is unlikely to result in adverse perioperative respiratory events. The neurological outcomes and ICU requirements may not be influenced by previous COVID-19 infection symptoms when delayed surgery is performed.

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Conflicts of interest
There are no conflicts of interest.

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