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## Outcomes and Surgical Considerations for Neurosurgical Patients Hospitalized with COVID-19—A Multicenter Case Series

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■ **OBJECTIVE:** Neurosurgical patients are at a higher risk of having a severe course of coronavirus disease 2019 (COVID-19). The objective of this study was to determine morbidity, hospital course, and mortality of neurosurgical patients during the coronavirus disease 2019 (COVID-19) pandemic in a multicenter health care system.

■ **METHODS:** A retrospective observational study was conducted to identify all hospitalized neurosurgical patients positive for COVID-19 from March 11, 2020 to November 2, 2020 at Mayo Clinic and the Mayo Clinic Health System.

■ **RESULTS:** Eleven hospitalized neurosurgical patients (0.68%) were positive for COVID-19. Four patients (36.6%) were men and 7 (63.3%) were women. The mean age was 65.7 years (range, 35–81 years). All patients had comorbidities. The mean length of stay was 13.4 days (range, 4–30 days). Seven patients had a central nervous system malignancy (4 metastases, 1 meningioma, 1 glioblastoma, and 1 schwannoma). Three patients presented with cerebrovascular complications, comprising 2 spontaneous intraparenchymal hemorrhages and 1 ischemic large-vessel stroke. One patient presented with an unstable traumatic spinal burst fracture. Four patients underwent neurosurgical/neuroendovascular interventions. Discharge disposition was to home in 5 patients, rehabilitation facility in 3, and hospice in 3.

Five patients had died at follow-up, 3 within 30 days from COVID-19 complications and 2 from progression of their metastatic cancer.

■ **CONCLUSIONS:** COVID-19 is rare among the inpatient neurosurgical population. In all cases, patients had multiple comorbidities. All symptomatic patients from the respiratory standpoint had complications during their hospitalization. Deaths of 3 patients who died within 30 days of hospitalization were all related to COVID-19 complications. Neurosurgical procedures were performed only if deemed emergent.

### INTRODUCTION

After the first cases identified in Wuhan, China, the coronavirus disease 2019 (COVID-19) disease rapidly spread, causing a global pandemic, resulting in immeasurable loss of life and a public health crisis.<sup>1</sup> According to the World Health Organization, as of February 22, 2021, there were 111,642,024 confirmed cases worldwide, of which 25.2% occurred in the United States, where approximately 500,071 individuals died of the virus.<sup>2</sup> The pandemic has affected all fields in medicine and has restructured neurosurgical care.<sup>3,4</sup> Patients commonly treated by the neurosurgical service have risk

### Key words

- Coronavirus
- COVID
- Neurosurgery
- Neurosurgical

### Abbreviations and Acronyms

- CNS:** Central nervous system  
**COVID-19:** Coronavirus disease 2019  
**DVT:** Deep venous thrombosis  
**GBM:** Glioblastoma  
**ICH:** Intraparenchymal hemorrhage  
**ICU:** Intensive care unit  
**MRI:** Magnetic resonance imaging

**PCR:** Polymerase chain reaction

**SARS-CoV-2:** Severe acute respiratory syndrome coronavirus 2

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factors that could predispose them to complications or severe coronavirus disease. For instance, neuro-oncologic patients are particularly susceptible to infection because of their older age, chronic steroid use, immunosuppression, hypercoagulable state, and disseminated disease.<sup>5</sup> Although severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) primarily targets the respiratory epithelium, neurologic manifestations are not uncommon.<sup>6</sup> In addition, COVID-19 has indirect effects on the central nervous system (CNS) as a result of hypoxemia, hypertension, and hypercoagulability, which places neurosurgical patients at a high risk for neurovascular complications that may require urgent intervention. There are limited data on the in-hospital course of neurosurgical patients who are COVID-19 positive.<sup>4</sup> We conducted a retrospective observational study to identify all neurosurgical-related patients with COVID-19 hospitalized at our Mayo Clinic sites to determine morbidity, hospital course, and mortality in this high-risk patient population.

## METHODS

The Mayo Clinic Neurological, Vascular and Neurovascular Events with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (MC NEWS) Study (institutional review board number 20-003457) is a prospectively collected study of all patients affected by the COVID-19 pandemic identified within the 3 major campuses of Mayo Clinic and the Mayo Clinic Health System, which includes hospitals in Arizona, Florida, Minnesota, and Wisconsin. Using the shared electronic medical record (Epic Systems, Verona, Wisconsin, USA), a registry of all patients with positive SARS-CoV-2 polymerase chain reaction (PCR) or serology as well as those with a documented diagnosis of COVID-19 in the electronic medical records was queried from March 11, 2020 to November 2, 2020. This registry is continuously monitored and updated by Mayo Clinic personnel. To account for patients diagnosed at other facilities and transferred to Mayo Clinic, this list was compared with manually updated registries of hospitalized patients with SARS-CoV-2. We performed a retrospective analysis of this prospectively collected database, only neurosurgical-related patients were identified, and data were extracted regarding their hospitalization and outcomes. The study protocol was reviewed and approved by the Mayo Clinic institutional review board and the COVID-19 task force and abides by PROCESS (Preferred Reporting of Case Series in Surgery) guidelines.<sup>7</sup> Written informed consent was not required because of the minimal risk nature of the study.

## Data Collection and Analysis

The variables collected included age, sex, diagnosis, underlying risk factors for COVID-19 severity (hypertension, diabetes, active smoking, chronic obstructive pulmonary disease, disseminated cancer, chronic steroid use, and obesity), body mass index ( $\text{kg}/\text{m}^2$ ), date of admission, symptoms at admission, neurologic examination at admission, admission chest radiography and/or chest computed tomography findings, lymphocyte count ( $\times 10^9/\text{L}$ ), status on mechanical ventilation or oxygenation needed, COVID-19 treatment, and inpatient complications. The following were considered inpatient complications of COVID-19: pneumonia, acute respiratory distress syndrome, deep venous thrombosis

(DVT), pulmonary embolism, and sepsis. Outcomes included length of hospital stay (days), length of intensive care unit (ICU) stay (days), progression of neurologic disease (neuro-oncologic patients), transient/permanent neurologic sequelae, postdischarge disposition (home, rehabilitation facility, or hospice), readmission, cause of readmission, and survival status. Patients were assessed for COVID-19 severity at admission using the American College of Emergency Physicians COVID-19 severity classification into mild, moderate, severe, and critical disease at presentation.<sup>8</sup> In addition, each patient was assessed for the need for any neurosurgical/neuroendovascular intervention. If the patient underwent surgical intervention, variables including the type of operation (elective or emergent), type of anesthesia (general vs. awake), duration of operation (minutes), intraoperative complications, and postoperative extent of resection in neuro-oncologic patients were collected. Neurologic disease progression was defined as the appearance of new or worsened neurologic deficits at follow-up. Extent of resection was defined as gross total resection (no residual enhancement), near-total resection (thin rim of enhancement in resection cavity), and subtotal resection (residual nodular fluid-attenuated enhancement) on T1-postgadolinium and T2 sequence on magnetic resonance imaging (MRI) performed within 48 hours after surgical intervention.

## RESULTS

A total of 15 (0.92%) neurosurgical-related patients of 1624 hospitalized with COVID-19 were identified. From this list of 15 patients, 4 were excluded from further review, because they had resolution/no active neuro-oncologic disease on MRI at the time of COVID-19 hospitalization. This process resulted in a series of 11 hospitalized neurosurgical patients (0.68%). During the same period, there were 3407 non-COVID-19-related discharges for elective neurosurgical procedures across campuses. Neurosurgical discharges in 2019 during a similar period between March 11, 2019 and November 2, 2019 were 4038, which shows a 16% decrease in practice volume caused by the pandemic.

## Patient Demographics and Risk Factors at Admission

Four patients (36.6%) were men and 7 (63.6%) were women. The mean age of all patients was 65.7 years (range, 35–81 years). Seven patients had a CNS malignancy (4 metastases, 1 meningioma, 1 glioblastoma [GBM], and 1 schwannoma). All patients with metastases had disseminated disease. Two patients were undergoing chemotherapy at the time of COVID-19 diagnosis. **Table 1** shows the demographic and clinical characteristics of the series. Three patients presented with a cerebrovascular complication either at admission or during the course of their hospitalization (2 spontaneous intraparenchymal hemorrhages (ICHs) and 1 large-vessel ischemic stroke). One patient with a past medical history of diffuse idiopathic skeletal hyperostosis presented with an unstable traumatic spinal burst fracture after sustaining a fall. Nine patients presented with respiratory symptoms at the time of admission; chest radiography showed atypical interstitial pneumonia. Two patients were asymptomatic from the respiratory perspective and COVID-19 infection was detected as part of their preoperative screening protocol. These 2 patients were the following: a 35-year-old woman with a metastatic sarcoma and a

**Table 1.** Demographic and Clinical Characteristics and COVID-19 Symptoms on Admission of Patients with Active Neurosurgical Conditions

Age (Years)/ Sex	Diagnosis	Comorbidities	Disseminated Cancer	Active/ Former Smoking	Steroid Use	Body Mass Index (kg/m <sup>2</sup> )	Respiratory Symptoms on Admission	COVID-19 Severity	Lymphocyte Count (×10 <sup>9</sup> /L)	Chest Radiography Findings	Mechanical Ventilation	Ongoing Chemotherapy	Treatment For COVID-19
35/F	Metastatic sarcoma	None	Yes	No	No	20.4	No	Mild—low risk	0.57	Multiple pulmonary masses and nodules	No	No	No
40/F	Metastatic human epidermal growth factor receptor 2—positive+ metastatic breast carcinoma	HTN	Yes	No	Yes (dex 4 mg twice a day)	28.25	Yes	Moderate—severe	0.68	Hyperinflation with areas of atelectasis at lung bases	No	Tucatib, herceptin/ pertuzumab	Remdesivir + 2 doses of convalescent plasma
79/F	O-6-Methylguanine DNA-methyltransferase methylated isocitrate dehydrogenase wild type glioblastoma	HTN, HCL hypothyroidism	No	No	Yes (dex 4 mg twice a day)	26.81	Yes	Moderate—severe	0.93	Bilateral patchy infiltrates. Small left pleural effusion	No	No	Remdesivir
60/F	Right parietal meningioma	HTN, HCL type II DM, chronic obstructive pulmonary disease, CKD	No	No	No	37.64	Yes	Moderate—severe	0.36	Bilateral multifocal ground-glass opacities	No	No	Lenzilumab
73/F	Metastasis	None	Yes	No	Yes (dex 6 mg/day)	22	Yes	Moderate—severe	1.5	3.2 cm apical mass, interstitial pneumonia	No	Gemcitabine fulvestrant	Remdesivir + convalescent plasma
81/F	Cavernoma	HTN, CKD, coronary artery disease, amyloid angiopathy	No	No	No	24.9	Yes	Moderate—severe	1.63	Interstitial pneumonia, right lung opacification, pleural effusion, left lung atelectasis	No	No	Convalescent plasma
75/M	Schwannoma	HTN, DM, CKD, HCL	No	No	No	30.39	Yes	Mild—low risk	0.96	Interstitial pneumonia	No	No	Convalescent plasma
61/F	ICH	HTN, DM, hypothyroidism	No	No	No	24.5	Yes	Critical	0.82	Interstitial pneumonia	Yes	No	Remdesivir
70/M	ICH	Stroke	No	Yes	No	41.5	Yes	Critical	0.38	Interstitial pneumonia	Yes	No	Remdesivir, tocilizumab

65/M	Left internal carotid artery thrombosis	HTN, HCL, hypothyroidism	No	Yes	—	30.3	No	Mild—low risk	0.89	Normal	No	No	No
80/M	Spinal fracture	DM, CKD	No	Yes	Yes (dex 6 mg/day)	42.37	Yes	Moderate—severe	1.63	Interstitial pneumonia, displaced traction fracture T7-T8, T8-T9 discs	Yes	No	Convalescent plasma

F, female; HTN, hypertension; dex, dexamethasone; HCL, hypercholesterolemia; DM, diabetes mellitus; CKD, chronic kidney disease; M, male; ICH, intracerebral hemorrhage.

65-year-old man with a large-vessel stroke, who both underwent neurosurgical or neurointerventional procedures. All patients had significant comorbidities.

### Hospital Course

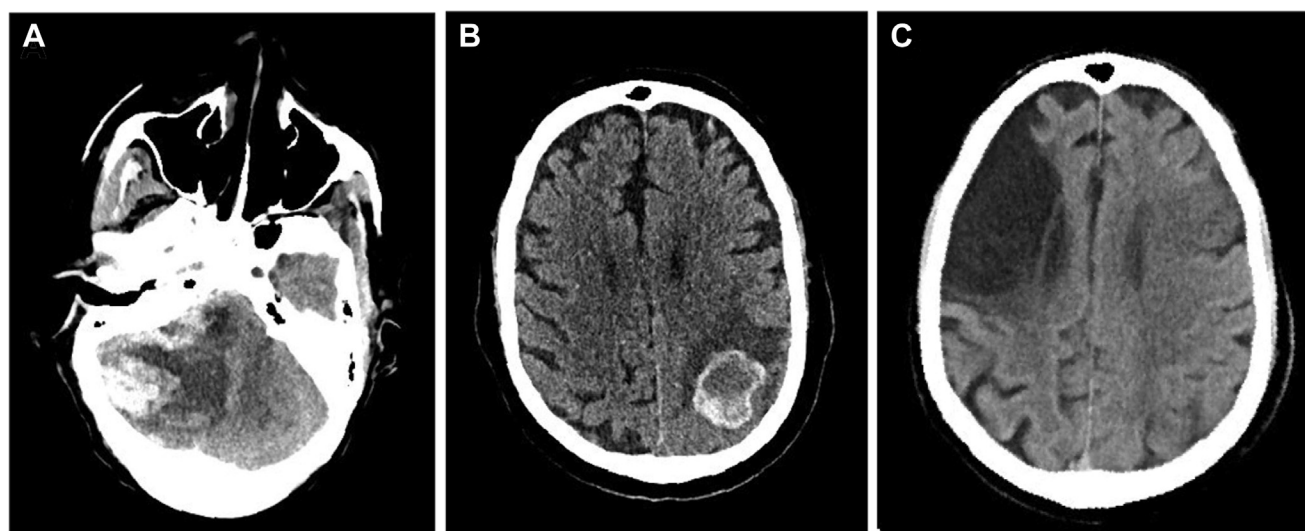
All symptomatic patients from the COVID-19 perspective received treatment for it and this included convalescent plasma, remdesivir, lenzilumab, and tocilizumab. Two patients (18.18%) developed acute respiratory distress syndrome requiring mechanical ventilation. Eight patients (66.6%) required ICU admission, with a mean length of stay of 8.5 days (range, 1–22 days). The mean length of hospital stay for all patients was of 13.4 days (range, 4–30 days). All patients symptomatic from the respiratory perspective developed complications during their hospitalization (4 pulmonary effusions, 2 ICH, 2 DVT, 1 sepsis, pulmonary embolism, and hemothorax).

Two patients developed spontaneous ICH. The first one was in a 61-year-old woman and the second one was a 70-year-old man. Both patients were admitted through the emergency department because of shortness of breath secondary to COVID-19 pneumonia. In both cases, the patients had several cerebrovascular risk factors, including hypertension, diabetes, chronic kidney disease, and hypercholesterolemia (Table 1). During their hospitalization, both patients developed acute kidney injury before the development of ICH (Figure 1A and B). Increased D-dimer levels preceded the cerebrovascular events, which were of 6799 ng/dL and 385 ng/dL, respectively. Both patients were placed on therapeutic anticoagulation with enoxaparin and heparin because of increasing D-dimer levels. One of the patients developed a ventral abdominal wall subcutaneous hematoma. The second developed bilateral lower extremity DVT and an occlusion of the left radial artery. The ICHs occurred 11 (Figure 1A) and 17 days after admission (Figure 1B). The patients developed the ICH after prolonged mechanical ventilation, at days 7 and 16 after intubation. Only 1 patient with ICH was intervened on with the placement of an external ventricular drain. After the cerebrovascular event, both patients deteriorated clinically and radiographically and were placed under hospice care. They both died in hospital on hospital day 20 and 22, respectively. The third death in this cohort was of an 81-year-old woman with a cavernoma, who required increased amounts of oxygen during her hospitalization. Although supportive therapy was provided, she progressively deteriorated and developed left-sided atelectasis with pleural effusion. Her family did not want to escalate care and she was placed in hospice care and died 15 days after initial diagnosis of COVID-19 pneumonia. All 30-day mortalities were caused by COVID-19 complications (mean, 19 days; range, 15–22 days).

### Neurosurgical Procedures

Four patients (36.36%) required urgent neurosurgical intervention. All operations were classified as emergent procedures (Table 2). Of these 4 patients, 2 did not have respiratory symptoms, but were positive for SARS-CoV-2 PCR testing at the time of preoperative screening. The decision to proceed with neurosurgical intervention was to the result of rapid neurologic deterioration with radiographic progression of underlying disease process. The operations performed included a right frontal craniotomy for





**Figure 1.** Imaging of hospitalized patients with COVID-19 with neurovascular complications. **(A)** Noncontrast head computed tomography (CT) showing large right cerebellar intraparenchymal hemorrhage with associated mass effect and leftward transtentorial herniation with effacement of the cerebral aqueduct. **(B)** Noncontrast head CT showing a multifocal intraparenchymal hemorrhage within the left parietal lobe

associated with surrounding edema. **(C)** Non-contrast-enhanced head CT showing a core infarction in the left frontotemporal region involving the anterior cerebral artery–middle cerebral artery and middle cerebral artery–posterior cerebral artery watershed regions and left opercular cortex.

resection of a metastatic sarcoma located on the right falx resulting from rapid radiographic progression with edema and midline shift (**Figure 2A** and **B**), a left parietal craniotomy for decompression of tumor mass effect on a O-6-methylguanine DNA-methyltransferase methylated isocitrate dehydrogenase wild type GBM causing global aphasia and cognition and memory impairment (**Figure 2C** and **D**) a T6-T10 spinal fusion for an unstable T7-T8 burst fracture (**Figure 3**) and a mechanical thrombectomy in a patient with a large-vessel stroke secondary to in-stent thrombosis (**Figures 1C** and **4**).

### Postoperative Course and Readmission

Five patients were discharged home, 3 patients were transferred to hospice care, and 3 patients were discharged to a rehabilitation facility. Two patients had neurologic progression of their underlying disease. Three patients required readmission because of shortness of breath and hypoxemia ( $n = 2$ ), wound dehiscence, and sepsis ( $n = 1$ ) (**Table 3**). At time of last follow-up (mean, 102 days; range, 15–307 days), 5 patients had died. Three patients died of pneumonia and complications related to COVID-19 infection (mean, 19 days; range, 15–22 days) and 2 patients died of metastatic cancer progression (mean: 95 days and range: 59–130 days) including one with a metastatic sarcoma and another with HER2+ metastatic breast cancer to the brain.

Disease progression in the patient with metastatic sarcoma and the patient with metastatic breast cancer was not unexpected. In the case of the patient with metastatic sarcoma, near-total resection was confirmed on postoperative MRI. She was readmitted with transient left hemiplegia secondary to transient supplementary motor area syndrome. A month after discharge, the patient

underwent Gamma Knife (Elekta, Stockholm, Sweden) irradiation to the right parafalcine residual lesion treated with 30 Gy at the 50% isodose line. Two months after her operation, computed tomography of the chest, abdomen, and pelvis showed significant progression of her extracranial disease. Brain MRI showed an area of persistent enhancing soft tissue extending and occluding the superior sagittal sinus. The patient was then offered to start chimeric antigen receptor T cell therapy. However, she died 4 months after surgical intervention.

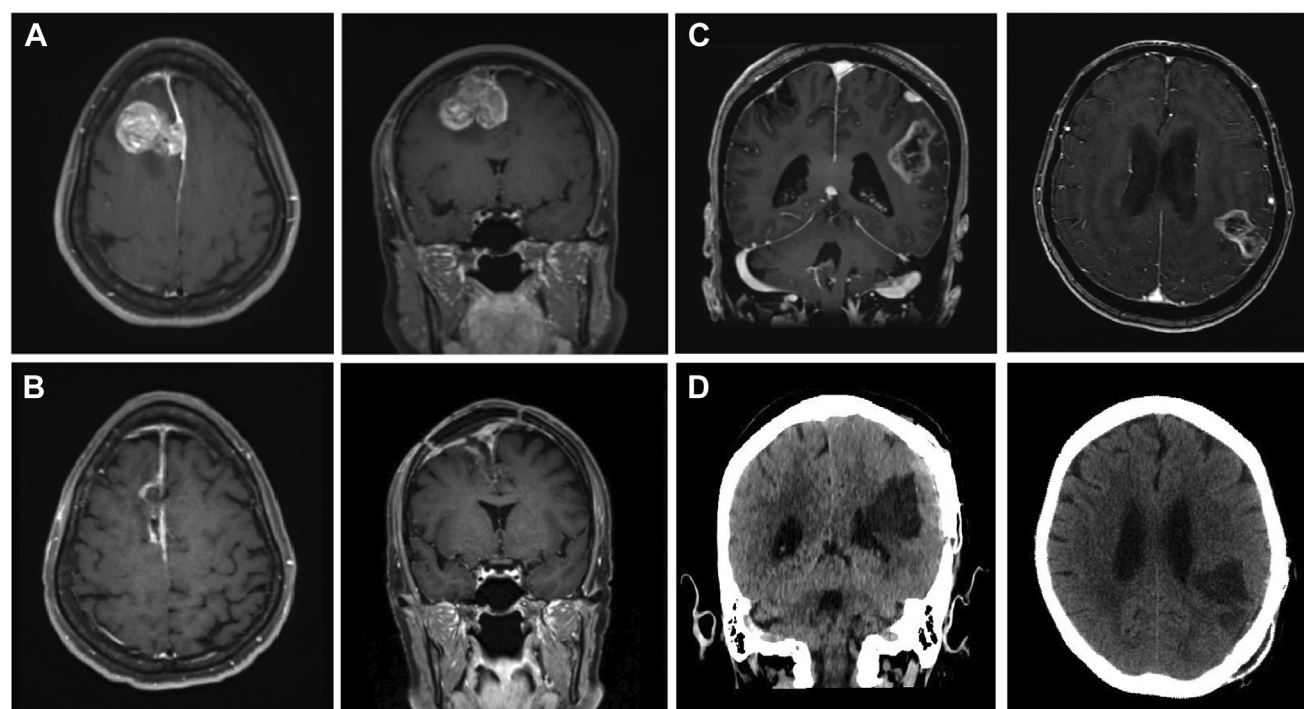
In the case of the patient with metastatic HER-2 breast carcinoma, she had metastases to the pons, right cerebellar hemisphere, left cerebellar hemisphere, and within the left postcentral gyrus. One month after discharge, she was readmitted because of hypoxemia secondary to aspiration pneumonia (a repeat SARS-CoV-2 PCR test was negative). During hospitalization, the patient became increasingly debilitated, with motor dysfunction (2/5 on upper and lower extremity strength bilaterally) and dysphagia. MRI showed substantial progression of the known pontine lesion. She was discharged to hospice care and died 1 week after discharge.

### DISCUSSION

The coronavirus pandemic has affected several aspects of neurosurgical care, leading to changes in clinical practice, including significant modifications to preoperative, perioperative, and postoperative care.<sup>4</sup> In initial phases of the pandemic, the spread of the virus led to a decline in inpatient surgical volume because of recommended cessation of all elective operations.<sup>9</sup> In our review, the number of hospitalized neurosurgical patients with COVID-19

**Table 2.** Emergent Neurosurgical and Neurovascular Procedures Performed in Four Patients with COVID-19

Diagnosis	Location	Neurologic Examination	Karnofsky Performance Status	Reasons for Surgery	Procedure	Neuromonitoring	Anesthesia	Duration (Hours:Minutes)	Intraoperative Complications	Surgical Outcome
Metastatic sarcoma	Right falx	Left hyperreflexia	70	Rapid tumor growth, edema	Right frontal craniotomy	SSEPs	General	3:22	None	NTR
O-6-methylguanine DNA-methyltransferase methylated isocitrate dehydrogenase wild type glioblastoma	Left parietal cortex	Global aphasia, impaired cognition and memory impairment	70	Impending uncal herniation	Left parietal free bone flap craniotomy	SSEPs	General	7:07	Subdural bleeding after decompression	NTR
Internal carotid artery thrombosis/hemorrhagic conversion	Left middle cerebral artery distribution ischemic stroke	Aphasia, left-sided gaze deviation	NA	Acute large-vessel infarction	Angioplasty/mechanical thrombectomy	None	Monitored anesthesia care	2:04	None	Thrombolysis in Cerebral Infarction scale grade 3 reperfusion
Unstable burst fracture T7-8	T7-T8	Normal	NA	Impending neurodeficit if untreated	T6-T10 fusion posterior thoracic spine	NA	General	4:07	None	Stabilization of fracture and posterior thoracic interbody fusion
SSEPs, somatosensory evoked potentials; NTR, near-total resection; NA, not applicable.										



**Figure 2.** Imaging of hospitalized patients with neuro-oncologic COVID-19 who underwent emergent neurosurgical operative intervention.

(A) Preoperative axial and coronal T1 postgadolinium magnetic resonance imaging (MRI) showing lobulated, heterogeneously enhancing right extra-axial mass (3.2 × 3.9 × 3.6 cm) with increased mass effect on the right dorsomedial premotor region. (B) Postoperative axial and coronal T1

postgadolinium MRI showing near-total resection of right frontal mass.

(C) Preoperative axial and coronal T1 postgadolinium MRI, showing a mass within the left parietal cortex and subcortical white matter with central necrosis and irregular thickened marginal enhancement. (D) Postoperative noncontrast head computed tomography showing removal of left parietal mass.

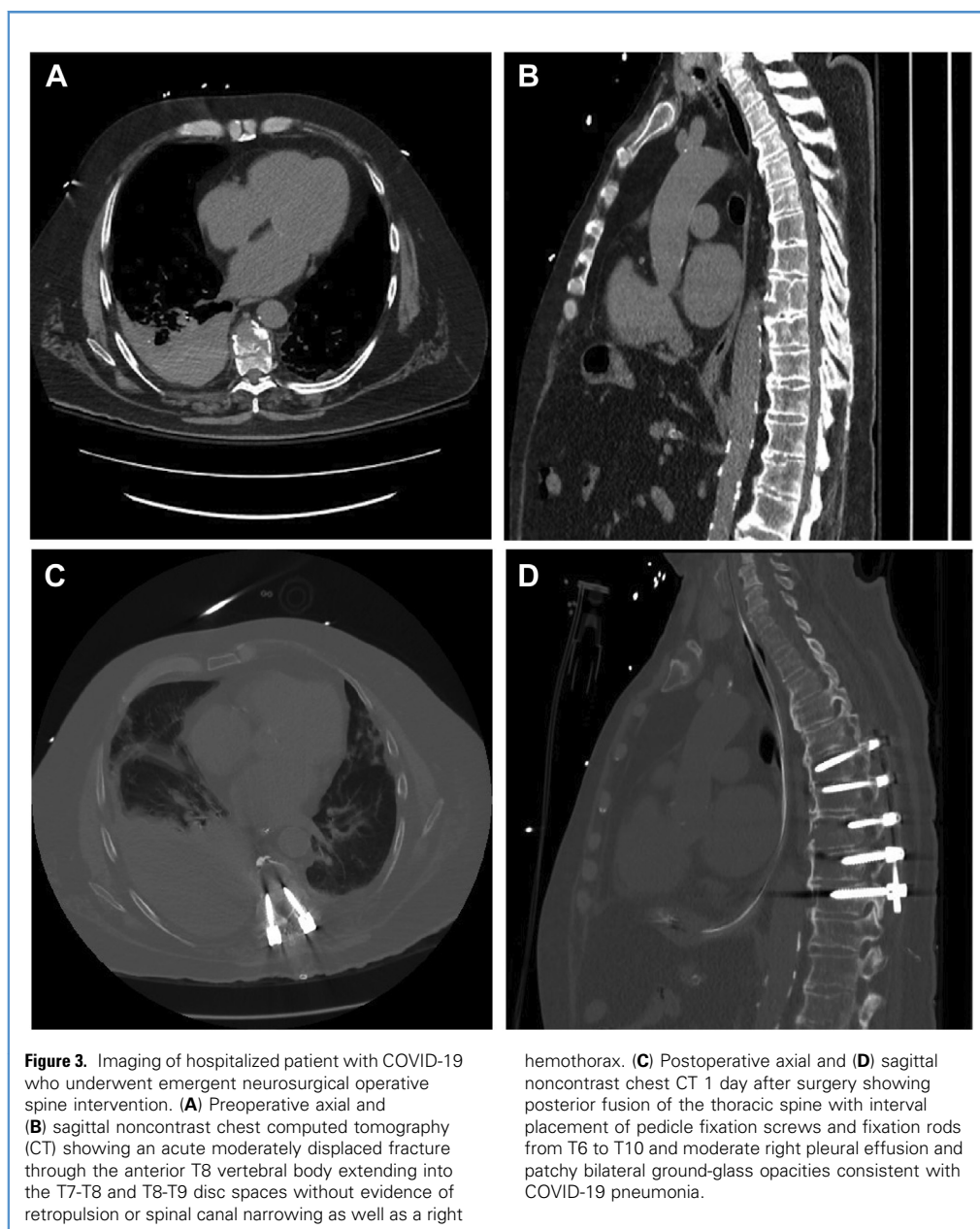
was lower than expected, because neurosurgical patients represented 0.68% of the total inpatient population who tested positive for COVID-19. This low prevalence is probably attributed to the measures enforced within Mayo Clinic to control the transmission of the virus within our hospital system.<sup>10</sup> Of these measures, telemedicine emerged as an excellent alternative for routine visits for services offered to our patients.<sup>11,12</sup> Moreover, in our series, none of the patients acquired the virus during their hospitalization. This finding contrasts with a recent report of hospitalized neurosurgical patients with low resources, in which half of the patients tested positive for SARS-CoV-2 infection after repeat testing after admission.<sup>13</sup>

In this series, the majority of patients were ≥65 years old with comorbidities. Most patients were hypertensive, diabetic, and overweight, with the average body mass index being 29.8 kg/m<sup>2</sup>, and 41.7% classifying as obese. All patients presented with lymphopenia at the time of admission and this laboratory finding has been previously identified as a predictor of hospitalization and increased risk for severity of symptoms.<sup>14,15</sup> Tan et al.<sup>16</sup> observed that patients with COVID-19 with lymphocyte counts <5% had a higher likelihood of becoming critically ill, requiring ICU care, and showing a higher mortality. The potential mechanism behind lymphopenia resulting in increased risk of severe signs and symptoms involves the release of inflammatory cytokines

(tumor necrosis factor  $\alpha$  and interleukin 6) leading to lymphocyte apoptosis or inducing lymphocyte deficiency. Most patients were hospitalized for a prolonged period, because the mean length of stay was 13.4 days (range, 4–30 days). However, this extended stay applied only to those patients with respiratory symptoms at the time of admission. Moreover, in this case series, the main cause of severe in-hospital course and poor prognosis resulted from respiratory distress secondary to coronavirus infection.

Patients with cancer have a higher mortality than the general population when infected with COVID-19 (5.6% vs. 2.3%).<sup>17</sup> This difference can be attributed to an immunosuppressed state as well as increased susceptibility to acquiring coronavirus as a result of frequent hospital visits. A total of 7 patients with CNS malignancy (4 metastasis, 1 meningioma, 1 GBM, and 1 schwannoma) who were infected with COVID-19 were admitted. Five patients died, 3 of COVID-19 complications and 2 of neuro-oncologic disease progression. Reports on outcomes of neuro-oncologic patients with COVID-19 are scarce, limited to case reports and few case series. In the early stages of the pandemic, the Society for Neuro-oncology released 2 guidelines addressing patients with gliomas.<sup>18,19</sup> Recommendations emphasize patient education and primary prevention (social distancing, hand washing, and minimizing unnecessary social interactions). Prioritization of patients is paramount, for those patients with indolent or slow-progressing

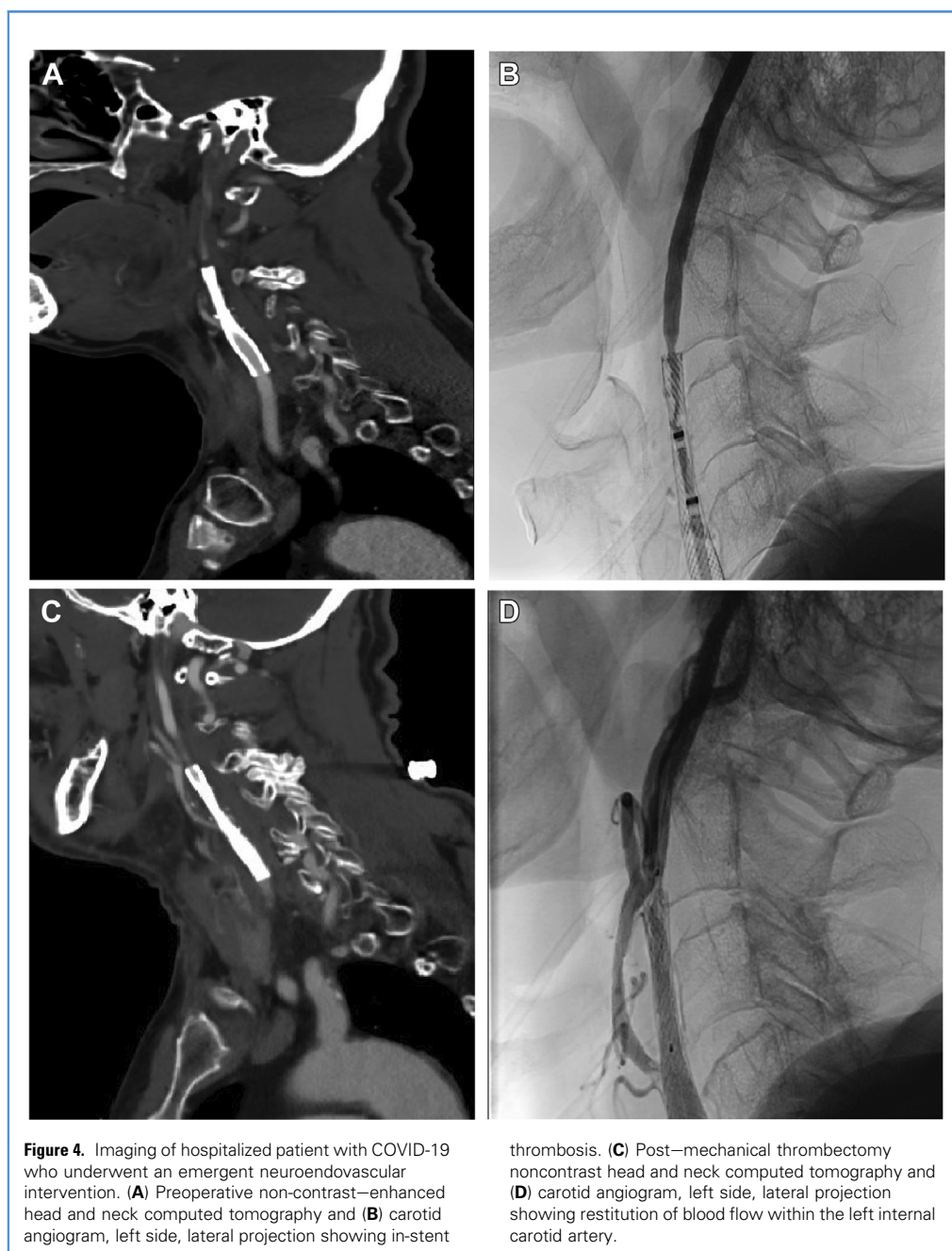




disease; they can have deferred interventions and be followed up with 3–6 months MRI. Evidence on the continuation of chemotherapy of patients with COVID-19 infection is controversial. In a large series of 800 oncologic patients, the mortality did not differ between COVID-19 patients receiving active chemotherapy versus individuals not receiving chemotherapy (27% vs. 29%, respectively).<sup>20</sup> Another study examining the outcomes of 366 patients who received chemotherapy treatment within 4 weeks of COVID-19 diagnosis noted that 160 patients (44%) who underwent cytotoxic therapy and 205 (56%) who did not receive therapy died.<sup>21</sup> These 2 studies may indicate that chemotherapy might not be related to increased mortality in patients with COVID-19. The Society

for Neuro-oncology recommends that if a patient becomes symptomatic, chemotherapy should be interrupted and resumed once the patient fully recovers from the infection.<sup>18</sup>

Regarding cerebrovascular events, 2 patients presented with ICH after admission and 1 patient presented with an ischemic stroke secondary to large-vessel occlusion. Hemorrhages occurred 11 and 17 days after admission, with both cases having onset after prolonged mechanical ventilation. It is reported that although COVID-19 can lead to cerebrovascular complications, the rate of ischemic or hemorrhagic stroke events is low.<sup>22,23</sup> In a recent review, among 844 patients hospitalized with COVID-19, only 20 (2.4%) and 8 (0.9%) had an ischemic stroke and ICH,



respectively,<sup>24</sup> with a median time of 21 days from COVID-19 diagnosis to the cerebrovascular event. In another series examining 1200 hospitalized patients with COVID-19, investigators identified only 3 patients (0.25%) with ICH.<sup>25</sup> More recently, a large case-control study across 13 hospitals in England and Scotland described the characteristics and outcomes of COVID-19-associated stroke. Overall, ischemic stroke was more common than hemorrhagic stroke in patients with COVID-19. However, the proportion of strokes secondary to multiple large-vessel occlusion in patients with COVID-19 doubled that of controls.<sup>23</sup> In addition,

patients with stroke and a positive COVID-19 status presented with a statistically significant increase in D-dimer levels as well as higher rates of inpatient death.<sup>23</sup>

The Congress of Neurological Surgeons released recommendations on the management of brain tumor patients in the COVID-19 era, emphasizing the importance of surgical case prioritization.<sup>26</sup> Emergent procedures defined as impending herniation or hydrocephalus should be performed as soon as possible using enhanced personal protective equipment. Because of the risk of aerosolization in endoscopic endonasal procedures,<sup>27,28</sup> the

**Table 3.** Outcomes for Eleven Neurosurgery-Related Patients with COVID-19 Infection

Age (Years)/ Sex	Diagnosis	Length of Stay (Days)	Intensive Care Unit Stay (Days)	COVID + Associated Complications	Transient Neurologic Deficit	Permanent Neurologic Deficits	Location After Discharge	Readmission	Reason for Readmission	Treatment After Admission	Final Status	Cause of Death
35/F	Metastatic monophasic synovial sarcoma*	13	1	None	Supplementary motor area syndrome, left hemiparesis	Yes	Rehabilitation	No	—	Fludarabine and cyclophosphamide SRS chimeric antigen receptor T cell	Deceased	Tumor progression
40/F	Metastatic human epidermal growth factor receptor 2 —positive metastatic breast carcinoma*	5	4	Acute respiratory failure, aspiration pneumonia, interstitial pulmonary edema	No	Increased weakness, progressive dysphagia, dysarthria, and diplopia	Home	Yes	Hypoxic respiratory failure	Palliative care	Deceased	Tumor progression
79/F	O-6-Methylguanine DNA- methyltransferase methylated isocitrate dehydrogenase wild type glioblastoma	19	2	Subsegmental pulmonary embolism	No	No	Rehabilitation	No	—	Temozolomide and radiotherapy	Alive	NA
60/F	Right parietal meningioma	8	2	Sepsis, interstitial pulmonary edema	No	No	Home	Yes	Shortness of breath	Gamma Knife SRS	Alive	NA
73/F	Metastasis	9	0	Interstitial pneumonia and aspiration pneumonia, hypophysitis	No	No	Home	No	—	Gemcitabine (continued), desmopressin, SRS (pending)	Alive	NA
81/F	Cavernoma*	12	0	Interstitial pneumonia, pulmonary effusion	No	No	Hospice	No	—	Palliative care	Deceased	Pneumonia
75/M	Schwannoma	4	0	Interstitial pneumonia	No	No	Home	No	—	Monitoring and repeat magnetic resonance imaging	Alive	NA
61/F	ICH*	18	16	Interstitial pneumonia, acute respiratory distress syndrome, intraparenchymal hemorrhage, AKI	Yes	Yes	Hospice	NA	NA	NA	Deceased	Pneumonia/ ICH

F, female; SRS, stereotactic radiosurgery; NA, not applicable; M, male; AKI, acute kidney injury; ICH: Intracerebral hemorrhage; DVT, deep vein thrombosis.

\*indicates patients who died.

Continues

Table 3. Continued

Age (Years)/ Sex	Diagnosis	Length of Stay (Days)	Intensive Care Unit Stay (Days)	COVID + Associated Complications	Transient Neurologic Deficit	Permanent Neurologic Deficits	Location After Discharge	Readmission	Reason for Readmission	Treatment After Admission	Final Status	Cause of Death
70/M	ICH*	22	22	Interstitial pneumonia, pulmonary edema, intraparenchymal hemorrhage, DVT, AKI	Yes	Yes	Hospice	NA	NA	NA	Deceased	Pneumonia/ ICH
65/M	Internal carotid artery thrombosis	9	8	Small hemorrhagic complication of stroke	Yes	Yes	Rehab	No	—	Observation	Alive	NA
80/M	Spinal fracture	30	13	Interstitial pneumonia, DVT, hemothorax	Yes	No	Home	Yes	Wound dehiscence	Second surgery and antibiotic treatment	Alive	NA

F, female; SRS, stereotactic radiosurgery; NA, not applicable; M, male; AKI, acute kidney injury; ICH, intracerebral hemorrhage; DVT, deep vein thrombosis.

\*indicates patients who died.

American Academy of Otolaryngology—Head and Neck Surgery recommends deferring all nonemergent, urgent, or time-sensitive cases unless COVID-19 testing can be performed.<sup>29</sup> Emergent cases including high-flow cerebrospinal fluid leak, pituitary apoplexy, and progressive neurologic deficits caused by an enlarging sellar lesion follow the same recommendations from the Congress of Neurological Surgeons and it is advised to consider a transcranial approach if feasible.<sup>30</sup> In our series, we followed Congress of Neurological Surgeons recommendations and only those individuals who were symptomatic from the neurosurgical perspective were offered operative intervention.

It is difficult to predict when we will return to standard practice, especially with an increase in the number of new cases as well as the emerging new strains of the virus. For now, the recommendations remain in place, and it is vital to understand the effect of the SARS-CoV-2 infection and its implication in neurosurgical practice.

### Limitations

This retrospective study provides a thorough overview of all neurosurgical-related patients with COVID-19 admitted to the Mayo Clinic during a period in 2020. The findings herein can provide helpful information to our colleagues of the increased risk that neurosurgical patients are exposed to once infected with COVID-19. The main limitations of this study are the small number of neurosurgical patients and the retrospective nature of the data collection.

### CONCLUSIONS

We observed a relatively low prevalence of neurosurgical patients among the COVID-19-positive inpatient population. Most admitted patients were older than 65 years and had multiple underlying comorbidities. Most neuro-oncologic patients who were SARS-CoV-2 positive had disseminated disease and were not actively undergoing chemotherapy or radiotherapy before admission. All symptomatic patients from the respiratory standpoint had complications during their hospitalization. Three patients, who died within 30 days of hospitalization were all related to COVID-19.

### CRedit AUTHORSHIP CONTRIBUTION STATEMENT

**Lina Marenco-Hillebrand:** Conceptualization, Methodology, Data collection, Data curation, Writing — original draft. **Young Erben:** Conceptualization, Methodology, Data collection, Data curation, Writing — original draft. **Paola Suarez-Meade:** Conceptualization, Methodology, Data collection, Data curation, Writing — original draft. **Camila Franco-Mesa:** Conceptualization, Methodology, Data collection, Data curation, Writing — original draft. **Wendy Sherman:** Visualization, Writing — review & editing. **Benjamin H. Eidelman:** Visualization, Writing — review & editing. **David A. Miller:** Visualization, Writing — review & editing. **Nancy L. O'Keefe:** Data collection, Investigation. **Bernard R. Bendok:** Visualization, Writing — review & editing. **Robert J. Spinner:** Visualization, Writing — review & editing. **Kaisorn L. Chaichana:** Visualization, Writing — review & editing. **James F. Meschia:** Visualization, Writing — review & editing. **Alfredo Quiñones-Hinojosa:** Conceptualization, Supervision, Writing — review & editing.

## REFERENCES

1. Helmy YA, Fawzy M, Elasad A, Sobieh A, Kenney SP, Shehata AA. The COVID-19 pandemic: a comprehensive review of taxonomy, genetics, epidemiology, diagnosis, treatment, and control. *J Clin Med*. 2020;9:1225.
2. World Health Organization Coronavirus Disease (COVID-19) Dashboard. Available at: [https://covid19.who.int/?gclid=CjwKCAiAouD\\_BRBIEiwALhJH6Pxm7\\_w27zRA2DVO\\_KDgXSqeiSoVeevCWRbyHVCn5Zau2rkojKvXhoCDT4QAvD\\_BwE](https://covid19.who.int/?gclid=CjwKCAiAouD_BRBIEiwALhJH6Pxm7_w27zRA2DVO_KDgXSqeiSoVeevCWRbyHVCn5Zau2rkojKvXhoCDT4QAvD_BwE). Accessed December 28, 2020.
3. Tsermoulas G, Zisakis A, Flint G, Belli A. Challenges to neurosurgery during the coronavirus disease 2019 (COVID-19) pandemic. *World Neurosurg*. 2020;139:519-525.
4. Díaz-Bello S, Hernández-Hernández A, Guinto-Nishimura GY, et al. Reconversion of neurosurgical practice in times of the SARS-CoV-2 pandemic: a narrative review of the literature and guideline implementation in a Mexican neurosurgical referral center. *Neurosurg Focus*. 2020;49:E4.
5. Simonelli M, Franceschi E, Lombardi G. Neuro-oncology during the COVID-19 outbreak: a hopeful perspective at the end of the Italian crisis. *Opinion Front Med*. 2020;7:594610.
6. Lima M, Siokas V, Aloizou AM, et al. Unraveling the possible routes of SARS-CoV-2 invasion into the central nervous system. *Curr Treat Options Neurol*. 2020;22:37.
7. Agha RA, Sohrabi C, Mathew G, Franchi T, Kerwan A, O'Neill N. The PROCESS 2020 guideline: updating consensus Preferred Reporting Of Case Series in Surgery (PROCESS) guidelines. *Int J Surg*. 2020;84:231-235.
8. American College of Emergency Physicians. Emergency Department COVID-19 Severity Classification 2020. Available at: <https://www.acep.org/globalassets/sites/acep/media/covid-19-main/acep-covid-19-ed-management-tool.pdf>. Accessed December 3, 2020.
9. COVID-19: Recommendations for Management of Elective Surgical Procedures. Available at: <https://www.facs.org/covid-19/clinical-guidance/elective-surgery>. Accessed January 2, 2021. <https://www.facs.org/covid-19/clinical-guidance/elective-surgery>.
10. De Biase G, Freeman W, Elder B, et al. Path to reopening surgery in the COVID-19 pandemic: neurosurgery experience. *Mayo Clin Proc Innov Qual Outcomes*. 2020;4:557-564.
11. De Biase G, Freeman WD, Bydon M, et al. Telemedicine utilization in neurosurgery during the COVID-19 pandemic: a glimpse into the future? *Mayo Clin Proc Innov Qual Outcomes*. 2020;4:736-744.
12. Erben Y, Franco-Mesa C, Hamid O, et al. Telemedicine in vascular surgery during the coronavirus disease 2019 (COVID-19) pandemic—a multi-site healthcare system experience. *J Vasc Surg*. 2021;74:1-4.
13. Sahoo SK, Dhandapani S, Singh A, et al. COVID-19: changing patterns among neurosurgical patients from North India, efficacy of repeat testing, and inpatient prevalence. *Neurosurg Focus*. 2020;49:E7.
14. Aggarwal S, Garcia-Telles N, Aggarwal G, Lavie C, Lippi G, Henry BM. Clinical features, laboratory characteristics, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): Early report from the United States. *Diagnosis (Berl)*. 2020;7:91-96.
15. Tavakolpour S, Rakhshandehroo T, Wei EX, Rashidian M. Lymphopenia during the COVID-19 infection: what it shows and what can be learned. *Immunol Lett*. 2020;225:31-32.
16. Tan L, Wang Q, Zhang D, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Transduct Target Ther*. 2020;5:33.
17. Zhang L, Zhu F, Xie L, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol*. 2020;31:894-901.
18. Mohile NA, Blakeley JO, Gatson NTN, et al. Urgent considerations for the neuro-oncologic treatment of patients with gliomas during the COVID-19 pandemic. *Neuro-Oncology*. 2020;22:912-917.
19. Bernhardt D, Wick W, Weiss SE, et al. Neuro-oncology management during the COVID-19 pandemic with a focus on WHO grade III and IV gliomas. *Neuro Oncol*. 2020;22:928-935.
20. Lee LY, Cazier JB, Angelis V, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet*. 2020;395:1919-1926.
21. Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet*. 2020;395:1907-1918.
22. Greenway MRF, Erben Y, Huang JF, et al. Yield of head imaging in ambulatory and hospitalized patients with SARS-CoV-2: a multi-center study of 8675 patients. *Neurohospitalist*. 2021;11:221-228.
23. Perry RJ, Smith CJ, Roffe C, et al. Characteristics and outcomes of COVID-19 associated stroke: a UK multicentre case-control study. *J Neurol Neurosurg Psychiatry*. 2021;92:242-248.
24. Rothstein A, Oldridge O, Schwennessen H, Do D, Cucchiara BL. Acute cerebrovascular events in hospitalized COVID-19 patients. *Stroke*. 2020;51:e219-e222.
25. Pavlov V, Beyerli O, Gareev I, Torres Solis LF, Solis Herrera A, Aliev G. COVID-19-related intracerebral hemorrhage. *Front Aging Neurosci*. 2020;12:600172.
26. Zacharia BE, Eichberg DG, Ivan ME, et al. Letter: Surgical management of brain tumor patients in the COVID-19 era. *Neurosurgery*. 2020;87:E197-E200.
27. Dhillon RS, Nguyen LV, Rowin WA, et al. Aerosolisation in endonasal endoscopic pituitary surgery. *Pituitary*. 2021;24:499-506.
28. Tuli IP, Trehan S, Khandelwal K, et al. Diagnostic and therapeutic endonasal rhinologic procedures generating aerosol during COVID-19 pandemic: a systematized review [e-pub ahead of print]. *Braz J Otorhinolaryngol*. 2021;87:469-477.
29. American Academy of Otolaryngology—Head and Neck Surgery. Guidance for Return to Practice for Otolaryngology—Head and Neck Surgery. Available at: <https://www.entnet.org/content/guidance-return-practice-otolaryngology-head-and-neck-surgery>; 2020. Accessed December 15, 2020.
30. American Academy of Otolaryngology—Head and Neck Surgery. Available at: <https://www.entnet.org/content/academy-supports-cms-offers-specific-nasal-policy>. Updated March 2018. Accessed December 15, 2020.

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