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Characteristics and operation outcomes of neuro-oncology patients after COVID-19 pandemic — A case series

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ARTICLE INFO	A B S T R A C T		
ARTICLEINFO Keywords: COVID-19 Pandemic Neuro-oncology	Background: COVID-19 has been spreading worldwide at hitherto unknown speed, and the treatment of neuro- oncology patients without COVID-19 has been greatly affected.Methods: To compare the medical records and surgical results of surgical patients before and after the pandemic. We collected a total of 80 patients form April 2020 to May 2020 after pandemic and from April 2019 to May 2019 before pandemic. The patient's demographics, past medical history, comorbidities, imaging, pathology, laboratory teat, and Karnofsky Performance Score (KPS) were analyzed. Results: The most common presenting symptom was intracranial hypertension and neurological deficit. Hyper- tension and diabetes were the most common comorbid diseases. The pre-operation KPS were 83.21 ± 15.60 , 80 ± 14.77 , 78.57 ± 12.83 and 74.14 ± 12.72 , respectively. The post-operation KPS were 94.64 ± 8.65 , 95.45 ± 6.56 , 91.43 ± 10.82 and 84.21 ± 22.55 , respectively. The tumor volume was larger and the midline shift distance was greater after the pandemic than before. For pathological grade, meningiomas were mostly grade I, while gliomas were mainly grade III and IV. Conclusion: Although affected by the COVID-19 pandemic, patients with glioma should be operated as soon as possible to obtain better surgical results, however, for patients with meningiomas, their operation can be postponed slightly when the patients are tolerable.		

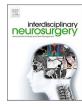
1. Introduction

Coronavirus disease 2019 (COVID-19) is a type of viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), which was first detected in Wuhan, Hubei, China in December 2019 [1]. Typical common clinical manifestations of COVID-19 include respiratory symptoms (e.g. fever and cough), loss of appetite, nausea, vomiting, diarrhea, and neurological manifestations [2–4]. Since the first detected case of COVID-19 in December 2019 in Wuhan, COVID-19 has rapidly spread across the globe with nearly 200 countries affected [5]. On the basis of previous experience with the SARS-CoV outbreak at the beginning of the century, the Chinese government has implemented strict measures, whereby millions of residents in cities in China were isolated to slow down the spread of the COVID-19. Moreover, many medical institutions invested substantial medical resources to fight against COVID-19 [6,7]. The COVID-19 pandemic has seriously disrupted health care, including the medical treatment of patients with neuro-oncology [8]. However, neuro-oncology cases are unique to that they can become critical at any time, and thus delays in treatment may affect surgical outcomes [9].

In April 2020, the epidemic was largely under control in Wuhan, the patients with COVID-19 were transferred to specialized hospitals for further treatment, our department began to gradually treat non-COVID-19 patients. With many countries having brought the epidemic situation under control, hospitals have been required to make adjustments to accommodate non-COVID-19 patients. In this paper, we compared clinical data, severity of disease, and surgical outcomes of the patients with common neuro-oncology (gliomas or meningiomas) from April to May for 2019 and 2020 to evaluate outcomes for operations. Our aim is to provide suggestions for the treatment of neuro-oncology following the

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Abbreviations: COVID-19, Coronavirus disease 2019; IQRs, Interquartile Ranges; KPS, Karnofsky Performance Score; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2.

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Table 1

Patient's basic characteristics, symptoms, underlying diseases, hospitalization time, complications and KPS score.

Demographics	Meningioma		Glioma	
	Pre- Pandemic (n = 28)	Pos- Pandemic (n = 11)	Pre- Pandemic (n = 22)	Pos- Pandemic (n = 19)
Sex (male/female)	9/19	4/7	13/9	11/8
Age(years)	56.54 \pm	49.48 \pm	53.73 \pm	49.16 \pm
	9.86	11.30	8.15	19.80
Recurrence	0 (0%)	0 (0%)	4 (18.18%)	3 (15.79%)
Chemoradiotherapy Symptoms	0 (0%)	0 (0%)	4 (18.18%)	1 (5.26%)
Intracranial	12	5 (45.45%)	9 (40.91%)	8 (42.11%)
hypertension	(42.86%)			
Neurological deficit	11	5 (45.45%)	8 (36.36%)	8 (42.11%)
	(39.26%)			
Seizure	1 (3.57%)	0 (0%)	4 (18.18%)	3 (15.79%)
Incidental	4 (14.29%)	1 (9.1%)	1 (4.55%)	0 (0%)
Hypertension	6 (21.43%)	5 (45.45%)	5 (22.73%)	5 (26.32%)
Diabetes	6 (21.43%)	0 (0%)	1 (4.55%)	2 (10.53%)
Lung disease	1 (3.57%)	0 (0%)	0 (0%)	1 (5.26%)
Chronic kidney disease	0 (0%)	0 (0%)	2 (9.09%)	1 (5.26%)
Hepatopathy	0 (0%)	0 (0%)	0 (0%)	2 (10.53%)
Heart disease	0 (0%)	1 (9.1%)	0 (0%)	1 (5.26%)
Totall	15.43 \pm	$18.09~\pm$	15.45 \pm	$21.05~\pm$
hospitalization time	2.49	4.79	2.89	6.68
Waiting time for surgery	$\textbf{6.18} \pm \textbf{2.05}$	$\textbf{7.73} \pm \textbf{2.04}$	$\begin{array}{c} \textbf{5.82} \pm \\ \textbf{1.92} \end{array}$	$\textbf{8.79} \pm \textbf{2.21}$
Postoperative	9.25 ± 2.38	10.86 \pm	9.64 ±	12.26 \pm
discharge time		4.81	2.23	6.13
Complications	4 (14.28%)	2 (18.18%)	4 (18.18%)	5 (26.32%)
New dyskinesia	3 (10.71%)	2 (18.18%)	2 (9.09%)	2 (10.53%)
New aphasia	0 (0%)	0 (0%)	0 (0%)	2 (10.53%)
New vision deficits	0 (0%)	0 (0%)	2 (0%)	1 (5.26%)
Intracranial infection	1 (3.57%)	0 (0%)	0 (0%)	0 (0%)
Pre-op KPS	83.21 \pm	80 ± 14.77	78.57 \pm	74.14 \pm
-	15.60		12.83	12.72
Pos-op KPS	94.64 ±	95.45 \pm	91.43 \pm	84.21 \pm
-	8.65	6.56	10.82	22.55

Abbreviations: KPS, karnofsky performance score.

COVID-19 pandemic.

2. Methods

2.1. Data collection

We retrospectively reviewed non-COVID-19 patients with gliomas or meningiomas confirmed by pathological examination post-operation from April to May for 2019 and 2020. Data on demographics, past medical history, comorbidities, imaging, pathology, laboratory teat, and outcomes were collected form patients who were hospitalized in our hospital system. Tumor sizes were calculated with the method of XYZ/2 that has been validated with the gold standard of computer volumetric calculation.

2.2. Surgery procedure

CT and MRI were performed in all patients before operation to check the characteristics of tumor and its surrounding anatomy for surgical planning. The surgical approach is based on the location and size of the tumor, tumor removal was accomplished using standard microsurgical technique. For meningioma resection, the same standard method was used for total resection of brain tumors before and after COVID-19 pandemic. For glioma resection, neuroelectrophysiological technique and yellow fluorescence technique were used to assist maximize remove glioma under the condition of protective function, but for the intraoperative wake-up technology, unlike before the pandemic, it not used

Table 2

Patient's imaging dates and pathological dates.

Demographics	Meningioma		Glioma	
	Pre- Pandemic(n = 28)	Pos- Pandemic (n = 11)	Pre- Pandemic(n = 22)	Pos- Pandemic (n = 19)
Tumor volume, median (IQR), cm ³	4.6 (14.9–27.3)	8.7 (17.2–37.0)	17.4 (34.2–46.0)	22.2 (43.7–52.8)
Tumor Edema (yes/no)	13/15	4/7	14/8	16/3
Ventricular compression (yes/no)	11/17	5/6	15/7	14/5
Midline shift, median (IQR), mm	0 (0–5.0)	2.0 (0–10.5)	2.0 (0–7.0)	7.0 (3.5–11.0)
WHO classification				
I	25 (89.29%)	11 (100%)	3 (13.64%)	1 (5.26)
II	2(7.14%)	0 (0%)	3 (13.64%)	4 (21.05%)
III	1 (3.57%)	0 (0%)	5 (22.73%)	3 (15.79%)
IV	0 (0%)	0 (0%)	11 (50%)	11 (57.89%)
Ki67, median (IQR), %	2.05 (1–3)	1.64 (1–2)	25.14 (8.5–27.5)	17.33 (8–15)

after pandemic due to lack of medical resources.

2.3. Statistical analysis

All normally distributed data are presented as mean \pm standard deviation, and non-normally distributed data are presented as medians with interquartile ranges (IQRs). All analyses were performed using SPSS 21.0 (IBM Corp., Armonk, NY, USA). Because the data analysis was retrospective and no additional blood or in vitro samples were collected, a full ethics review of the terms of the ethics committee of Wuhan University Zhongnan Hospital was not required.

3. Results

In total, we collected date form 80 patients that underwent surgery only in our center which was categorized into four groups: 28 and 11 meningiomas patients before and after the pandemic, respectively, and 22 and 19 gliomas patients before and after the pandemic, respectively. The average ages for each group were 56.54, 49.48, 53.73, and 49.16 years, respectively. There were four patients (18.18%) with recurrent gliomas before the pandemic, who all received normal chemoradiotherapy, while only one of the three (15.79%) relapsed patients after the pandemic received chemoradiotherapy. The most common presenting symptoms were intracranial hypertension and neurological deficit. Hypertension and diabetes were the most common comorbid diseases. For hospitalization time, the time to wait for an operation and the time from operation to discharge was longer after than before the pandemic, the specific data are shown in Table 1. The pre-operation KPS were 83.21 \pm 15.60, 80 \pm 14.77, 78.57 \pm 12.83, and 74.14 \pm 12.72, respectively. The post-operation KPS were 94.64 \pm 8.65, 95.45 \pm 6.56, 91.43 \pm 10.82, and 84.21 \pm 22.55, respectively (Table 1).

In terms of imaging features, tumor volumes were larger and the midline shift distance was greater after the pandemic than before. For pathological grade, meningiomas were mostly grade I, while gliomas were mainly grade III and IV. The median (IQR) Ki67 were 2.05 (1–3), 1.64 (1–2), 25.14 (8.5–27.5), and 17.33 (8–15), respectively (Table 2).

Laboratory examination before and after surgery were also collected to assess the patient's condition, the median (IQR) post-operation white blood cell counts (\times 109/L) were 10.6 (8.1–14.7), 14.5 (10.8–16.8), 9.8 (7.1–11.4), and 10.8 (7.0–12.7), respectively. The median (IQR) postoperation hemoglobin levels (g/L) were 101.3 (85.4–115.6), 111.0 (102.3–120.5), 101.8 (92.7–111.5), and 99.6 (84.5–114.0),

Table 3

Laboratory data of 80 patients before and after COVID-19 pandemic.

Demographics	Meningioma		Glioma		
	Pre-Pandemic (n = 28)	Pos-Pandemic (n = 11)	Pre-Pandemic(n = 22)	Pos-Pandemic (n = 19)	
WBC counts, median (IQR), $\times 10^9$ /L					
Pre-operation	5.0 (4.2-6.4)	5.7 (5.1–6.6)	6.4 (5.6-8.0)	5.47 (4.5-6.6)	
Post-operation	10.6 (8.1–14.7)	14.5 (10.8–16.8)	9.8 (7.1–11.4)	10.8 (7.0–12.7)	
Hemoglobin, median (IQR), g/L					
Pre-operation	132.4 (121.3–140.1)	140.0 (123.9–142.1)	137.5 (127.0–145.2)	129.0 (112.7–134.7)	
Post-operation	101.3 (85.4–115.6)	111.0 (102.3–120.5)	101.8 (92.7–111.5)	99.6 (84.5–114.0)	
Platelet counts, median (IQR), $\times 10^9$ /L					
Pre-operation	191.5 (149.5–217.0)	167.0 (152.5–183.5)	195.5 (183.5–245.3)	213.0 (183.5-240.0)	
Post-operation	139.0 (107.3-165.5)	168.0 (147.5–187.5)	165.0 (124.5–188.3)	173.0 (143.0-213.0)	
Neutrophil Ratio, median (IQR), %					
Pre-operation	57.3 (50.7-69.9)	55.7 (52.0-67.3)	59.8 (52.0-72.4)	63.3 (57.9–70.0)	
Post-operation	85.5 (80.7-89.8)	87.0 (86.3-89.3)	81.6 (77.1-85.6)	86.6 (82.3-88.6)	
ALB, median (IQR), g/L					
Pre-operation	40.1 (37.9-43.9)	38.7 (37.1-40.9)	42.1 (38.1-43.9)	37.8 (35.8-41.4)	
Post-operation	30.9 (28.8–34.3)	32.0 (31.0-35.1)	31.3 (29.1–34.8)	30.3 (28.7–32.2)	
GLB, median (IQR), g/L			. ,		
Pre-operation	23.9 (21.8-26.8)	30.9 (29.0-32.8)	23.4 (22.2–27.8)	27.8 (25.2-30.7)	
Post-operation	20.7 (19.8–20.7)	28.2 (24.0-32.1)	23.0 (20.9–25.4)	24.6 (22.4–27.0)	
ALT, median (IQR), U/L					
Pre-operation	15.5 (10.0-24.5)	17.0 (12.0-22.5)	14.0 (12.0-22.5)	13.0 (10.0-37.8)	
Post-operation	14.0 (10.5–17.0)	16.0 (10.8–25.8)	15.0 (11.0–25.0)	13.0 (10.0–23.5)	
AST, median (IQR), U/L			. ,		
Pre-operation	17.5 (14.0-22.3)	18.0 (14.5-22.5)	17.0 (14.0-20.5)	16.0 (13.2–29.8)	
Post-operation	17.0 (13.0–28.5)	24.0 (21.2–32.2)	24.0 (15.0-42.0)	22.0 (19.8–34.2)	
CREA, median (IQR), µmol/L					
Pre-operation	56.4 (50.5–69.0)	58.7 (51.6-71.5)	67.0 (56.3-81.7)	64.2 (53.1-68.3)	
Post-operation	49.0 (45.8–60.9)	56.0 (49.8–62.2)	59.4 (48.5–74.6)	56.2 (43.8–56.2)	
FIB, median (IQR), mg/dL			. ,		
Pre-operation	309.0 (264.5-355.0)	273.0 (249.5-329.3)	291.0 (276.3-316.8)	276.5 (237.0-332.3)	
Post-operation	361.5 (280.0-418.8)	340.0 (298.5-420.5)	331.0 (264.0–377.0)	332.0 (296.0-395.0)	
D-dimer, median (IQR), μg/mL					
Pre-operation	125.0 (92.3–177.0)	98.0 (67.5–148.5)	138.5 (93.8-218.0)	182.0 (84.5-370.0)	
Post-operation	848.5 (686.8–1367.0)	860.0 (623.5–1245.5)	834.0 (607.0–1463.5)	848.5 (578.0–1314.8)	
K ⁺ , median (IQR), mmol/L					
Pre-operation	4.0 (3.6-4.1)	3.8 (3.6-4.1)	3.7 (3.8, 4.2)	4.0 (3.8-4.2)	
Post-operation	3.4 (3.2–3.7)	3.7 (3.5–4.0)	3.6 (3.2–4.0)	3.5 (3.3–3.9)	
Na ⁺ , median (IQR), mmol/L					
Pre-operation	141.3 (140.0–142.0)	140.0 (139.2–141.0)	140.0 (139.0–140.0)	140.0 (138.3–142.0)	
Post-operation	141.9 (140.0–143.3)	142.0 (137.8–143.0)	139.3 (136.2–141.0)	141.0 (139.0–142.0)	

Abbreviations: WBC, White blood cell; ALB, albumin; GLB, globulin; ALT, alanine transaminase; AST, aspartate transaminase; CREA, creatinine; FIB, fibrinogen; IQR, interquartile range.

respectively. The median (IQR) post-operation neutrophil ratios (%) were 85.5 (80.7–89.8), 87.0 (86.3–89.3), 81.6 (77.1–85.6), and 86.6 (82.3–88.6), respectively. The median (IQR) post-operation albumin levels (g/L) were 30.9 (28.8–34.3), 32.0 (31.0–35.1), 31.3 (29.1–34.8), and 30.3 (28.7–32.2), respectively. The median (IQR) post-operation K^+ levels (mmol/L) were, 3.4 (3.2–3.7), 3.7 (3.5–4.0), 3.6 (3.2–4.0), and 3.5 (3.3–3.9), respectively. The median (IQR) post-operation Na⁺ levels (mmol/L) were, 141.9 (140.0–143.3), 142.0 (137.8–143.0), 139.3 (136.2–141.0), and 141.0 (139.0–142.0), respectively. Additional laboratory results are summarized in Table 3.

4. Discussion

Covid-19 is a kind of virus infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the typical common clinical manifestations of COVID-19 include respiratory symptoms (fever and cough), loss of appetite, nausea, vomiting and diarrhea [2]. In addition, a few cases are accompanied by neurological manifestations, including acute cerebrovascular disease (i.e., cerebral hemorrhage), olfactory/taste disorders, myalgia and headache [3,4]. Although much remains to be discovered about the COVID-19, China's observation shows that 2.3% of patients need ventilatory support, and 1.4% of them died[8], less than 30% mortality in SARA [7]. However, the transmission rate (number of new infections per infected person) of 2.5 to 3 is very high, which leads to the current worldwide pandemic [7]. By contrast, the annual transmission rate for the common cold is less than 1.4. Furthermore, respiratory failures caused by COVID-19 have led to high intubation rates and an increased need for respiratory machines, which has resulted in insufficient ICU capacities and made the treatment of all critical diseases, especially neuro-oncology, extremely difficult or even impossible [7,10]. For neurosurgeons, the most important thing is to evaluate the operation priority and pay attention to self-protection when resources are severely limited. At present, most individuals and consensus recommendations have given high priority to neuro-oncology cases during the pandemic to not delay surgeries [8,9,11–13], However, there is limited data to support these recommendations. Our clinical data analysis may fill some of these gaps.

Compared with the same period of last year, the number of neurooncology surgeries after the pandemic was significantly reduced, despite conditions being more critical (Tables 1 and 2). During this period, there were no medical infection in our department, and no patients were diagnosed with COVID-19. Compared with the same period of 2019 year of , we found that the outcomes of glioma operations were greatly affected by the pandemic, while the outcomes of meningioma operations were not. On the basis of the statistical results and personal experience, this could be attributed to a number of reasons. First, because of the COVID-19 pandemic, there were more patients in critical conditions. Many patients were not able to receive timely medical treatment following symptom onset. Even upon admission to the hospital, the waiting time for surgery was prolonged due to the delay of detection results of COVID-19 virus throat swab. Second, because of the epidemic, chemoradiotherapy was not being offered. Many patients with recurrent gliomas had poor outcomes because of delays in chemoradiotherapy plans. Third, because of the lack of hospital resources, intraoperative wake-up technology that maximizes protection of function could not be employed for motor area glioma operations. Finally, because of the insufficient numbers of doctors and nurses during the COVID-19 pandemic, changes in patients' conditions may not have been detected and attended to in a timely manner.

To the best of our knowledge, this is the first and largest study on the effects of neuro-oncology surgery before and after the outbreak of COVID-19. The uniqueness of our research is that we compared clinical data, severity of disease, and surgical outcomes in patients with meningiomas and gliomas before and after the pandemic. Our data may provide guidance for the treatment of neuro-oncology after the COVID-19 pandemic. For patients who are suspected of neuro-oncology in need of medical treatment, it is recommended to choose video or telephone consultation. Even if need to go to the outpatient clinic, the patients should keep a good physical protection, wear masks scientifically, pay attention to hand hygiene, avoid taking public transportation, and keep a safe distance of more than one meter from others. For clinicians, apart from doing their daily work and personal protection, they also need to evaluate which patients to concentrate limited healthcare resources, and preoperative imaging is very important in the evaluation. In addition to the basic MRI scan and enhancement and CT examination to reflect the morphology, location, mass effect of the tumor, more MRI series are needed. As a new noninvasive magnetic resonance perfusion imaging technology, arterial spin labeling can be well qualified to distinguish the characteristics of brain tumor, grading of gliomas, recurrence and radiation necrosis [14,15].

However, the number of cases studied was small and we did not have long-term follow-up data and thus, more research is necessary. In principle, we recommend that surgery can postpone slightly if medical resources are limited for patients with meningiomas. However, for patients with gliomas, surgery should be performed as soon as possible if medical resources allow, to ensure good prognosis.

5. Conclusion

Compared with the pre-pandemic, the complexity and criticality of neuro-oncology after the pandemic have an upward trend. In terms of surgical treatment, meningioma patients are not affected, while the surgical effect of glioma patients has significantly decreased. The decreased operation effectiveness of gliomas may be related to the shortage of medical resources and the delay of the patient's condition. Therefore, we recommend that patients with meningioma can be postponed for surgery and given conservative treatment first if medical resources are tight. But for patients with gliomas, we recommend that surgery should be performed as soon as possible if medical resources allowed to obtain better clinical results.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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