HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2023.47123
Haydarpasa Numune Med J 2024;64(3):408–415

ORIGINAL ARTICLE

Effect of COVID-19 on Vasospasm in Patients with Aneurysmal Subarachnoidal Hemorrhage

Eyüp Varol[1], Yunus Emre Çakıcı[1], Furkan Avcı[1], Mustafa Umut Etli[2], Serdar Onur Aydın[3], Mustafa Efendioğlu[4], Mehmet Reşid Önen[5], Abuzer Güngör[6], Cumhur Kaan Yaltırık[1]

[1]Department of Neurosurgery, Ümraniye Training and Research Hospital, İstanbul, Türkiye
[2]Department of Neurosurgery, Siverek State Hospital, İstanbul, Türkiye
[3]Department of Neurosurgery, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye
[4]Department of Neurosurgery, University of Health Sciences Türkiye, Haydarpaşa Numune Training Hospital, İstanbul, Türkiye
[5]Department of Neurosurgery, Medicalpark Hospital, İstanbul, Türkiye
[6]Department of Neurosurgery, Bakırköy Psychiatric and Neurological Diseases Hospital, İstanbul, Türkiye

Abstract

Introduction: In our article, our aim was to compare patients with aneurysmal SAH (subarachnoid hemorrhage) treated during and before the COVID-19 pandemic—regardless of whether they have COVID-19 pneumonia or not—in terms of clinical course, mortality, and morbidity.

Methods: In this study, we retrospectively analyzed 100 patients undergoing surgery at our institution between 02/2018 and 02/2021. These patients were followed up for a period of 1 month during the period with the highest risk of vasospasm. Patients were compared based on sex, aneurysm location, presence of single or multiple aneurysms, WFNS grade, Fisher grade, complications, frequency of vasospasm, and mortality and morbidity. Complication rate and vasospasm rate were found to be higher in aneurysmal subarachnoid hemorrhage patients seen during the COVID pandemic period. This may be due to the late admission of patients to the hospital.

Results: Of those patients, 51% were female and 49% were male. The mean age was 51.33±12.94. The vasospasm frequency was 18% before the COVID-19 pandemic; during the pandemic, the rate significantly increased to 58%. Of the 38 patients with vasospasm, 26 were symptomatic and 12 were asymptomatic; symptomatic vasospasm was seen during the pandemic. Mean GCS scores and WFNS grades were significant, and the mean Hunt-Hess Scale score was nearly significantly higher during the pandemic in comparison to pre-pandemic time periods. During the pre-pandemic period, the complication rate was 40%, the presence of hydrocephalus was 8%, and vasospasm was unseen. During the pandemic, the complication rate significantly increased to 64%, hydrocephalus to 26%, and vasospasm to 26%.

Discussion and Conclusion: The higher complication rate and vasospasm rate in patients with aneurysmal subarachnoid hemorrhage seen during the COVID pandemic may be due to the late admission of these patients to the hospital. In SAH patients, the onset of symptoms instead of the date of hospital admission should be considered when determining the disease course, and the possibility of earlier vasospasm should always be kept in mind due to delays in diagnosing and treating the condition.

Keywords: COVID-19; Subarachnoid hemorrhage; Vasospasm.

Correspondence: Eyüp Varol, M.D. Department of Neurosurgery, Ümraniye Training and Research Hospital, İstanbul, Türkiye
Phone: +90 544 234 12 03 **E-mail:** dreyupvarol@gmail.com
Submitted Date: 08.04.2023 **Revised Date:** 06.06.2023 **Accepted Date:** 12.06.2023
Haydarpaşa Numune Medical Journal

A subarachnoid hemorrhage (SAH) develops between the pia and arachnoid mater of three membranous layers surrounding the brain parenchyma. In addition to head trauma, SAH can develop due to underlying vascular pathologies. Since aneurysmal SAH is associated with high morbidity and mortality (30%), and the possibility of rebleeding is high in the early period, surgical and/or endovascular treatment is vital[1-3].

The COVID-19 pandemic, which gained increased prevalence in 2020, has caused changes in the number of patients with cerebral aneurysms and SAH, as it did for many other diseases. Since symptoms such as headache and nausea can also be seen in COVID-19 pneumonia, the diagnosis of SAH may be delayed in some patients. Decreased admission to hospitals due to the increased risk of infection is another factor for delayed diagnosis. For these reasons, some studies argue that the number of patients admitted to hospitals for headache and being diagnosed with SAH is decreasing[4-11]. Studies have shown that intracranial bleeding and mortality are more frequent in patients with recent positive cases of COVID-19[12,13].

Vasospasm is seen in around 30% of patients with SAH. However, its effect on vasospasm in SAH patients during the COVID-19 pandemic has not been fully investigated. In this study, we aimed to compare the clinical course, mortality, and morbidity of SAH patients treated during the COVID-19 pandemic, regardless of their COVID PCR test results, and of SAH patients treated before the COVID-19 pandemic.

Materials and Methods

In this study, we retrospectively analyzed 100 patients undergoing surgery at our institution between 02/2018 and 02/2021. Since the COVID-19 pandemic started in February 2020, patients were divided into two groups: a pre-pandemic group (02/2018-02/2020) and a far-pandemic group (02/2020-02/2021). Patients were compared based on sex, aneurysm location, presence of single or multiple aneurysms, World Federation of Neurosurgical Societies (WFNS) SAH grade, Fisher Grade, perioperative complications, frequency of vasospasm, and mortality and morbidity. Each patient group was evaluated and compared within itself. Ethics committee approval or patient consent was not required due to the retrospective nature of our study.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA) was used to analyze our findings. Normality was assessed using graphical and statistical methods for the continuous variables. The Shapiro-Wilk test was used to test the normality of the scores derived by the statistical analysis of a continuous variable. Other than descriptive methods (count, percent, mean, median, standard deviation), the Mann-Whitney U test was used to compare the quantitative data. Chi-square tests (Pearson's Chi-square, Continuity Correction Test, and Fisher's Exact Test) were used to compare the categorical variables. Multiple logistic regression analyses were used to define the independent factors associated with mortality. The results were evaluated with a 95% confidence interval; the significance level was set at $p<0.05$.

Results

One hundred patients diagnosed with SAH were included in our study; 50 of these were diagnosed before the COVID-19 pandemic and 50 were diagnosed during the COVID-19 pandemic. Of those patients, 51% were female and 49% were male. The mean age was 51.33±12.94; 13% of the patients were under the age of 40, 37% were between 41 and 50, 30% were between 51 and 60, and 20% were older than 61. Moreover, 58% of the patients were diagnosed with a chronic disease. According to the findings from the radiologic imaging studies, the aneurysm location was the anterior communicating artery (ACom) in 39 patients, the middle cerebral artery (MCA) in 28 patients, the posterior communicating artery (PCom) in 19 patients, the proximal internal carotid artery (ICA) in 10 patients, and other locations in four patients. Single aneurysms were found in 22 patients and multiple aneurysms were present in 77 patients.

SAH Patients before the COVID-19 Pandemic

A total of 58% of the patients diagnosed before the pandemic were male and 42% were female. After imaging studies, the aneurysm locations of the patients in this group were: ACom (18 patients), MCA (13 patients), PCom (8 patients), posterior inferior cerebellar artery (PICA) (9 patients), and proximal ICA (9 patients). Multiple aneurysms were detected in 40 patients (80%).

Among the patients undergoing surgery, 20 had perioperative complications; the most common complication was hydrocephalus (8%) followed by malignant edema (10%) and neurologic deficits (10%).

The WFNS grades of the patients in this group were: I in 33 patients, II/III in 9 patients, IV/V in 8 patients. According to computed tomography (CT) examinations, the Fisher scores of the patients in this group were I in 3 patients, II in 11 patients, III in 19 patients, and IV in 17 patients.

Vasospasm was seen in 9 patients, 9 of whom were asymptomatic.

Table 1. Patient characteristics (n=100)

	All (n=100)	Pre-pandemic (n=50)		Post-pandemic (n=50)		$\chi^{2/t}$	p
	n	n	%	n	%		
Age, mean (SD)	51.33 (12.94)	50.36 (12.77)		52.30 (13.17)		0.748[c]	0.456
Age group						3.368[a]	0.338
≤40	13	8	16	5	10		
41-50	37	16	32	21	42		
51-60	30	18	36	12	24		
≥61	20	8	16	12	24		
Sex						2.561	0.110
Female	51	21	42	30	60		
Male	49	29	58	20	40		
Presence of chronic disease						1.026[b]	0.311
Yes	58	26	52	32	64		
No	42	24	48	18	36		
Localization of aneurysm						7.247[a]	0.123
ACom	39	18	36	21	42		
MCA	28	13	26	15	30		
PCom	19	8	16	11	22		
Proximal ICA	10	9	18	1	2		
Other	4	2	4	2	4		
Presence of multiple aneurysm						0.226[b]	0.635
Single	23	10	20	13	26		
Multiple	77	40	80	37	74		
Vasospasm						**15.323[b]**	**<0.001***
Yes	38	9	18	29	58		
No	62	41	82	21	42		
Type of vasospasm						**35.452[a]**	**<0.001***
Symptomatic vasospasm	26	0	0	26	52		
Asymptomatic vasospasm	12	9	18	3	6		
Not detected	62	41	82	21	42		

*: $p<0.05$; χ^2: Chi-Square Tests. [a]: Pearson Chi-Square; [b]: Continuity correction; [c](t): Independent Sample t-Test. SD: Standard deviation; ACom: Anterior communicating artery; MCA: Middle cerebral arteryl PCom: Posterior communicatinng artery; ICA: Internal carotid artery.

When the patients were evaluated according to the morbidity and mortality rates, in the pre-pandemic group, death at the time of admission was seen in 10 (20%) patients. Ten pre-pandemic patients with SAH died during their hospital stay, three patients needed lifetime care, and the remaining 37 patients were neurologically intact and were discharged without the need for additional surgery.

SAH Patients during the COVID-19 Pandemic

Of the 50 patients diagnosed with SAH during the pandemic, 40% were male and 60% were female. Thirty-three (66%) of these patients underwent digital subtraction angiography. In our study, 75% of the patients were vaccinated and 28% had COVID-19 before hospital admission. Three of our patients had active COVID-19 at the time of SAH diagnosis. After imaging studies, the aneurysm location of the patients in this group were: ACom (21 patients), MCA (15 patients), PCom (11 patients), proximal ICA (1 patient), PICA (1 patient), and basilar tip aneurysm (1 patient). Multiple aneurysms were detected in 37 patients (74%).

Twenty-six (52%) patients had a history of hypertension. Of the patients undergoing surgery, 32 had perioperative complications; the most common of these were hydrocephalus (40%) followed by malignant edema (20%) and neurologic deficit (20%). Two patients tested positive for COVID-19 during their postoperative follow-up.

The WFNS grades of the patients in this group were I in 20 patients, II/III in 12 patients, IV/V in 18 patients. The Fisher scores of the patients in this group were I in 8 patients, II in 11 patients, III in 13 patients, and IV in 18 patients.

Table 2. Results of GCS, WFNS, fisher grade, hunt-hess scale evaluation

	All (n=100)	Pre-pandemic (n=50)		Post-pandemic (n=50)		$\chi^{2/Z}$	p
	n	n	%	n	%		
GCS, mean (SD)	12.90 (3.34)	13.50 (3.06)		12.30 (3.54)		**-2.225[a]**	**0.026***
GCS						**4.018[c]**	**0.045***
Stupor/perikoma/coma	28	9	18	19	38		
Oriented/Confused	72	41	82	31	62		
WFNS, mean (SD)	2.12 (1.45)	1.74 (1.26)		2.50 (1.54)		**-2.722[a]**	**0.008***
WFNS						**7.463[b]**	**0.024***
I	53	33	66	20	40		
II/III	21	9	18	12	24		
IV/V	26	8	16	18	36		
Fisher Grade, mean(SD)	2.91 (1.01)	3.00 (0.90)		2.82 (1.10)		-0.664[a]	0.507
Fisher Grade						0.800[d]	0.371
I	11	3	6	8	16		
II	22	11	22	11	22		
III	32	19	38	13	26		
IV	35	17	34	18	36		
Hunt-Hess Scale, mean (SD)	2.41 (1.14)	2.18 (1.00)		2.64 (1.23)		-1.909[a]	0.056
Hunt-Hess Scale						**4.085[d]**	**0.043***
I	18	12	24	6	12		
II	50	25	50	25	50		
III	12	6	12	6	12		
IV	7	1	2	6	12		

*: p<0.05; χ^2: Chi-Square Tests. [a](Z): Mann-Whitney U Test; [b]: Pearson Chi-Square; [c]: Continuity correction; [d]: Linear-by-linear association. GCS: Glasgow coma scale; WFNS: World Federation of Neurosurgery; SD: Standard deviation.

In 26 (52%) patients, symptomatic vasospasm was detected and in 15 patients there was a need for intensive care unit care. Neurologic deficits were seen in 10 (20%) patients.

Mortality and morbidity assessment revealed that 14 (28%) patients treated during the pandemic died during their hospital stay, five (10%) patients needed lifetime care, and the remaining 31 patients (62%) were neurologically intact and discharged without the need for additional surgery.

Comparison of the Results Before and During the Pandemic

No statistical significance was found between the patients diagnosed before and during the COVID-19 pandemic in relation to age, sex, presence of chronic disease, aneurysm location, and number (single/multiple) of aneurysms (p>0.05) (Table 1).

The vasospasm frequency was 18% before the COVID-19 pandemic; during the pandemic, the rate significantly increased to 58% (χ^2=15.323; p<0.001). Of the 38 patients with vasospasm, 26 were symptomatic and 12 were asymptomatic; symptomatic vasospasm was seen during the pandemic (χ^2=35.452; p<0.001) (Table 1).

Mean GCS (Glasgow Coma Scale) scores (12.30±3.54 vs. 13.5±3.06, p=0.026) and WFNS grades (1.74±1.26 vs. 2.5±1.54, p=0.008) were significant, and the mean Hunt-Hess (H&H) Scale score was nearly significantly higher during the pandemic in comparison to pre-pandemic time periods (Table 2).

During the pre-pandemic period, the complication rate was 40%, the presence of hydrocephalus was 8%, and vasospasm was unseen. During the pandemic, the complication rate significantly increased to 64% (p=0.028), the presence of hydrocephalus increased to 26% (p=0.031), and the presence of vasospasm increased to 26% (p<0.001). All these changes were significant. In the pre-pandemic period, mortality was 20% and it increased to 28% during the pandemic, but this change was not statistically significant (p>0.05) (Table 3).

Without dividing patients into the pre- and during pandemic groups, according to the GCS scores, the mortality rate was lower in the confusion/orientation patient group in comparison to the stupor/pre-coma-coma group (13.9% vs. 50%, p≤0.001). An increase in mortality

Table 3. Perioperative and postoperative status evaluation results of the patients

		All (n=100)	Pre-pandemic (n=50)		Post-pandemic (n=50)		$\chi^{2/Z}$	p
	Presence	n	n	%	n	%		
Complication	Yes	52	20	40	32	64	**4.848[b]**	**0.028***
	No	48	30	60	18	36		
Hydrocephalus	Yes	17	4	8	13	26	-[c]	**0.031***
	No	83	46	92	37	74		
Perioperative vasospasm	Yes	13	0	0	13	26	-[c]	**<0.001***
	No	87	50	100	37	74		
Re-operation	Yes	21	10	20	11	22	0.000[b]	1
	No	79	40	80	39	78		
Periopertive third ventriculostomy	Yes	52	17	34	35	70	**11.579[b]**	**0.001***
	No	48	33	66	15	30		
Perioperative lumbar drainage	Yes	9	0	0	9	18	-[c]	**0.003***
	No	91	50	100	41	82	-[c]	
External ventricular drainage	Yes	9	0	0	9	18	-[c]	**0.003***
	No	91	50	100	41	82		
Perioperative ES transfusion	Yes	34	15	30	19	38	0.401[b]	0.527
	No	66	35	70	31	62		
Perioperative FFP transfusion	Yes	25	11	22	14	28	0.213[b]	0.488
	No	75	39	78	36	72		
Postoperative intubation	Yes	36	13	26	23	46	4.516[b]	0.061
	No	64	37	74	27	54		
Perioperative bleeding (ml)	Mean (SD)	356.30 (253.82)	353.60 (276.04)		359.0 (232.27)		-0.693[d]	0.488

*: $p<0.05$; χ^2=: Chi-Square Tests. [a]: Pearson Chi-Square; [b]: Continuity correction; c: Fisher's Exact test; [d](Z): Mann-Whitney U Test. ES: Erythrocyte suspension; FFP: Fresh frozen plasma; SD: Standard deviation.

was detected with increased WFNS grade and increased H&H Scale score ([WFNS→grade I, 11.3%, II/III, 23.8%, IV/V 50%; p=0.001] and [H&H→grade I, 5.6%, II/III, 17.7%, IV/V, 60%; p≤0.001]). The analyses also demonstrated that the peri- and post-operative complications significantly increased the mortality rate (6.3% vs. 40.4%; p<0.001) (Table 4). According to the logistic regression analysis, the factors that independently determined mortality were found to be the GCS category of stupor/pre-coma-coma (OR=4.49 [1.49–13.51], p=0.008) and the presence of complications (OR=7.52 [1.92–29.48]; p=0.004) (Table 5).

Discussion

With its increasing prevalence in 2020, the COVID-19 pandemic caused differences in the number of cerebral aneurysm and SAH cases as it did for many other diseases. Although therapy for severe COVID-19 infections often focuses on acute respiratory distress syndrome, vasculopathy, and coagulopathy, cerebral damage may occur. Evidence-based therapies that reduce COVID-19 mortality may increase the likelihood of acquiring an intracranial hemorrhage[8-15]. Despite the increase in this frequency, there are delays in the admission process of patients, and patients go to the hospital with worse neurological conditions.

Although the comparison of age, sex, presence of chronic diseases, aneurysm localization, and the number of aneurysms between the pre-pandemic group and the pandemic group did not show a significant difference (p>0.05) in our study, significantly low levels of pre-operative GCS and high post-operative morbidity levels were observed in both patient groups. During the pandemic, peri-operative vasospasm, and complications along with post-operative radiologic and symptomatic vasospasm, significantly increased in comparison to the pre-pandemic period. In addition to these findings, the frequency of hydrocephalus increased during the pandemic.

Symptoms such as headache and nausea, which are also reported in COVID-19 pneumonia, can cause delays in the diagnosis of SAH. Decreased admission rates due to increased infection risk are also another factor that

Table 4. Mortality rates by patient characteristics

	Category	All (n)	Mortality		χ^2	p
			n	%		
Patient group	Pre-pandemic	50	10	20	0.493[b]	0.482
	Post-pandemic	50	14	28		
Age	≤40	13	1	7.7	2.997[a]	0.392
	41-50	37	8	21.6		
	51-60	30	9	30		
	≥61	20	6	30		
Sex	Female	51	14	27.5	0.348[b]	0.555
	Male	49	10	20.4		
Presence of chronic disease	Yes	58	16	27.6	0.562[b]	0.454
	No	42	8	19		
Localization	ACom	39	11	28.2	0.620[a]	0.733
	MCA	28	6	21.4		
	Other	33	7	21.2		
Presence of multiple aneurysm	Single	23	6	26.1	0.000[b]	1.000
	Multiple	77	18	23.4		
GCS	Confused/Oriented	72	10	13.9	**12.501[b]**	**<0.001***
	Stupor/Pericoma-coma	28	14	50		
WFNS	I	53	6	11.3	**14.308[a]**	**0.001***
	II/III	21	5	23.8		
	IV/V	26	13	50		
Fisher Grade	I/II	33	6	18.2	0.500[b]	0.480
	III/IV	67	18	26.9		
Hunt-Hess Scale	I	18	1	5.6	**18.899[a]**	**<0.001***
	II/III	62	11	17.7		
	IV/V	20	12	60		
Complication	Evet	52	21	40.4	-[c]	**<0.001***
	Hayır	48	3	6.3		
Hydrocephalus	Evet	17	6	35.3	0.783[b]	0.376
	Hayır	83	18	21.7		
Peroperative Vasospasm	Evet	13	4	30.8	-[c]	0.506
	Hayır	87	20	23		
Re-operation	Evet	21	8	38.1	2.000[b]	0.157
	Hayır	79	16	20.3		

*: p<0.05; χ^2: Chi-Square Tests. [a]: Pearson Chi-Square; [b]: Continuity correction; [c]: Fisher's Exact test. GCS: Glasgow coma scale; WFNS: World Federation of Neurosurgery.

Table 5. Independent factors associated with mortality

	Category	β	SE	OR (95% CI)	p
Age	All	0.043	0.023	1.044 (0.997-1.093)	0.067
GCS	Confused/Oriented			1^R	
	Stupor/Pericoma-coma	1.501	0.562	4.485 (1.489-13.505)	**0.008***
Complication	No			1^R	
	Yes	2.017	0.697	7.519 (1.918-29.483)	**0.004***

*: p<0.05. Multivariate Logistic Regression Analysis (Method=Enter), 1^R: Reference value. The dependent variable=Mortality. SE: Standard error; OR: Odds ratio; CI: Confidence interval; GCS: Glasgow coma scale.

delays SAH diagnosis. Consequently, some studies have reported a decrease in the number of patients admitted to hospitals with headaches and SAH[2,5-7,10,11,16]. Possible explanations for this epidemiological situation include:

1. A decrease in the number of people seeking medical help because they are afraid of becoming infected with COVID-19.
2. Excessive pressure on the healthcare system, which may lead to misdiagnosis, particularly in patients who present with headache, which can be one of the first symptoms of COVID-19 infection, along with altered mental status.
3. Some of the quarantined people died for reasons that are yet unclear.

In patients undergoing surgery for an aneurysmal SAH, the main reason for altered consciousness is vasospasm, which can be followed by CT angiography and digital subtraction angiography; moreover, SAH can be symptomatic or present without any clinical outcomes[17,18]. Some studies have investigated diseases that cause non-aneurysmal cerebral vasospasm and their relationship with COVID-19 infection[19,20]. Thrombocyte dysfunction in COVID-19 patients has been described in the literature[21]. Furthermore, an increase in cerebral venous thrombosis in relation to COVID-19 cases has been reported[19]. Arterial vasospasm without obstruction in systemic and cerebral arteries caused by COVID-19 has also been reported[14,19].

Inflammation resulting from infections that cause vasospasm has also been reported in the literature[22]. Increased C-reactive protein and acute phase reactant levels in the setting of infection and inflammation are associated with angiographic or clinical vasospasm[23]. The clinical course of patients is affected by a wide range of comorbidities and inflammation[22]. Our study found that the two main reasons for the more frequent occurrence of vasospasm during the COVID-19 pandemic period were delayed admission to the hospital and, consequently, delayed initiation of treatment. The effects of the drugs used to treat COVID-19 may also trigger the development of ischemic events.

Our study has some limitations, including its retrospective nature, the limited number of cases, and the lack of detailed information on thrombocyte functions. Prospective studies with larger cohorts and more information on thrombocyte functions should be conducted. We believe that it is necessary to reevaluate the timing of hemorrhage in light of the onset of symptoms, delay surgery in patients with high WFNS grades, and, if present, treat the COVID-19 infection first. Then, it is beneficial to surgically address the aneurysm.

Conclusion

Symptoms such as headache and nausea, which are also reported in COVID-19 pneumonia, can cause delays in the diagnosis of SAH. This delay significantly affects the development of vasospasm in patients with SAH. In SAH patients, the onset of symptoms instead of the date of hospital admission should be considered when determining the disease course, and the possibility of earlier vasospasm should always be kept in mind due to delays in diagnosing and treating the condition.

Peer-review: Externally peer-reviewed.

Use of AI for Writing Assistance: Not declared.

Authorship Contributions: Concept: C.K.Y.; Design: M.U.E.; Supervision: M.E.; Fundings: A.G.; Materials: F.A.; Data Collection or Processing: E.V.; Analysis or Interpretation: S.O.A.; Literature Search: Y.E.Ç.; Writing: E.V.; Critical Review: M.R.Ö.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Diringer MN, Zazulia AR. Aneurysmal subarachnoid hemorrhage: Strategies for preventing vasospasm in the intensive care unit. Semin Respir Crit Care Med 2017;38:760–7. [CrossRef]
2. Nguyen TN, Haussen DC, Qureshi MM, Yamagami H, Fujinaka T, Mansour OY, et al. Decline in subarachnoid haemorrhage volumes associated with the first wave of the COVID-19 pandemic. Stroke Vasc Neurol 2021;6:542–52. [CrossRef]
3. Petridis AK, Kamp MA, Cornelius JF, Beez T, Beseoglu K, Turowski B, et al. Aneurysmal subarachnoid hemorrhage. Dtsch Arztebl Int 2017;114:226–36. [CrossRef]
4. Akbik F, Yang C, Howard BM, Grossberg JA, Danyluk L, Martin KS, et al. Delayed presentations and worse outcomes after aneurysmal subarachnoid hemorrhage in the early COVID-19 era. Neurosurgery 2022;91:66–71. [CrossRef]
5. Antony J, James WT, Neriamparambil AJ, Barot DD, Withers T. An Australian response to the COVID-19 pandemic and its ımplications on the practice of neurosurgery. World Neurosurg 2020;139:e864–e71. [CrossRef]
6. Bernat AL, Gaberel T, Giammattei L, Rault F, Gakuba C, Magro E, et al. Intracranial hemorrhage related to brain vascular disease and COVID-19 containment: Where are the patients? Neurochirurgie 2020;66:400–1. [CrossRef]
7. De Bonis P, Cavallo MA, Sturiale CL, Martellucci C, Flacco ME, Dughiero M, et al. Incidence of hemorrhagic cerebrovascular

disease due to vascular malformations during the COVID-19 national quarantine in Italy. Clin Neurol Neurosurg 2021;202:106503. [CrossRef]
8. Daly SR, Nguyen AV, Zhang Y, Feng D, Huang JH. The relationship between COVID-19 infection and intracranial hemorrhage: A systematic review. Brain Hemorrhages 2021;2:141–50. [CrossRef]
9. Nawabi J, Morotti A, Wildgruber M, Boulouis G, Kraehling H, Schlunk F, et al. Clinical and imaging characteristics in patients with SARS-CoV-2 infection and acute intracranial hemorrhage. J Clin Med 2020;9:2543. [CrossRef]
10. Theofanopoulos A, Fermeli D, Boulieris S, Kalantzis G, Kefalopoulou Z, Panagiotopoulos V, et al. Effects of COVID-19 on the admissions of aneurysmal subarachnoid hemorrhage: the West Greece experience. Neurol Sci 2021;42:2167–72. [CrossRef]
11. You Y, Niu Y, Sun F, Zhang J, Huang S, Ding P, et al. Impact of COVID-19 pandemic on haemorrhagic stroke admissions: A systematic review and meta-analysis. BMJ Open 2021;11:e050559. [CrossRef]
12. Abbas R, El Naamani K, Sweid A, Schaefer JW, Bekelis K, Sourour N, et al. Intracranial hemorrhage in patients with coronavirus disease 2019 (COVID-19): A case series. World Neurosurg 2021;154:e473–e80. [CrossRef]
13. Kafadar S, Yucetas SC, Gezgin I, Kaya H, Gulacti U, Bilek O. Influence of COVID-19 disease on subarachnoid hemorrhage and intracerebral hemorrhage. Bratisl Lek Listy 2022;123:140–3.
14. Sümerkan MÇ, Er Kara A, Doğan GM, Alyan Ö. Spontaneous, severe, and diffuse coronary vasospasm in a patient with COVID-19. Anatol J Cardiol 2021;25:E36–E7. [CrossRef]
15. Santana MF, Frank CHM, Almeida TVR, Jeronimo CMP, de Araújo Pinto RA, Martins YF, et al. Hemorrhagic and thrombotic manifestations in the central nervous system in COVID-19: A large observational study in the Brazilian Amazon with a complete autopsy series. PLoS One 2021;16:e0255950. [CrossRef]
16. Aboukaïs R, Devalckeneer A, Boussemart P, Vromant A, Bricout N, Verdin MF, et al. Impact of COVID-19 pandemic on patients with intracranial aneurysm rupture. Clin Neurol Neurosurg 2021;201:106425. [CrossRef]
17. Craen A, Logan G, Ganti L. Novel coronavirus disease 2019 and subarachnoid hemorrhage: A case report. Cureus 2020;12:e7846. [CrossRef]
18. van der Steen WE, Leemans EL, van den Berg R, Roos YBWEM, Marquering HA, Verbaan D, et al. Radiological scales predicting delayed cerebral ischemia in subarachnoid hemorrhage: Systematic review and meta-analysis. Neuroradiology 2019;61:247–56. [CrossRef]
19. Arandela K, Samudrala S, Abdalkader M, Anand P, Daneshmand A, Dasenbrock H, et al. Reversible cerebral vasoconstriction syndrome in patients with coronavirus disease: A multicenter case series. J Stroke Cerebrovasc Dis 2021;30:106118. [CrossRef]
20. Dakay K, Kaur G, Gulko E, Santarelli J, Bowers C, Mayer SA, et al. Reversible cerebral vasoconstriction syndrome and dissection in the setting of COVID-19 infection. J Stroke Cerebrovasc Dis 2020;29:105011. [CrossRef]
21. Sharifian-Dorche M, Bahmanyar M, Sharifian-Dorche A, Mohammadi P, Nomovi M, Mowla A. Vaccine-induced immune thrombotic thrombocytopenia and cerebral venous sinus thrombosis post COVID-19 vaccination; A systematic review. J Neurol Sci 2021;428:117607. [CrossRef]
22. Ahn SH, Savarraj JPJ, Parsha K, Hergenroeder GW, Chang TR, Kim DH, et al. Inflammation in delayed ischemia and functional outcomes after subarachnoid hemorrhage. J Neuroinflammation 2019;16:213. [CrossRef]
23. Rasmussen R, Bache S, Stavngaard T, Møller K. Plasma levels of IL-6, IL-8, IL-10, ICAM-1, VCAM-1, IFNγ, and TNFα are not associated with delayed cerebral ıschemia, cerebral vasospasm, or clinical outcome in patients with subarachnoid hemorrhage. World Neurosurg 2019;128:e1131–e6. [CrossRef]