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Impact of COVID-19 pandemic on patients with intracranial aneurysm rupture

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ABSTRACT

Background/objectives: The present study aimed at evaluating the impact on the early outcome of patients with ruptured intracranial aneurysms.
Methods: Our study prospectively included 26 consecutive patients with ruptured intracranial aneurysm managed at our institution in context of COVID-19 pandemic between March 1st, 2020 and April, 26th, 2020 (2020 group). A group control included other 28 consecutive patients managed at the same institution for the same disease in 2019, during the same time frame (2019 group). On admission, poor neurological status was defined as WFNS score >3. Severe radiological status was defined by the presence of intracerebral hematoma, or/and acute hydrocephalus requiring further EVD or/and the presence of vasospasm on presentation. Statistical analysis was performed to compare the 2 distinct groups.
Results: Rates of poor neurological presentation and severe radiological presentation on hospital admission were higher in the 2020 group ($p = 0.01$ and $p = 0.02$, respectively). The delayed hospital admission was 2.7 days in 2020 group and 0.75 days in 2019 group ($p = 0.005$). Therefore, vasospasm's rate on presentation was also higher in the 2020 group ($p = 0.04$).
Conclusion: To our knowledge, this is one of the first studies demonstrating influence of the COVID-19 pandemic on patients with urgent and severe intracranial aneurysmal disease. In case of recurrent COVID-19 pandemic, educating the population concerning specific symptoms such as sudden headache, neurological deficit or even sudden chest pain should be emphasized.

1. Introduction

COVID-19 pandemic has a considerable impact on the life of the whole humanity and in several aspects. There is a social behavior impact with the lockdown at home in several countries [1], the social distancing and the containment measures. Moreover, the public health impact is alarming [2]. Emergency and intensive care units (ICU) are becoming saturated by the massive influx of COVID-19+ patients. Indeed, all health systems in the world are focusing on the COVID-19 pandemic [3]. However, other urgent and severe diseases should not be neglected, as they might endanger people's life. Indeed, cardiologists and neurologists are reporting a reduction in the number of patients admitted at hospital for myocardial infarction [4,5] or stroke [6]. In the department of neurosurgery, we noticed a higher rate of patients with ruptured aneurysm who had a deteriorated neurological presentation on admission. We suggest that this fact might be partly related to the patient's fear and further engendering a delayed hospital admission (DHA) in the context of the COVID-19 pandemic [7].

Our present study aimed to evaluate the impact of COVID-19 pandemic on the early outcome of patients with ruptured intracranial

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aneurysm in a single institution (CHU Roger Salengro, Lille, France).

2. Methods

2.1. Population data

Our institution drains an area of about 4 million inhabitants in the North of France. It is the unique hospital center managing an aneurysmal subarachnoid hemorrhage (aSAH) in this area. All patients with aSAH are first admitted to the Emergency unit of our institution before neurosurgical intensive care admission. They are immediately transferred from all the hospitals of our area (no delay is possible at this stage) or they are directly admitted to the Emergency unit of our institution when they live nearby. The annual incidence of patients with an aSAH managed at our institution is almost 130 per year [8].

Our study prospectively included a series of consecutive adult patients (age > 18 years) with ruptured aneurysm managed at our institution over 8 weeks period, between March 1st, 2020 and April, 26th, 2020 (2020 group, n = 26, female to male ratio 18:8). During this period, the social distancing, the containment measures and the lockdown were largely respected in our country because of COVID-19 pandemic. Using our own hospital database, we included a control group of consecutive adult patients with a ruptured aneurysm managed at our institution over the same period the year before (when there was no pandemic), between March 1st, 2019 and April 26th, 2019 (2019 group, n = 28, 19 Females/9 Males).

Treatment (endovascular or microsurgical) was decided in a multidisciplinary discussion between neurosurgeons, neuroradiologists and intensive care colleagues. No COVID tests were systematically performed in 2020 group at this period.

2.2. Pre-therapeutic clinical evaluation

Age, date of the first symptom, date of hospital admission, World Federation of Neurosurgical Societies (WFNS) score [9], Glasgow coma scale (GSC) score [10] and presence of mydriasis were recorded for each patient on hospital admission. Poor neurological presentation was defined by a WFNS score >3. The delayed hospital admission (DHA) was defined as the exact delay (in days) between the first symptom and the admission to the emergency unit of our institution. The date of the first symptom was obtained after questioning the patient and/or her/his family.

2.3. Pre-therapeutic radiological evaluation

Standard Fisher score [11], presence of intracerebral hematoma (ICH) and presence of acute hydrocephalus requiring external ventricular draining (EVD) were noted. All patients with acute hydrocephalus received EVD.

Presence of a significant vasospasm on CT angiography and digital subtraction angiography (DSA) was recorded upon admission. Ischemic lesions potentially related to vasospasm were noted on contrast enhanced CT scan.

Severe radiological status was defined by the presence of ICH, or/and acute hydrocephalus requiring EVD or/and presence of vasospasm on admission.

Aneurysm characteristics were recorded for each case.

2.4. Post-treatment evaluation

Early (<7days) outcome and treatment complications were noted.

2.5. Statistical analysis

All variables on admission were compared between the 2 groups using ANOVA test (Age), Mann Whitney Wilcoxon test (DHA, GSC score), and Fisher's exact test (neurological and radiological presentation, EVD and vasospasm). A P value < 0.05 was considered as a significant result.

3. Results

3.1. Population data

The population data and the clinical and radiological presentation are presented in Tables 1 and 2. The mean age at diagnosis was 56.7 years (Ranging from 31 to 93) in 2020 group and 55.8 years (Ranging from 35 to 90) in 2019 group. The mean delay between the first symptom and the admission to an emergency unit was respectively 2.7 days (Ranging from 0 to 14) in 2020 group and 0.75 days (Ranging from 0 to14) in 2019 group.

3.2. Clinical presentation

Poor neurological presentation was more common in 2020 cohort (Table 2). Presence of mydriasis was recorded in 4 patients of 2020 group and in 1 patient of 2019 group. Seizure was noted in 6 patients of 2020 group and in 8 patients of 2019 group. No patient in 2020 group had COVID. The number of patients presented directly to our emergency room institution was 9 in 2020 and 11 in 2019. No delay in transfers from other hospitals was noted.

3.3. Radiological presentation

Severe radiological presentation, acute hydrocephalus requiring EVD and vasospasm on admission were more common in the 2020 group (Table 2). Obstructive hydrocephalus was noted in 10 patients of 2020 group and in 4 patients of 2019 group. Ischemic lesions were noted in 3 of the 6 patients with vasospasm on admission of 2020 group and no ischemic lesions on admission were noted in 2019 group. ICH was noted in 11 patients of 2020 group and in 9 patients of 2019 group.

In the 2020 group, the aneurysm location was on middle cerebral artery (MCA) in 6 patients, on anterior communicating artery (AcoA) in 10 patients, on pericallosal artery in 1 patient, on posterior communicating artery (PcomA) in 5 patients, on posterior and inferior cerebellar artery (PICA) in 3 patients, on posterior cerebral artery (PCA) in 1 patient (Table 3). The mean maximal diameter of aneurysm was 7.3 mm (Ranging from 3 to 19).

In the 2019 group, the aneurysm location was on MCA in 12 patients, on AcoA in 7 patients, on pericallosal artery in 2 patients, on PcomA in 4 patients, on PICA in 2 patients, on PCA in 1 patient. The mean maximal diameter of aneurysm was 6.7 mm (Ranging from 3 to 14).

3.4. Treatment

In the 2020 group, endovascular procedure was performed in 14 patients and microsurgical treatment in 10 patients. No aneurysm treatment was proposed in 2 patients with severe cardiovascular comorbidities. One patient was considered too old (93 years) by the multidisciplinary team and the second one had a poor neurological

Table 1
Neurological status on admission of patients.

WFNS score	2020 group (n = 26)	2019 group (n = 28)	P value
1	6 (23 %)	11 (39 %)	0.25
2	4 (15 %)	9 (32 %)	0.2
3	1 (4%)	2 (7%)	1
4	5 (19 %)	5 (18 %)	1
5	10 (39 %)	1 (4%)	0.001**

WFNS: World Federation of Neurosurgical Societies.
** Very significant.

Table 2
Statistical analysis comparing 2020 group and 2019 group using appropriate test.

	2020 group (n = 26)	2019 group (n = 28)	P value
Age (years)	56.7	55.8	0.827
DHA (days)	2.7	0.75	0.005*
Poor neurological presentation	15	6	0.006*
GSC score <13	15	6	0.002*
Severe radiological presentation	21	14	0.03*
ICH	11	9	0.05
EVD	14	6	0.02*
Vasospasm on admission	6	1	0.04*
Fisher score >2	24	21	0.18

ICH: Intracerebral hematoma.
EVD: External ventricular drain for acute hydrocephalus.
* Significant with a confidence interval of 95 %.

Table 3
Aneurysm location.

Aneurysm location	2020 group (n = 26)	2019 group (n = 28)
Middle cerebral artery	6	12
Anterior communicating artery	10	7
Pericallosal artery	1	2
Posterior communicating artery	5	4
Posterior and inferior cerebellar artery	3	2
Posterior cerebral artery	1	1
Microsurgery/Endovascular ratio	10/14	8/20
	Absence of therapeutic procedure in 2 patients	

presentation (ICH) with vasospastic cerebral infarction and Takotsubo syndrome on admission. This patient had a sudden headache 14 days before hospital admission. She died 5 days after the hospital admission and CT scan demonstrated a large cerebral infarction of the ICA territory.

In 2019 group, endovascular procedure was performed in 20 patients and microsurgical treatment in 8 patients.

3.5. Treatment complications

In the 2020 group, ischemic lesions were noted in 3 patients after endovascular treatment. Among these 3 patients, 2 had post-procedural neurological deficit. In 1 of these 2 patients, the WFNS score was 4 on admission, intraprocedural aneurysmal rupture occurred and a large cerebral infarction of the MCA territory was noted on postoperative CT scan. The patient died 4 days after treatment. Ischemic lesions were noted in 2 patients after microsurgical procedure. In 1 of these 2 patients, the WFNS score was 5 on admission, intraoperative aneurysmal rupture occurred and a temporary interruption of the flow was necessary during procedure. A large hemispheric cerebral infarction was noted on postoperative CT scan. Decompressive hemicraniectomy was performed.

In 2019 group, ischemic lesions were noted in 4 patients after endovascular procedure. Among these 4 patients, 3 had postprocedural neurological deficit. Ischemic lesions were noted in 2 patients after microsurgical procedure. In 1 of these 2 patients, the WFNS score was 5 on admission, intraoperative aneurysmal rupture occurred and a temporary interruption of the flow was necessary during the procedure. Decompressive hemicraniectomy was performed.

3.6. Early complications after treatment

In the 2020 group, of the 26 patients, death was noted in 2 patients and 15 patients were still in neurosurgical ICU at the end of the study. A symptomatic vasospasm requiring active treatment was noted in 6 patients in post-treatment course.

In the 2019 group, malignant swelling brain with death was noted in 2 patients within the first week after treatment and 1 patient died from prolonged decubitus complications 2 months after treatment. A symptomatic vasospasm requiring active treatment was noted in 5 patients in post-treatment course.

3.7. Statistical analysis

All statistical results were summarized in Table 2.

In sum, rates of poor neurological presentation and severe radiological presentation on hospital admission were higher in the 2020 group ($p = 0.01$ and $p = 0.02$, respectively). Moreover, the delayed hospital admission was 2.7 days in 2020 group and 0.75 days in the 2019 group ($p = 0.005$). Therefore, vasospasm's rate on presentation was also higher in the 2020 group ($p = 0.04$).

4. Discussion

The patients may prefer to remain housebound instead of going to the emergency unit of the hospital center in order to avoid COVID-19 contamination. In this pandemic context, patients might have given less attention to headache as it may be a part of COVID-19 symptoms. Of course, patients were immediately admitted to hospital when their symptoms were severe. However, the treatment and the prognosis of their aneurysm rupture might have been worsened by this delay in medical management. In particular, there was a delayed hospital admission, with higher rates of poor neurological and severe radiological presentation, as well as higher vasospasm rate, as compared to a group control during the same period of time, the year before.

4.1. Higher rate of severe clinical presentation

In our institution, we noticed that the incidence of severe aSAH increased in the period of COVID-19 pandemic. Indeed, a poor neurological presentation was recorded in 58 % of patients on admission. At the same period in 2019, this rate was much lower (21 % patients on admission). Moreover, a study was performed on patients with aSAH managed between January and December 2009 in our institution. Of the 121 included patients in this period, only 24 % had a poor neurological presentation on admission [8]. In his study on 195 consecutive patients with aSAH, Natarajan [12] reported that 38 % had a high WFNS score (>3) on admission. These differences in results between the 2020 group and the others could be explained by different hypotheses. In 2020, the patients might have feared immediate hospital admission because of the potential contact with COVID-19+ patients. This might partly explain the low rate of patients with a good neurological status in the pandemic period. Indeed, the patients with only a headache and without a severe neurological disorder might prefer to stay at home in lockdown situation to prevent any COVID-19 contamination. In the same way, the difficulties of contacting the emergency services due to a saturation of the phone networks related to COVID-19 pandemic would discourage these same patients with a good neurological status to seek healthcare [13]. Perhaps, some patients followed the recommendations of the media that was to stay at home in the absence of severe respiratory signs related to COVID-19 infection. Moreover, some of the patients might have considered that their headache was probably explained by a mild form of COVID-19 disease and not related to a brain vascular disease. Persistent headache or the occurrence of neurological deficit (WFNS score = 3) was the reason that the 2020 cohort eventually seeked medical attention. In his series of 509 patients with aSAH, Goertz [14]

reported a higher rate of poor neurological presentation in patients with DHA. An alert from the health authorities [15] should be perhaps considered in order to make the population aware of the potential gravity of sudden and violent headache or mild neurological deficit. The reluctance to refer a patient to the Emergency unit of our institution from other hospitals with headache but good clinical condition could also explain the higher frequency of severe cases in 2020. However, it seems that it was not the case in 2019 cohort. The rate of admission seems to be similar in 2019 and 2020, it is, however, unknown if there were other cases dying from aSAH before reaching the hospital and that these numbers may be different in 2020 and 2019. Nevertheless, other authors [16] reported a dramatic decrease of patients with acute SAH admitted in leading neurosurgical departments in Paris during the pandemic. They proposed some explanations to "such "strange" epidemiological situation: 1) decrease of people seeking for medical help fearing to get infected; 2) excessive pressure on healthcare system that may lead to misdiagnosis especially for patients presenting headache which can be, along altered mental status, also one of initial symptoms of COVID-19 infection; 3) some still unknown deaths of quarantined people.

4.2. Higher rate of severe radiological presentation

The neurological presentation of patients with an aSAH with ICH is usually more severe than patients without ICH [17]. In 2020 group, the high rate of patients (42 %) with ICH can partly explain the higher rate of the poor neurological presentation and the significant change in endovascular/surgical treatment ratio between 2019 and 2020. Indeed, surgical intracerebral hematoma evacuation with aneurysm clipping was more frequent in 2020. In Wan [18] series of 5362 consecutive patients with aSAH, only 21 % had an aSAH with ICH. In his series, the patients with ICH experienced poorer neurological presentation and poorer outcome than those without ICH. The higher rate of severe radiological presentation with poor neurological presentation might be related to an aneurysmal rebleeding before hospital admission in some patients of 2020 group. Indeed, the significant DHA may support this hypothesis in this group. In his series of 326 patients with aSAH, Guo [19] reported a rebleeding in 21.5 % of patients admitted at hospital until 72 h after the first symptom. Moreover, uncontrolled hypertension and aspirin self-medication for a persistent headache after the aSAH might have been contributing factors of massive aSAH or potential rebleeding in 2020 group [20,21,19,10,22]. Moreover, all patients with vasospasm at admission from 2020 were WFNS 4 or 5 - which is a strong indicator of rehemorrhage, probably as one of the cause of poor clinical state. ICH, acute hydrocephalus and vasospasm on admission are predictive factors of poor prognosis in patients with aSAH according to many authors [11,18,23–27]. Some authors [28] reported that higher World Federation of Neurological Surgeons (WFNS) grade ($P < 0.001$), surgical aneurysm treatment ($P = 0.002$), and angiographic vasospasm ($P = 0.005$) are independent predictors of shunt-dependent hydrocephalus with poorer long term outcomes in multivariable analysis.

4.3. Delayed hospital admission

It has been previously acknowledged that the delay in medical treatment most usually worsens the prognosis of diseases [29,30], especially when such diseases are severe and urgent and require immediate treatment. Several specialties modified their daily organization to provide immediate medical care and intensive care unit (ICU) to COVID-19+ patients [31–33]. In our department of neurosurgery, as in other similar national and international centers and following strict recommendations, we suspended all the non-urgent surgical procedures in order to provide help from our anesthesia and neurosurgical intensive care teams to emergency physicians and medical intensivists in the management of patients COVID-19 + . This organization could also potentially provide additional ventilators from non-used operating rooms. However, during this challenging period, we have maintained the management of all urgent and severe cerebral and spinal neurosurgical diseases, which accounted for almost half of our neurosurgical activity. Concerning aSAH, the delay between aneurysmal rupture and neurosurgical management of patients should be as short as possible because of the risk of rebleeding especially within the first hours [19, 27]. In the same way, the treatment of cerebral vasospasm related to the aSAH must be introduced as soon as possible to prevent the occurrence of ischemic lesions [34]. Acute hydrocephalus must also be quickly managed to improve the outcome of patients [35]. Indeed, in our study, in 2019 group, the rate of EVD was close to other studies but in 2020 group, it was significantly higher [36]. Therefore, the DHA might also explain the severe neurological presentation of the patients [14]. Indeed, the mean delay between the first symptom and the admission into emergency unit was 2.7 days in 2020 group and the rate of patients with vasospasm on admission appears also higher. Delayed cerebral ischemia was noted in 3 of the 6 patients with vasospasm on admission. In this group, the delay from the sudden headache to the admission was more than 3 days in 9 patients (vs 3 patients in 2019 group). Three of them had sudden headache associated to cough and hyperthermia respectively 4, 7 and 10 days before their hospital admission but their COVID-19 test was negative. In his series of patients with aSAH [14], Goertz reported a higher vasospastic infarction rate in DHA group (41.5 %) than in early hospital admission group (22.6 %). In our opinion, the presence of vasospasm on admission is a good parameter to confirm the delay of SAH management in some cases because cerebral vasospasm after aSAH usually occurs between 4 and 10 days after aneurysm rupture [37]. The delay in disease management is also an important prognostic factor in other diseases like ischemic stroke [38,39] or myocardial infarction [6]. Some authors [16] reported a marked reduction in the number of patients presenting with transient ischemic attack and stroke in the Emergency departments of their institution during COVID-19 pandemic and it may have affected stroke outcome. "Time is brain" and "Time is heart" are also true during COVID-19 pandemic.

5. Conclusion

To the best of our knowledge, this is one of the first studies demonstrating the impact of the COVID-19 pandemic on the prognosis of urgent and severe intracranial aneurysmal disease. In case of recurrent COVID-19 pandemic, educating the population concerning specific symptoms such as sudden headache, neurological deficit or even sudden chest pain should be emphasized. However, it may be difficult for public health authorities and hospital organization to create a massive access to ICU for COVID-19+ patients whilst maintaining normal access to other emergency networks.

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name of institute/committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. "For this type of study formal consent is not required."

Informed consent

Informed consent was obtained from all individual participants included in the study.

"This article does not contain any studies with human participants performed by any of the authors."

CRediT authorship contribution statement

Rabih Aboukaïs: Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft, Writing - review & editing. **Antoine Devalckeneer:** Data curation, Methodology, Validation. **Pierre Boussemart:** Data curation, Methodology, Validation. **Amélie Vromant:** Methodology, Software, Validation. **Nicolas Bricout:** Data curation, Methodology, Validation. **Marie-Francoise Verdin:** Data curation, Methodology, Validation. **Philippe Bourgeois:** Data curation, Methodology, Validation, Supervision. **Cédric Cirenei:** Data curation, Methodology, Validation. **Patrick Goldstein:** Data curation, Methodology, Validation, Supervision. **Benoit Tavernier:** Data curation, Methodology, Validation, Supervision. **Xavier Leclerc:** Data curation, Methodology, Validation, Supervision. **Jean-Paul Lejeune:** Conceptualization, Data curation, Methodology, Validation, Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors report no declarations of interest.

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