

Impact of the COVID-19 outbreak on acute stroke pathways – insights from the Alsace region in France

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Background and purpose: To date, no study has attempted to quantify the impact of the COVID-19 outbreak on the incidence and treatment of acute stroke.

Methods: This was a retrospective review of acute stroke pathway parameters in all three stroke units in the Alsace region during the first month of the outbreak (1–31 March 2020), using the similar period from 2019 as a comparator. A secondary detailed analysis of all stroke alerts and stroke unit admissions was performed in the centre with the largest case volume.

Results: Compared to the same period in 2019, in March 2020 there were 39.6% fewer stroke alerts and 33.3% fewer acute revascularization treatments [40.9% less intravenous thrombolysis (IVT) and 27.6% less mechanical thrombectomy (MT)]. No marked variation was observed in the number of stroke unit admissions (−0.6%). The proportion of patients with acute revascularization treatments (IVT or MT) out of the total number of stroke unit admissions was significantly lower in March 2020 (21.3%) compared to 2019 (31.8%), $P = 0.034$. There were no significant differences in time delays or severity of clinical symptoms for patients treated by IVT or MT, nor in the distribution of final diagnosis amongst stroke alerts and stroke unit admissions.

Conclusion: These results suggest that the overall incidence of stroke remained the same, but fewer patients presented within the therapeutic time window. Increased public awareness and corrective measures are needed to mitigate the deleterious effects of the COVID-19 outbreak on acute stroke care.

Introduction

The COVID-19 pandemic is an ongoing pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2). The outbreak was identified in China in December 2019 and then spread to Europe in January 2020. The first three cases in Europe were reported in France on 24 January [1]. Epidemic

response measures were triggered in France on 1 March and gradually developed until 17 March when nationwide lockdown was enforced, with strict home confinement of the entire population.

Alsace was the first French region affected by the outbreak. It is a region in the east of France with a population of approximately 1.9 million people. On 31 March there were 2004 hospitalized patients diagnosed with COVID-19 (of which 410 were in intensive care units) and 591 reported deaths [2].

Since the onset of the pandemic, several groups reported marked and unexplained decreases in the

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volume of patients with acute cardiovascular pathologies apparently unrelated to COVID-19 infection, such as myocardial infarction [3,4] and acute ischaemic stroke [5,6]. However, up to now, no study has attempted to quantify the impact of the COVID-19 outbreak on incidence and treatment rates of acute stroke.

The aim was to perform a detailed analysis of variations in the acute stroke pathway activity for the Alsace region, during the first month of the outbreak, using the same time period from 2019 as a comparator.

Materials and methods

A retrospective review was performed of acute stroke pathway parameters in all three stroke units in the Alsace region, for 1–31 March 2020 and 1–31 March 2019. For each centre the number of patients processed as stroke alerts, the number of admissions in the stroke units, the number of acute revascularization treatments [intravenous thrombolysis (IVT) and mechanical thrombectomy (MT)] as well as time delays for treated patients were collected. In addition, a more detailed analysis within the centre with the largest case volume (Strasbourg) was performed, collecting characteristics and final diagnosis for all patients processed as stroke alerts and characteristics and final diagnosis of all patients admitted on the stroke unit.

Brief description of the stroke pathway in the Alsace region

There are three hospitals with stroke units in the region, of which two have endovascular treatment (EVT) facilities. The north of the region (population approximately 1.1 million) is covered by Strasbourg (EVT), whilst Colmar (EVT) and Mulhouse are situated in the south (population approximately 800 000 people). Patients are accepted as stroke alerts following a telephone consultation between the paramedic/physician in the field and the on-call neurologist, if there are symptoms suggestive of stroke dating <6 h from last seen well (up to 24 h in selected cases). Stroke alerts bypass the emergency department and are seen directly by the on-call neurologist in the Radiology Department, before imaging. All three centres use magnetic resonance imaging (MRI) for patient selection.

Statistical analysis

Continuous variables are presented as median with interquartile range and were compared using the Mann–

Whitney *U* test. The normality of the distributions was assessed graphically and using the Shapiro–Wilk test. Categorical variables are presented as numbers with percentages and were compared using Pearson's χ^2 test or the Fisher exact test depending on theoretical numbers. A *P* value < 0.05 was considered statistically significant. Analyses were performed using GraphPad Prism, Version 6.0 (GraphPad Software, San Diego, CA, USA).

The study was approved by the institutional ethical review board of Strasbourg University Hospitals (reference CE-2020-70, 29 April 2020). Due to the retrospective nature of the study, the board waived the need for signed informed consent.

Results

Compared to the same period in 2019, in March 2020 there were 39.6% fewer stroke alerts (174 vs. 288 in 2019) and 33.3% fewer acute revascularization treatments (34 vs. 51 in 2019; 40.9% fewer IVT and 27.6% fewer MT). No marked variation was observed in the number of stroke unit admissions (159 vs. 160 in 2019 – 0.6%). Table 1 outlines the detailed evolution of activity in each centre.

The proportion of patients with acute revascularization treatments (IVT or MT) out of the total number of stroke unit admissions was significantly lower in March 2020 – 34/159 (21.3%) compared to 51/160 (31.8%) in March 2019, *P* = 0.034. Amongst patients who benefited from IVT or MT, there were no significant differences in pre-hospital, intra-hospital time delays or severity of clinical symptoms (Table 2).

Age and distribution of final diagnosis (cerebrovascular disease or stroke mimic) amongst stroke alerts did not differ significantly between the two time periods (Table 3). The time interval from hospital admission to imaging was not significantly longer in 2020.

Similarly, there was no significant difference of final diagnosis for patients admitted on the stroke unit, nor of age and National Institutes of Health Stroke Scale scores amongst patients admitted for ischaemic strokes (Table 4).

Discussion

During the first month of the COVID-19 outbreak a marked reduction in stroke alerts, IVT and MT, was observed with a relatively stable number of stroke unit admissions. This result suggests that the overall incidence of stroke remained stable but fewer patients presented within the therapeutic time window.

Two centres from northern Italy reported similar findings. Baracchini *et al.* [5] observed a reduction of 26% in IVT and 30% in MT, as well as onset-to-door

Table 1 Evolution of stroke alerts, admissions and treatments

	March 2019	March 2020	Variation
Strasbourg			
Stroke alerts	167	122	-26.9%
Patients admitted to stroke unit	93	94	+1.1%
Acute revascularization treatments	31	22	-29.0%
IV thrombolysis	15	6	-60.0%
Mechanical thrombectomy (with or without prior IV thrombolysis)	16	16	0%
Colmar			
Stroke alerts	37	18	-51.4%
Patients admitted to stroke unit	30	39	+30%
Acute revascularization treatments	16	10	-37.5%
IV thrombolysis	3	5	+66.7%
Mechanical thrombectomy (with or without prior IV thrombolysis)	13	5	-61.5%
Mulhouse			
Stroke alerts	84	34	-59.5%
Patients admitted to stroke unit	37	26	-29.7%
Acute revascularization treatments	4	2	-50%
IV thrombolysis	4	2	-50%
Mechanical thrombectomy (with or without prior IV thrombolysis)	Not applicable	Not applicable	Not applicable
Total for Alsace region			
Stroke alerts	288	174	-39.6%
Patients admitted to stroke unit	160	159	-0.6%
Acute revascularization treatments	51	34	-33.3%
IV thrombolysis	22	13	-40.9%
Mechanical thrombectomy (with or without prior IV thrombolysis)	29	21	-27.6%

IV, intravenous.

and door-to-treatment times for major strokes. They also note a 50% reduction in minor strokes, transient ischaemic attacks and transfers from primary stroke units. The authors do not provide further details for these findings and the number of stroke unit admissions and study periods are not specified. In the editorial of Morelli *et al.* [6] the authors note a marked reduction in emergency admissions with symptoms of acute stroke – only six admissions between 21 February and 25 March 2020, compared to a monthly average of 51 cases in previous years.

Table 2 Evolution of time delays and severity of neurological deficits for acute revascularization treatments

	Treatments in the entire region		
	March 2019 (n = 51)	March 2020 (n = 34)	P value
Intravenous thrombolysis (n)	22	13	
Symptom onset to hospital arrival (min) (median, IQR)	132 (87–175)	110 (87.5–149.2)	0.531
Hospital arrival to needle (min) (median, IQR)	52 (40.5–68.5)	64 (53.5–81)	0.143
Symptom onset to needle (min) (median, IQR)	185 (160–236)	190 (172.5–222.7)	0.911
Initial NIHSS score (median, IQR)	5 (2–10)	4 (4–5)	0.417
Mechanical thrombectomy (n)	29	21	
Symptom onset to hospital arrival (min) (median, IQR)	144 (122.5–163.7)	111 (98–178.5)	0.220
Hospital arrival to groin puncture (min) (median, IQR)	97.5 (80.2–119.2)	106 (86.5–149.5)	0.308
Symptom onset to groin puncture (min) (median, IQR)	246 (212.5–270.2)	257 (199.5–326)	0.787
Initial NIHSS score (median, IQR)	13 (8–19)	15.5 (7–18)	0.886

IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale.

Table 3 Patient characteristics and final diagnosis for stroke alerts (stroke pathway based on MRI screening)

	Stroke alerts in Strasbourg		
	March 2019 (n = 167)	March 2020 (n = 122)	P value
Final diagnosis			
Cerebrovascular disease (n) (%)	93 (55.6%)	59 (48.3%)	0.217
Acute ischaemic stroke	60/93 (64.5%)	39 (66.1%)	0.485
TIA	25/93 (26.8%)	14 (23.7%)	
Haemorrhagic stroke	7 (7.5%)	5 (8.4%)	
Retinal artery occlusion	0 (0%)	1 (1.6%)	
Cervical artery dissection (without ischaemic stroke)	1 (1.0%)	0 (0%)	
Stroke mimics (n) (%)	74 (44.3%)	63 (51.6%)	0.217
Age (median, IQR)	64 (49–78)	65.5 (49.2–78)	0.938
Time from hospital admission to imaging (min) (median, IQR)	38 (23–72)	30 (21–61)	0.303

IQR, interquartile range; MRI, magnetic resonance imaging; TIA, transient ischaemic attack.

Table 4 Final diagnosis and patient characteristics amongst stroke unit admissions

	Stroke unit admissions in Strasbourg		<i>P</i> value
	March 2019 (<i>n</i> = 93)	March 2020 (<i>n</i> = 94)	
Diagnosis (<i>n</i>) (%)			
Cerebrovascular disease	83 (89.2%)	77 (81.9%)	0.153
Ischaemic stroke	66 (70.9%)	60 (63.8%)	0.327
Haemorrhagic stroke	5 (5.3%)	5 (5.3%)	
TIA	9 (9.6%)	7 (7.4%)	
Cerebral venous thrombosis	0 (0%)	3 (3.1%)	
Cervical artery dissection without stroke	2 (2.1%)	1 (1.0%)	
Retinal artery occlusion	0 (0%)	1 (1.0%)	
Reversible cerebral vasoconstriction syndrome	1 (1.0%)	0 (0%)	
Other diagnosis	10 (10.7%)	17 (18.0%)	0.153
NIHSS score (median, IQR) ^a	3 (1–8)	4 (1.5–10)	0.399
Age (median, IQR) ^a	68.5 (58.5–79.75)	69 (58.5–81)	0.821
Time from symptom onset to hospital admission (h) (median, IQR) ^b	2.9 (1.7–7.2)	3.1 (1.5–10.5)	0.847

IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischaemic attack. ^aFor ischaemic strokes only. ^bFor ischaemic strokes only, excluding in-hospital strokes.

Several factors could potentially explain this phenomenon. First, some patients with milder neurological symptoms might delay or avoid medical consultation due to fear of contamination. This could potentially account for a reduction in stroke alerts but less so in IVT or MT, as patients in this group generally do not have mild deficits. Secondly, care systems, and in particular pre-hospital and hospital emergency services, are undergoing significant pressures due to the volume of COVID-19 patients. Moreover, protocols are burdened by personal protection measures across all phases of patient care. This might induce supplemental delays or errors during patient triage and transport, thus reducing the proportion of patients eligible for acute treatments. In our region, stroke care and interventional treatments remained available around the clock; the effects of the outbreak could potentially become even more significant if stroke pathways are affected or even interrupted by illness amongst the medical personnel or redistribution to other departments. Albeit not statistically significant, in our study longer in-hospital delays were observed for patients who underwent IVT or MT. This is probably explained by additional anamnesis and clinical examination needed in patients with suspected COVID-19 infection, as well as by the

additional personal protection measures taken to avoid contamination of medical personnel.

Thirdly, epidemic response measures might also represent a contributing factor. Home confinement reduces social connections, especially in the elderly population. Isolation can lead to delayed notification of emergency services and can thus contribute towards a reduced proportion of patients who present within the therapeutic time window.

From a physiopathological standpoint, an increase in the incidence of ischaemic stroke should be being seen. Initial findings point towards a hypercoagulable state in COVID-19 patients. High levels of thrombosis and inflammation serum markers, such as D-dimers, fibrinogen and C-reactive protein, have been reported [7–9].

In a single-centre Chinese cohort [9] of 221 patients with COVID-19, 11 (5%) developed acute ischaemic stroke, one (0.5%) cerebral venous sinus thrombosis and one (0.5%) cerebral haemorrhage. In our centre [10] brain MRI was performed for 13 patients hospitalized in the intensive care unit with severe COVID-19 infection and acute respiratory distress syndrome. Three cases (23%) had evidence of acute or subacute ischaemic stroke. Of note, these patients did not have focal signs suggestive of stroke; they underwent MRI because of unexplained encephalopathic features. These findings suggest that ischaemic stroke might be frequent in patients with severe COVID-19 infection, but a significant proportion of cases are not detected because clinical symptoms are masked by the severity of respiratory features and sedation.

The strength of the present study lies in the fact that data were collected from all stroke units in the region and there were no organizational changes between the two time periods. Consecutively, the results should be representative for the total number of strokes for this geographical area.

There are, however, a number of limitations, however. The analysis was restricted to a period of 31 days at the beginning of the COVID-19 outbreak. As the epidemic continues, the care systems may adapt and tendencies might change. Furthermore, our results might not be representative for other countries or regions with different stroke care protocols and geographical specificities.

CONCLUSION

During the first month of the COVID-19 outbreak, a marked reduction in stroke alerts, IVT and MT rates and a relatively stable number of stroke unit admissions were observed. This suggests that the overall

incidence of stroke remained the same but fewer patients presented within the therapeutic time window. Further research is warranted to better characterize this phenomenon. Increased public awareness and corrective measures are needed, in order to mitigate the deleterious effects of the COVID-19 outbreak on acute stroke care.

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Disclosure of conflicts of interest

None declared.

Author contributions

All authors have made a substantial contribution to all categories established by the ICMJE guidelines on authorship.

Data sharing statement

Data are available upon reasonable request.

References

1. Bernard Stoecklin S, Rolland P, Silue Y, *et al.* First cases of coronavirus disease 2019 (COVID-19) in France: surveillance, investigations and control measures, January 2020. *Eurosurveillance* 2020; **25**.
2. Available from: <https://www.gouvernement.fr/info-coronavirus/carte-et-donnees> (accessed 20/03/2020).
3. Oriol R-L, Belén C-Á, Soledad O, *et al.* Impacto de la pandemia de COVID-19 sobre la actividad asistencial en cardiología intervencionista en España. *REC: Interv Cardiol* 2020; **2**: 82–89.
4. Tam CF, Cheung KS, Lam S, *et al.* Impact of coronavirus disease 2019 (COVID-19) outbreak on ST-segment-elevation myocardial infarction care in Hong Kong, China. *Circ Cardiovasc Qual Outcomes* 2020; **13**: 1–4.
5. Baracchini C, Pieroni A, Viaro F, *et al.* Acute stroke management pathway during Coronavirus-19 pandemic. *Neurol Sci* 2020; **41**: 1003–1005.
6. Morelli N, Rota E, Terracciano C, *et al.* The baffling case of ischemic stroke disappearance from the casualty department in the COVID-19 era. *Eur Neurol* 2020; 1–3.
7. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020; **395** (10229): 1033–1034.
8. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system. A review. *JAMA Cardiol* 2020.
9. Li Y, Wang M, Zhou Y, *et al.* Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study.
10. Helms J, Kremer S, Merdji H, *et al.* Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med* 2020.