



# Stroke admissions during the COVID-19 pandemic: a single-center retrospective analysis

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## Abstract

**Background and aims** The SARS-CoV-2 pandemic affected the organization of the healthcare system, and several studies analyzed the impact on hospitalization for non-COVID diseases, in particular during the first wave period. We sought to analyze the impact of the pandemic on stroke care in the province of Ferrara during a longer pandemic period and its different phases.

**Methods** We retrospectively analyzed data of all patients with acute ischemic stroke admitted to the University Hospital of Ferrara from March 2020 to April 2021. Data were compared with nonpandemic reference periods (RP, March–April 2018 and 2019).

**Results** We observed a 31% reduction in monthly admission rate for ischemic stroke (IRR 0.69; 95% CI 0.51–0.94) and monthly thrombolysis rate (IRR 0.3; 95% CI 0.15–0.66) during the first-COVID-wave (March–April 2020), as compared to RP. A nonsignificant difference was recorded for admission rate when comparing RP with subsequent pandemic phases, but the thrombolysis rate was confirmed reduced. A significant increase in onset to door time (OTD) was observed in the CP-I period (median 230 vs 120 in the RP;  $p < 0.05$ ) with improvement in the subsequent phases but without returning to baseline. Nonsignificant differences in the thrombectomy rates were found over the study period.

**Conclusion** These findings reflect changing patient attitudes during the COVID-19 pandemic or the success of health system and public health campaigns to reassure patients about the safety of seeking emergency care when needed, not only for more severe stroke symptoms.

**Keywords** Stroke · COVID pandemic · Admission rate · Stroke treatment

## Introduction

During the SARS-CoV-2 pandemic, concerns have arisen regarding patient access and delivery of acute stroke (as well as other time-dependent diseases) care, due diversion of resources, conflicting demands on emergency care utilization, stay-at-home order, and social distancing. Several studies have reported a decline in stroke admissions, delay in hospital arrival, and, as a result, reduction of acute therapeutic procedures, in many countries, including Italy during

the first wave of the pandemic [1–6]. Little is known about the hospitalization trend during later pandemic stages.

We sought to analyze the impact of SARS-CoV-2 on stroke care in the province of Ferrara, northeastern Italy, over the course of the pandemic, from March 2020 to April 2021.

## Methods

The study was conducted in the province of Ferrara, northeastern Italy. The population of the study area was 346,563 inhabitants, 179,968 women and 166,595 men. The Ferrara University Hospital is the major hospital and the only comprehensive stroke center of the study area. Other small hospitals provide outpatient neurological services, but lack neurological and neurosurgical divisions, so that according to our acute stroke pathway, all stroke patients are directly

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referred to our hospital. This mothership model remained unchanged over the study period. The pathway for acute stroke treatment was fully maintained, without any restriction in the capacity and personnel of the Stroke Unit/Neurological ward. Contingency plans to contain the pandemic were implemented beginning from the end of February 2020. The national lockdown was started on March 8 and removed on June 3. Since the beginning of the fall, a second epidemic wave took place: Italy rode out its second wave using a three-tiered system of localized restrictions on movements, leading to a partial, transient reduction in transmission. The vaccination campaign began on 27 December 2020. More than 1 year after the start of the pandemic, Italy experienced a new lockdown since mid-March 2021, due to a third wave of SARS-CoV-2 infections.

Our hospital arranged ad hoc measures to avoid viral spread within the hospital including a pre-triage to identify suspected/confirmed SARS-CoV-2 infections and channel them into a dedicated pathway, separated from unsuspected patients /non-COVID-19 patients. Resources for acute stroke care were not restricted.

We reviewed data of all patients with ischemic stroke (ICD code 433.\*, 434.\*) admitted to the hospital during the period March–April 2020 (COVID-19 period–first wave–CP-I). The same months in 2018 and 2019 were considered as reference period (RP). To evaluate the trend of admission rates during the entire pandemic, we collected also data regarding the months August–September 2020 (post-lockdown period (PLP)), October–November 2020 (COVID-19 period–second wave–CP-II), and March–April 2021 (COVID-19 period–third wave–CP-III).

The study was approved by the Local Ethics Committee.

## Statistical analysis

We calculated the monthly rate per 100,000 of hospital admission during the reference and the COVID-19 periods, and the incidence rate ratio (IRR) with the use of Poisson regression. Other data were presented as absolute numbers, percentages, mean  $\pm$  standard deviation (SD) or median and interquartile ranges (IQR) as appropriate on the basis of data distribution. Comparative analysis of clinical data

were performed between the RP, the first and third waves of COVID-19. Comparison between continuous variables was performed using a two-tailed, independent samples Student *t*-test or Mann–Whitney *U* test. Dichotomous variables were compared using the chi-squared test.

## Results

A total of 164 ischemic stroke patients were admitted to hospital, with a mean monthly admission rate of 11.8 per 100,000 in the RP. During the CP-I, we registered 57 admission for ischemic stroke giving an average admission rate of 8.2 per 100,000. Compared to the RP, we observed a 31% reduction in hospitalization for ischemic stroke (IRR 0.69; 95% CI 0.51–0.94). The decline in admission rate was similar in the two genders (IRR 0.69–95% CI 0.44–1.09 for men, and 0.69–95% CI 0.46–1.04) for women.

In the post-lockdown period, the mean admission rate increased to 10.7 per 100,000 (95% CI 8.8–12.9) nonsignificantly lower than that recorded in the RP (IRR 0.9 per 100,000; 95% CI 0.7–1.15).

During the second wave of the pandemic, we estimated a mean monthly admission rate of 10.8 per 100,000 (95% CI 8.5–13.5) giving a IRR of 0.92 (95% CI 0.7–1.2) as compared to the RP.

The monthly admission rate in the course of the third wave was 12.1 per 100,000 (95% CI 9.6–15).

The results are summarized in Table 1.

The monthly intravenous thrombolysis (IVT) rate (Table 2) decreased from 3.68 per 100,000 (95% CI 2.7–4.8) in the RP to 1.15 (95% CI 0.5–2.3) in the CP-I with an IRR of 0.3 (95% CI 0.15–0.66). The same rate increased in the post-lockdown period but remained significantly lower (–43%) as compared to the RP (IRR 0.57; 95% CI 0.35–0.95). During the RP, the proportion of stroke patients treated with IVT was 31%, and it significantly declined to 14% during the CP-I. The most frequent reason not to administer IVT was delayed hospital arrival. The fall in thrombolysis rates accounts for the reduced proportion of patients who underwent combined treatment (Table 2) during the pandemic. We confirmed the decline of the monthly

**Table 1** Monthly admission rates during RP, CP-I, PLP, CP-II, and CP-III

	No. of cases	Monthly admission rate (95% CI)	Rate ratio (95% CI)
Reference period (March–April 2018–2019)	164	11.8 (10.09–13.8)	Reference
COVID-I wave period	57	8.2 (6.2–10.7)	<b>0.69 (0.51–0.94)</b>
Post-lockdown period (July–September 2020)	111	10.7 (8.8–12.9)	0.9 (0.71–1.15)
COVID-II wave (October–November 2020)	75	10.8 (8.5–13.5)	0.92 (0.7–1.2)
COVID-III wave (March–April 2021)	84	12.1 (9.6–15)	1.02 (0.79–1.33)

*p* value < 0.05 Monthly admission rate CP-I vs RP

**Table 2** Thrombolysis and thrombectomy for ischemic stroke during RP, CP-I, PLP, CP-II, and CP-III

	No. of cases	Proportion of patients treated with IVT (%)	P value	Monthly thrombolysis rate (95% CI)	Rate ratio (95% CI)	Proportion of patients treated with EVT (%)	P value	Monthly thrombectomy rate (95% CI)	Rate ratio (95% CI)	Proportion of EVT patients pretreated with IVT (%)	P value
Reference period (March–April 2018–2019)	164	31.1	Reference	3.68 (2.7–4.8)	Reference	11	Reference	1.37 (0.85–2.1)	Reference	61.1	Reference
COVID-I wave period	57	14.0	< 0.05	1.15 (0.5–2.2)	<b>0.31 (0.15–0.66)</b>	15.8	< 0.01	1.00 (0.45–2.2)	0.74 (0.3–1.7)	11.1	< 0.05
Post-lockdown period (July–September 2020)	111	19.8	< 0.05	2.12 (1.36–3.15)	<b>0.57 (0.35–0.95)</b>	12.6	0.68	1.35 (0.77–2.21)	1.04 (0.52–2.1)	42.8	0.3
COVID-II wave (October–November 2020)	75	21.3	0.12	2.31 (1.37–3.67)	0.63 (0.36–1.10)	14.7	0.07	1.59 (0.83–2.76)	1.22 (0.58–2.59)	27.3	0.07
COVID-III wave (March–April 2021)	84	15.5%	< 0.05	1.88 (1.04–3.13)	<b>0.510 (0.28–0.94)</b>	10.7	0.95	1.3 (0.63–2.38)	1.0 (0.45–2.23)	22.2	0.055

p value < 0.005 Monthly thrombolysis rate CP-I vs RP

p value < 0.05 Monthly thrombolysis rate post-lockdown period vs RP, CP-II vs RP

EVT endovascular thrombectomy, IVT intravenous thrombolysis

IVT rate, as well as of the proportion of IVT-treated patients during the two subsequent infection waves (Table 2). The thrombectomy rates and the proportion of admitted patients treated with thrombectomy were substantially stable during the study period (Table 2).

We made a comparison of clinical data between RP, CP-I, and CP-III (Table 3).

No significant differences in mean age at presentation, and stroke severity at onset were detected, although there was a nonsignificant trend toward a younger age as well as a lower severity of stroke at presentation during the CP-I.

A significant increase in onset to door time (OTD) was observed in the CP-I period (median 230 vs 120 in the RP;  $p < 0.05$ ); OTD improved in subsequent phases without returning to baseline figures.

There were otherwise no significant differences in the ambulance call to scene arrival time and in the median ambulance scene arrival to hospital arrival time.

Moreover, we observed a significant increase in door to needle time with a median delay of about 20 min compared to the RP. The onset to groin puncture time during the CP-I was significantly longer than in the RP, with a subsequent return to baseline values.

## Discussion

One major concern related to the first COVID-19 wave was its negative effect on acute stroke care, with significant reduction of admission rates, IVT rates, and an impairment of workflow metrics.

The impact of the pandemic on stroke admissions has been reported by multiple studies across countries with different COVID-19 burden. Despite SARS-CoV-2 infection could in itself be associated with an increased risk of cerebrovascular events [1], many studies detected a

significant decline in hospitalization due to stroke during the pandemic period [2–7]. A national investigation showed a significant reduction in hospital admission and in thrombolysis rates across Italy [4].

In our study, the COVID-19 pandemic reduced the stroke admissions during the CP1 by a third and strongly affected the ODT and the quality of in-hospital care metrics. As a result, while endovascular treatments remained unchanged, we observed a significant decline in thrombolysis rates compared to before the pandemic due to reduced or delayed admission of stroke patients.

These results were in accordance with a cross-sectional, observational, retrospective study across 6 continents [5]. The most likely interpretation of these findings is that stroke patients were not seeking emergency care or adopted a wait-and-see behavior, mainly due to fear of contagion and safety concerns, or nonrecognition of symptoms by isolated or older patients during the first lockdown period.

According to a mothership model, in our area, the stroke pathway remained unchanged during the COVID-19 pandemic with prehospital notification of stroke cases to the neurologist and direct transfer of the patient to our hospital. An overload of emergency ambulance services did not seem to account for a lengthening in stroke-onset-to-hospital arrival time, since the ambulance response time did not increase over the pandemic. Thus, the lack of prompt activation of the emergency services remains the dominant obstacle in the prehospital phase of the stroke chain of survival.

The substantial stability of the thrombectomy rates indirectly indicates that patients with more severe symptoms did not modify their health-seeking attitude. These findings are in agreement with other studies [4, 8–10], even if some reports showed a significant reduction also in endovascular procedures [11–13].

**Table 3** Clinical data and comparison between RP, CP-I, and CP-III

	Reference period (4 months)	COVID-I period (2 months)	<i>p</i> value*	COVID-III period (2 months)	<i>p</i> value**
No	164	57		84	
Age (mean, SD)	75.7, 12.6	73.3, 14.9	n.s	76.4, 12.1	n.s
Baseline NIHSS (median, IQR)	5, 3–11	6, 4–11.5	n.s	4.5, 2–10.5	n.s
Onset to door (median, IQR)	120 (74.5–190)	230 (79–600)	<0.05	190 (85–824)	<0.05
Call to scene time	14 (11–18.75)	16 (12–19)	n.s	16.4 (12.1–19.9)	n.s
Scene to hospital arrival time	38.7 (29.3–50.3)	39.3 (30–52)	n.s	39.1 (30.6–51.8)	n.s
Door to needle (median, IQR)	60 (49–76.5)	76 (59.5–124)	<0.05	80 (59.5–134.5)	<0.05
Door to groin (median, IQR)	99 (64.5–119.5)	125 (75–136.5)	<0.01	90 (60–111.2)	n.s

\*Comparisons between RP and CP-I

\*\*Comparisons between RP and CP-III

There were significant variations across and within countries reflecting differences in the sociocultural behaviors and healthcare organization [11].

Another study carried out in Italy [14] showed that during all the COVID-19 pandemic, despite a global reduction in the emergency department accesses, there was only a non-significant decrease in admissions for ischemic stroke and the rate of reperfusion therapies remain unchanged, but with longer onset to door time.

In our study, the admission rate fell during the first wave, and returned to normality after the relaxing of the restriction measures where has remained ever since. Stroke physicians have been increasingly implementing information campaigns, encouraging patients to present early to the emergency room. It remains unclear whether the appeals of the scientific community during the first wave would have lessened the effect of any subsequent social containment mandates on stroke admissions.

Nevertheless, a Greek study reported a persistent decline in hospitalization for acute stroke during the second wave of the COVID-19 pandemic [15]. The magnitude of reduction in admissions in the above study was similar to that of the first lockdown, suggesting that, regardless of the impact that COVID-19 has had on our community, social distancing mandates, restrictive measures and fear of infection have a negative impact on cerebrovascular diseases.

In agreement with our findings, a nationwide Danish study showed that hospital admission rates returned to baseline levels during the post-lockdown phase of gradual reopening [16], even if with a transient drop during the second lockdown [17]. No significant declines in stroke alerts were observed during the largest second and third COVID-19 cases surge in Northern California [18].

On the contrary, in a severely COVID-affected area of Germany, there was a significant drop in total number of stroke patients presented during the second wave as compared to the first wave of the pandemic [19]. However, a nationwide study in the same country documented a smaller decline in hospitalizations for stroke during the second more severe wave than during the first one [20].

After all, in a state-wide analysis covering all types of acute cerebrovascular diseases in Austria [21], hospital admissions for TIA and ICH were reduced during and after the first wave of the COVID-19 pandemic while hospitalizations and recanalization treatments for IS were not affected in these two periods.

The discrepancies in findings across different areas could be dependent on the degrees of severity of the infection rates. However, the impact of COVID pandemic in noninfectious acute diseases has proven to be independent from the local incidence of SARS-CoV-2 infection. More likely, transcultural differences in health-seeking behaviors and in reaction to sustained pandemic-related challenge played a role. The

avoidance of seeking healthcare may not be driven directly by lockdowns per se but may be dependent on factors such as fear of the virus, not wanting to a further burden to hospital staff or fearing restrictions leading to further isolation from family members in hospitals. This, in conjunction with other variables (in particular the presence of a bystander at the onset of symptoms) could have influenced the prehospital notification and so the activation of the rescue chain [22].

The main limitation of the study is the small sample size due to the monocentric nature of this investigation. However, the study covers a relatively long observational period—including the first three waves of the COVID-19 pandemic—allowing to follow the changing patient attitudes, partly due to the success of public health campaigns encouraging patients to seek emergency care when needed.

The decline in acute stroke admission rates during societal pandemic lockdowns is avoidable, and public health efforts to improve the collateral damage of potential future waves of COVID-19 pandemic is warranted. The impact of the pandemic on cerebrovascular diseases may be seen in the months and years to come.

## Declarations

**Ethical approval** Approval was obtained from the ethics committee of the University of Ferrara. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

**Conflict of interest** The authors declare no competing interests.

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