

COVID-19 Lockdown Effects on Acute Stroke Care in Latin America

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American Stroke Registry (LASE) COVID-19 Collaborators.

Objectives: COVID-19 pandemic has forced important changes in health care worldwide. Stroke care networks have been affected, especially during peak periods. We assessed the impact of the pandemic and lockdowns in stroke admissions and care in Latin America. *Materials and Methods:* A multinational study (7 countries, 18 centers) of patients admitted during the pandemic outbreak (March-June 2020). Comparisons were made with the same period in 2019. Numbers of cases, stroke etiology and severity, acute care and hospitalization outcomes were assessed. *Results:* Most countries reported mild decreases in stroke admissions compared to the same period of 2019 (1187 vs. 1166, $p = 0.03$). Among stroke subtypes, there was a reduction in ischemic strokes (IS) admissions (78.3% vs. 73.9%, $p = 0.01$) compared with 2019, especially in IS with NIHSS 0–5 (50.1% vs. 44.9%, $p = 0.03$). A substantial increase in the proportion of stroke admissions beyond 48 h from symptoms onset

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was observed (13.8% vs. 20.5%, $p < 0.001$). Nevertheless, no differences in total reperfusion treatment rates were observed, with similar door-to-needle, door-to-CT, and door-to-groin times in both periods. Other stroke outcomes, as all-type mortality during hospitalization (4.9% vs. 9.7%, $p < 0.001$), length of stay (IQR 1–5 days vs. 0–9 days, $p < 0.001$), and likelihood to be discharged home (91.6% vs. 83.0%, $p < 0.001$), were compromised during COVID-19 lockdown period. *Conclusions:* In this Latin America survey, there was a mild decrease in admissions of IS during the COVID-19 lockdown period, with a significant delay in time to consultations and worse hospitalization outcomes.

Key Words: Latin America—Developing countries—Stroke—Acute stroke therapy—COVID-19—Lockdown
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The Coronavirus disease (COVID-19) pandemic has sparked an unprecedented international public health crisis. It has prompted numerous countries to implement lockdowns to mitigate the spread of the virus and to reduce the burden on health systems.¹ The decrease in the use of health institutions for non-COVID medical conditions and mobility restrictions due to social isolation measures had a potential impact on the care of several non-communicable diseases, including stroke.^{2–6}

The beginning of the pandemic first in Asia and Europe allowed Latin American governments to implement different prevention and control measures. However, this region has a historical lag in acute stroke care strategies compared to high-income countries.⁷ Data on the influence of the COVID-19 pandemic, including potential collateral consequences of different lockdown measures as “stay-at-home” campaigns taken by governments, in the care of stroke in Latin America is scarce. Argentina and Brazil showed an early decrease in hospital admissions for transient ischemic attack and mild-moderate strokes during the COVID-19 pandemic.^{5,8,9}

LASE (Latin American Stroke rEgistry) is an initiative that explores several topics related to stroke in Latin America through a multicenter, population-based sample from tertiary hospitals in the region using robust data compilation and methodology. The aim of this study was to assess the influence of COVID-19 pandemic and the implementations of quarantines in acute stroke care in several Latin American countries using a standardized survey.

Methods

Latin American Stroke rEgistry (LASE)

LASE is a multicenter initiative from tertiary referral hospitals with ongoing stroke registries from across Central and South America. Participating centers were recruited through formal invitations because of their known work in stroke care in their respective country/region. A total of 18 centers of 7 countries from Central and South America provided information for the LASE COVID-19 initiative. Participants included 5 centers from

Buenos Aires (Argentina), 1 center from Porto Alegre (Brazil), 2 centers from Santiago de Chile (Chile), 1 center from Bogotá and 1 center from Cali (Colombia), 2 centers from Mexico City, 1 center from Monterrey, 1 center from Aguascalientes and 1 center from Guadalajara (Mexico), 1 center from Asunción (Paraguay), and 2 centers from Lima (Peru). All participant centers meet accepted criteria for primary stroke centers and 12 centers (4 from Argentina, 1 from Brazil, 2 from Chile, 2 from Colombia, 2 from Mexico, 1 from Peru) offer 24/7 endovascular treatment.

Patients admitted with diagnosis of acute stroke between March 1st and June 30th 2020 (COVID-19 period) were included. All variables were compared with data from the same period of 2019 (pre-COVID-19). All countries were on strict lockdowns of different characteristics during the period reported in this work. The primary aim of the study was to evaluate if stroke admissions, type of strokes (ischemic stroke [IS], transient ischemic attack [TIA], intracerebral hemorrhage [ICH]), stroke severity classified as mild (National Institutes of Health Stroke Scale [NIHSS] score 0–5), moderate (NIHSS score 6–9), and severe (NIHSS score > 10), and revascularization therapies (intravenous thrombolysis [IVT] or mechanical thrombectomy [MT]) were affected by COVID-19 pandemic and/or lockdown measures. Other variables of acute stroke hospitalization were also evaluated.

The study protocol was approved by each Institutional Ethics Committee according to international and local research regulations. Because of the non-interventional and retrospective characteristics of the registry, the study was exempted from informed consent. The individual data that support the findings of this study are not publicly available because of certain institutional policies but are available from the corresponding author on reasonable request.

Statistical methods

Continuous variables were reported as means and standard deviations (SD), or as median and interquartile range (IQR), according to normality distribution (Kolmogorov-Smirnov test). Categorical variables were reported as counts and proportions. Univariate analyses were performed in continuous variables using the Student *t* test or Mann-Whitney *U* test, according to normality

distribution; for categorical variables comparisons were done using χ^2 or Fisher's exact test. The analysis was performed using IBM SPSS Statistics Version 22.0 (SPSS Statistics for Macintosh, IBM Corp., Armonk, NY), and the level of significance was established at a 0.05 level (2-sided), with Yates's correction.

Results

Patients baseline characteristics and presentation

Most countries reported mild decreases in all-type stroke admissions during COVID-19 period (1187 vs. 1166, $p = 0.03$),

except México where admissions significantly increased in 2020 (Table 1). Stroke patients in the COVID-19 period were more frequently females (44.7% vs. 49.3%, $p = 0.03$). Among stroke subtypes, the reduction was observed in IS (78.3% vs. 73.9%, $p = 0.01$), while there was an increase in ICH (9.4% vs. 14.2%, $p < 0.001$). TIAs admissions were unchanged between both periods when the region was evaluated as a whole. However, there was a substantial difference among countries, with a significant reduction in Argentina and Chile, no changes in Paraguay, Peru, Colombia and México, and an increase in Brazil (Table 2). Median NIHSS at admission was higher in 2020 (6 [IQR 2-12] vs. 5 [IQR 1-12], $p = 0.02$). There

Table 1. Main characteristics of the patients admitted during COVID-19 period (March-June 2020) in relation to pre-COVID-19 period (March-June 2019).

	March-June 2019 (n = 1187)	March-June 2020 (n = 1166)	P value
Country Distribution, n (%)			
Argentina	380 (32)	368 (31.6)	0.8
Brazil	88 (7.4)	95 (8.4)	0.5
Chile	123 (10.4)	119 (10.2)	0.9
Colombia	93 (7.8)	88 (7.5)	0.8
México	250 (21.1)	329 (28.2)	<0.001
Paraguay	108 (9.1)	55 (4.7)	<0.001
Peru	145 (12.2)	112 (9.6)	0.04
Stroke subtype, n (%)			
IS	930 (78.3)	862 (73.9)	0.01
TIA	134 (11.3)	124 (10.6)	0.6
ICH	112 (9.4)	165 (14.2)	<0.001
IS etiology, n (%)			
Cardioembolic	210 (21.7)	207 (24.2)	<0.001
Small vessel	173 (17.9)	104 (12.1)	0.22
Other causes	73 (7.5)	51 (6.0)	0.94
Cryptogenic	173 (17.9)	139 (16.2)	0.13
UIS	162 (16.7)	236 (27.6)	<0.001
LVO, n (%)	160 (16.5)	108 (12.6)	0.84
Admission NIHSS scale in IS patients			
NIHSS, median (IQR)	5 (1-12)	6 (2-12)	0.02
NIHSS 0-5, n (%)	437 (50.1)	367 (44.9)	0.03
NIHSS 6-10, n (%)	183 (21)	188 (23)	0.3
NIHSS >10, n (%)	253 (29)	263 (32.2)	0.1
Time to emergency consultation (symptom onset to hospital arrival), n (%)			
<24 h	720 (69.4)	682 (64.3)	0.28
24-48 h	88 (7.4)	95 (8.4)	0.50
>48 h	143(13.8)	217 (20.5)	<0.001
Acute reperfusion treatment, n (%)			
IVT	109 (9.2)	85 (7.3)	0.22
MT alone	30 (2.5)	28 (2.4)	0.22
IVT + MT	21 (1.8)	26 (2.2)	0.19
Acute intra-hospital time metrics, median minutes (IQR)			
Door-to-CT	25 (17-27)	20 (12-31)	0.96
Door-to-needle	43 (25-80)	49 (27-105)	0.46
Door-to-groin	141 (100-180)	115 (76-200)	0.09

COVID-19 indicates coronavirus disease 2019; CT, computed tomography; CVT, cerebral venous thrombosis; hs, hours; ICH; intracerebral hemorrhage; IQR, interquartile range; IS, ischemic stroke; IVT, intravenous thrombolysis; LVO, large vessels occlusion; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; and UIS, undetermined with incompletely studies.

Table 2. Cerebrovascular events admitted during COVID-19 period (March-June 2020) in relation to pre-COVID-19 period (March-June 2019) by country.

	IS n (%)			TIA n (%)			ICH n (%)		
	2019	2020	P value	2019	2020	P value	2019	2020	P value
Argentina	271 (71.3)	267 (72.6)	0.70	76 (20)	76 (20.7)	0.01	27 (7.1)	41 (11.1)	0.07
Brazil	65 (73.9)	54 (56.8)	0.01	15 (17)	35 (36.8)	0.02	8 (9.1)	6 (6.3)	0.48
Chile	103 (83.7)	97 (81.5)	0.64	14 (11.4)	6 (5)	0.05	5 (4.1)	15 (12.6)	0.01
Colombia	75 (80.6)	69 (78.4)	0.70	11 (11.8)	10 (11.4)	0.92	7 (7.5)	9 (10.2)	0.52
Mexico	217 (86.8)	247 (75.1)	<.001	11 (4.4)	16 (4.9)	0.06	18 (7.2)	62 (18.8)	<.001
Paraguay	76 (70.4)	38 (69.1)	0.86	3 (2.8)	2 (3.6)	0.76	18 (16.7)	15 (27.3)	0.95
Peru	123 (84.8)	90 (80.4)	0.34	4 (2.7)	5 (4.5)	0.46	18 (12.4)	17 (15.2)	0.52

ICH; intracerebral hemorrhage; IS, ischemic stroke; TIA, transient ischemic attack.

was reduction in mild (NIHSS 0-5) IS admissions compared to the same period in 2019 (50.1% vs. 44.9%, $p = 0.03$). A slight non-significant increase in IS patients with moderate (NIHSS 6-10) and severe (NIHSS > 10) IS was observed. The most common etiologies reported in COVID-19 period for IS were cardioembolic (24.2%) and undetermined etiology for incomplete studies (27.6%), both were more frequent than in the same period in 2019 ($p < 0.001$, Table 1).

IS acute management

During the COVID-19 period, there was a significant increase in stroke admissions beyond 48 h from symptoms onset (13.8% vs. 20.5%, $p < 0.001$; Table 1). Nevertheless, no differences in total reperfusion treatment rates were observed, with similar door-to-needle, door-to-CT, and door-to-groin times in both periods (Table 1).

Hospitalization outcomes

Length of stay in hospital was shorter in the COVID-19 period with a median of 2 days vs. 4 days in pre-COVID-19 period (IQR 1–5 days vs. 0–9 days, $p < 0.001$). All-type mortality during hospitalization increased in 2020 (4.9% vs. 9.7%, $p < 0.001$), and patients were less likely to be discharged home (91.6% vs. 83.0%, $p < 0.001$), and were discharged more frequently to long-term facility (2.0% vs. 8.1%, $p < 0.001$) or transfer to other hospitals (2.0% vs. 4.3%, $p < 0.001$). The same proportion were discharged to acute rehabilitation centers (4.4% vs. 4.6%, $p = 0.89$).

Discussion

The present study found a mild decrease of IS admissions to emergency departments in Latin America during the COVID-19 lockdown period, with a significant delay in time to consultation. Reperfusion treatment rates and metrics related were maintained. However, there was an increase in all-cause mortality and worsening of other in-hospital outcomes during hospitalization.

The pandemic of COVID-19 has challenged capacities of healthcare systems' response around the world.¹⁰ In the area

of acute medical emergencies, especially in acute stroke care, several changes have been implemented to deal with the economic and structural impact of COVID-19 pandemic. Moreover, there have been campaigns throughout the world to educate the general population about the availability of safe centers for stroke care, and to recognize stroke signs and to activate emergency medical services, with the motto: "stroke doesn't stay at home".^{11–13} However, despite all efforts, several reports showed a decrease of acute stroke consultations, with impacts in therapeutic times, and a subsequent decrease in quality-of-care parameters for stroke patients.¹⁴ Latin America, as a region, has been struggling to reduce the burden of stroke. The complexity of the healthcare systems throughout the region, economic disparities, and scarce availability of infrastructure with lack of regional stroke networks difficult this objective.⁷ COVID-19 pandemic has posed an even greater challenge to this situation in the region, with some reports showing a reduction in the global number of stroke admissions in some individuals centers.^{6,8,9} Our study reports a mild decrease of IS admissions during the first four months of the pandemic in several countries of Latin America. Centers in Mexico, instead, had an increase in the number of IS and ICH cases, probably due to a redistribution of admissions to hospitals classified as non-COVID-19 centers. The decrease in stroke admissions was significant for mild IS, with a trend for increase of severe cases, in accordance with prior studies.^{6,9} This phenomenon may be attributed to the behavior of patients not seeking medical attention for "minor" emergencies during the pandemic, fearing of COVID-19 infection in large hospitals.^{7,14} This could also explain that the proportion of cardioembolic strokes was higher during the pandemic, probably reflecting severe cases with higher NIH scores.

There is scant previous data on the effect of the COVID-19 pandemic in acute TIAs admissions. In our study, we observed a great disparity in consultation for TIAs among centers in the region. Some of the referral centers manage TIA not only at the emergency department, but also at TIA clinics, which could explain some differences found among countries and periods. However, this aspect deserves further analysis.

A meta-analysis including centers from Europe, Asia and the United States, but not Latin American countries, showed that the number of reperfusion therapies during the early part of the pandemic (February-March 2020), decreased compared to the pre-pandemic period.¹⁵ In our study, reperfusion therapies were maintained during the early COVID-19 period, reflecting preservation of in-hospital pathways in participating centers. Most of them adapted their current protocols to organize a protected stroke code pathway for patients with suspicion of COVID-19 and implemented safety measures for the health personnel in stroke units.^{16–19} Nevertheless, some hospital outcomes of stroke care were compromised during COVID-19 lockdown period in our region. Higher all-type intra-hospital mortality limited etiological evaluation (more undetermined IS secondary to incomplete studies), and less likelihood of being discharged to home showed a worrisome situation in terms of in-hospital management. It is likely that the decrease in the length of stay was not due to the improvement in the management of the hospitalized patient, but rather to a requirement of beds in the context of the COVID-19 pandemic. It is possible that the great effort that has been made maintaining acute stroke treatment has not been enough for an adequate comprehensive care during hospitalization.

The strengths of the current study mainly include a detailed dataset of compiled information, which was critically analyzed, from representative stroke centers in the different participating countries. We were also able to demonstrate some positive aspects of acute stroke management in the region to maintain quality standards despite the pandemic outbreak. Our study had some limitations. Number of patients entered in each country were not proportional to the country population with the possibility of introducing some biases. Most of the participating centers serve as referral institutions for their cities, many of them as primary neurological centers. There is variability in health systems in the 7 countries and perhaps other cultural or demographic reasons for some of these differences. Furthermore, as these centers represent a particular area in each city, taking into account the mobility restrictions that occurred during lockdown,²⁰ it is difficult to extrapolate the results to other areas of the same cities and countries. Other variables that could also be related such as number of available personnel at the stroke unit 24/7, delay time for patient transfers to referral stroke centers for acute therapies, results of SARS-COV-2 diagnostic test, were not included in the analysis. Finally, this is an ongoing pandemic, with different outbreak patterns in each region of Latin America, where the amount of cases is increasing daily. Thus, the present information may not represent the current situation of these centers and follow-up studies are needed.

In conclusion, in this Latin America survey, there was a mild decrease in admissions of IS during the COVID-19 lockdown period, with a significant delay in time to

consultations. Acute treatment parameters were maintained but there was an increase in all-cause mortality and worsening of other in-hospital outcomes during hospitalization. Therefore, the need to maintain an adapted chain of stroke care in our region is essential to keep offering adequate acute stroke management, especially in the context of probable new outbreaks of the COVID-19 pandemic in the coming months.

Declarations of Competing Interest

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