





Temporal analysis of the administration of encephalic reperfusion therapies during the COVID-19 pandemic in a Chilean hospital: An analytical cross-sectional study

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ABSTRACT

INTRODUCTION The COVID-19 pandemic had a major impact on emergency services, including stroke care. Changes in the administration times of brain reperfusion therapies for stroke have been little explored in Chile. The aim of this study was to analyze the impact that the pandemic had on critical stroke treatment times, the number of patients treated, clinical severity, and the presence of major vessel occlusion.

METHODS We performed a retrospective analysis of patients undergoing encephalic reperfusion therapy in a hospital in Valparaíso, Chile. Two groups of patients treated one year before (pre-pandemic group) and one year after (pandemic group) the start of health restrictions were compared.

RESULTS 104 patients were included, with a mean age of 67.4 ± 13 years and a clinical severity of 13.5 ± 6.5 in the NIHSS. 91.5% received thrombolytic therapy. No significant intergroup differences were found in the metrics of treatment time, number of patients treated, clinical severity, or presence of major vessel occlusion. Although there was a non-significant trend towards delayed institutional therapeutic times, a significant correlation was found suggesting that the shorter the time from symptom onset to door, the shorter the time to access therapy ($r = 0.84$).

CONCLUSIONS There were no significant differences in the therapeutic times of stroke in the period prior to the COVID-19 pandemic and the pandemic period, showing similarities to the experience reported in Chile and highlighting the adaptation of the health system during the health crisis. Studies with more complex epidemiological designs analyzing larger samples of patients will allow us to complement these results.

KEYWORDS Stroke, thrombolytic therapy, pandemics, COVID-19

INTRODUCTION

Acute ischemic stroke is a frequent neurological emergency, with an incidence in Chile of 117 per 100 000 people per year [1]. It is one of the leading causes of death and disability in the adult population. It is also the leading cause of disability in

Western countries [2]. According to current national statistics, stroke is, together with acute myocardial infarction, the leading cause of death in Chile among cardiovascular diseases [3]. Encephalic reperfusion therapies, both systemic thrombolysis and mechanical thrombectomy, strongly influence its prognosis. However, the application of both interventions depends on time, with a narrow therapeutic window and recommended hospital care times, given the favorable clinical impact of their early administration [4]. Thus, their implementation during the COVID-19 pandemic may be hampered.

The impact of the COVID-19 pandemic on the care of patients with ischemic stroke has been well described, being associated with delays in critical treatment times, decreased volumes of encephalic reperfusion therapies performed, activation of stroke

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Citation Zambrano K, Arancibia M, Soto C, Riquelme J. Temporal analysis of the administration of encephalic reperfusion therapies during the COVID-19 pandemic in a Chilean hospital: An analytical cross-sectional study. Medwave 2025;25(08):e3081

DOI 10.5867/medwave.2025.08.3081

Submitted Mar 7, 2025, Accepted Jul 21, 2025,

Published Sep 3, 2025

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MAIN MESSAGES

- Acute ischemic stroke is a frequent neurological emergency, which constitutes one of the leading causes of death and disability in the adult population.
- The Valparaíso Region, Chile, has a high incidence of stroke. However, the effects of socio-health restrictions during the COVID-19 pandemic have been little studied.
- No significant differences were observed in the encephalic reperfusion delay between the pre-pandemic period and the critical period of the COVID-19 pandemic. However, there was a non-significant trend towards a delay in institutional time metrics and a decrease in the number of patients treated.
- Limitations of this study include the low sample size, the small number of thrombectomies performed due to the low availability of endovascular therapy during the COVID-19 pandemic, and the changes imposed during that period in the clinical practice of thrombolytic therapy.

codes, consultations, and hospitalizations for cerebral vascular disease [5–9]. In addition, increased clinical severity and mortality from ischemic stroke have been reported. In Chile, as in the world, during the initial phase of the health emergency, there was a decrease in the number of emergency consultations for stroke, as well as in hospitalizations for this cause [3,5–8]. This impact would be attributed to the fear of contagion due to the rapid spread of the virus and the significant increase in the burden of care for patients with COVID-19, as well as to the measures of restriction and social isolation implemented worldwide [10]. In addition, factors such as the reduction in the use of diagnostic imaging equipment may also play a role [11]. For this reason, international organizations urged the effort to try to maintain standards of care during the critical period of the pandemic [5,6,11]. This decrease in the number of consultations and hospitalizations is worrisome, as it suggests that many patients with cerebral infarctions did not consult, particularly those with mild forms, who may also benefit from early care and treatment to reduce the recurrence rate.

The Carlos van Buren Hospital is the main referral center for the treatment of acute ischemic stroke in the Valparaíso Region, an area with a high morbidity and mortality rate associated with this pathology compared to other regions of Chile [12]. However, national scientific publications on the impact of the COVID-19 pandemic on stroke management do not include this region. From the beginning of the pandemic, the use of protective equipment for all healthcare personnel was standardized, as well as disinfection measures for imaging equipment among patients. The hospital maintained the continuity of emergency neurological care without changing the inclusion and exclusion criteria that govern the Stroke Code. In our center, this code establishes the performance of computed tomography angiography of the brain and neck in all patients, ruling out the presence of occlusion of a major vessel of the anterior or posterior circulation.

This study aimed to analyze the impact of the COVID-19 pandemic on critical stroke treatment times in our hospital, as well as the number of patients undergoing encephalic reperfusion therapy, clinical severity and major vessel occlusion rate, during the implementation of socio-health restrictions in

Chile. To this end, different clinical indicators were compared before and after the implementation of the health measures and their correlations were evaluated, to explore associations that would allow tentative answers to the observed phenomena to be formulated.

METHODS

Design

An analytical cross-sectional study was performed in patients undergoing encephalic reperfusion therapy for acute ischemic stroke at the Carlos van Buren Hospital, one year before and one year after the onset of the pandemic.

Sample

All patients over 18 years of age who were admitted to the hospital with a diagnosis of acute ischemic stroke and who met the inclusion criteria for encephalic reperfusion therapy were included. The period analyzed was between March 2019 and March 2021. Patients who suffered an in-hospital stroke were excluded.

Procedures

Electronic hospital statistics were reviewed to obtain the total number of patients admitted for ischemic stroke in both periods. The clinical records, both physical and electronic, of patients treated with encephalic reperfusion therapy were analyzed. In this way, the times from the onset of symptoms, pre- and in-hospital care (expressed in minutes) and the other study variables were obtained. As a bias control and data validation, these were additionally verified with the nursing records, prehospital care ambulance system records, and with the image viewer program of our center. Group 1 (pre-pandemic) was comprised of patients seen between March 1, 2019 and February 29, 2020, while group 2 (pandemic) was comprised of those seen between March 1, 2020 and February 28, 2021. The project was approved by the Ethical-Scientific Committee of the Valparaíso-San Antonio Health Service (No. 46/2022).

Statistical analysis

The Stata 17 program was used. Absolute numbers, proportions and means were used for descriptive statistics. Different clinical variables and procedure times were compared between the pre-pandemic and pandemic groups (Table 1). Student’s t-test and Chi-square test were applied for the comparison of means and proportions, respectively. To analyze the level of correlation between the variables age, National Institutes of Health Stroke Scale (NIHSS) score and procedure times, the Pearson correlation test was applied. A significance level of 5% was used.

RESULTS

There were a total of 980 patients admitted for ischemic stroke in the study period, evidencing a 21% reduction in the pandemic period (548 versus 432), of which 104 patients were selected for analysis, since only this group met the criteria for encephalic reperfusion therapy. This group had a mean age of 67.4 ± 13 years and a NIHSS of 13.5 ± 6.5. Forty-eight percent were women (n = 50). 59.6% (n = 62) corresponded to group 1 (Table 2).

There were no intergroup differences in demographic characteristics, clinical severity (NIHSS), presence of major vessel occlusion, type of therapy or procedure times (Table 3).

The correlation between the different therapeutic times was explored (Table 4). Concerning significant correlations, a high and positive correlation was found between door-to-needle onset time and needle onset time (r = 0.84), a moderate and positive correlation between door-to-needle time and door-to-computed tomography time (r = 0.57), and a low and positive correlation between door-to-needle time and door-to-needle time (r = 0.34). Positive correlations indicate that, as one variable increases in magnitude, the other also increases. The degrees of correlation correlate with the strength of the association between variables.

DISCUSSION

This study included 104 patients who received encephalic reperfusion therapy. When comparing the pre-pandemic period with the pandemic period, no significant intergroup differences were found in the metrics of treatment time, number of patients treated, clinical severity, or presence of major vessel occlusion. However, a significant correlation was found, suggesting that the shorter the time from symptom onset to door, the shorter the time to access therapy.

After the declaration of social distancing imposed in Chile on March 18, 2020, the implementation of restrictive measures that changed the hospital flow of stroke was promptly activated [7]. During the first months of the pandemic, a 10% decrease in emergency care for stroke and an 8.6% decrease in hospitalizations for stroke was reported [3]. Despite the above, the national experience reported in different studies did not show significant changes in the volume of patients who underwent endovenous thrombolysis or mechanical thrombectomy [14,15],

Table 1. Description of variables.

Variable	Description
NIHSS	Score from 1 to 45 points assigned by a neurologist for the assessment of basic neurological functions in the acute phase of stroke (clinical severity indicator). The dimensions evaluated in the scale are level of consciousness, conjugate gaze, visual fields, facial paresis, upper limb paresis, lower limb paresis, limb ataxia, sensibility, language, dysarthria, and extinction-negligence-inattention. The version with validation studies in Chile was used [13].
Large vessel occlusion on admission	Results of computed tomography angiography of the brain at the beginning of care. Large vessel occlusion was considered to be the involvement of the MCA in its M1, ICA, and BA segments.
Thrombolysis	Administration of thrombolytic treatment to patients with stroke of up to 4.5 hours of evolution.
Thrombectomy	Endovascular removal of a thrombus.
Mixed therapy	Administration of thrombolytic therapy as bridging therapy and subsequent mechanical thrombectomy in patients with stroke and proximal occlusion of large vessels.
Onset-door time	Time in minutes from symptom onset to admission to the adult emergency unit.
Door-to-CT time	Time in minutes from the patient’s admission to the adult emergency unit to the first imaging study (computed tomography or magnetic resonance imaging of the brain). Recommended time < 20 minutes.
Door-to-needle time	Time in minutes from admission to the adult emergency unit to the start of intravenous thrombolysis. Recommended time < 60 minutes.
Start-needle time	Time in minutes from symptom onset to start of intravenous thrombolysis. Recommended time < 120 minutes.

NIHSS, *National Institutes of Health Stroke Scale*. MCA, middle cerebral artery. ICA, internal carotid artery. AB, basilar artery. CT, computed tomography.

Source: Prepared by the authors of this study.

Table 2. Description of the total sample.

Variable	Total (n = 104)
Major vessel occlusion	50.9% (n = 53)
Therapy	Thrombolysis 91.3% (n = 95)
	Thrombectomy 4.8% (n = 5)
	Combined 3.8% (n = 4)
Start-door time	113.7 ± 88.2
Door-CT time	26.7 ± 16.8
Door-to-Needle time	62.5 ± 32.5
Start-needle time	170.6 ± 96.1

CT, computed tomography.

Results in proportions and averages ± standard deviation.

Source: Prepared by the authors.

Table 3. Clinical and procedural time differences according to groups.

	Prepandemic group (n = 62)	Pandemic group (n = 42)	p-value
Female	46.7% (n = 29)	50% (n = 21)	0.74 (-0.03; 95% CI: -0.16 to 0.22) ¹
Age (years)	66 ± 12.8	69.5 ± 13.2	0.17 (-3.53; 95% CI: -8.7 to 1.6) ²
NIHSS (score)	13.5 ± 6.8	13.5 ± 6	0.9 (0.01; 95% CI: -2.58 a 2.61) ²
Presence of major vessel occlusion	51.6% (n = 32) MCA M1 75% (n = 24) ICA 21.9% (n = 7) BA 3.1% (n = 1)	45.2% (n = 19) MCA M1 63.2% (n = 12) ICA 31.6% (n = 6) BA 5.3% (n = 1)	0.5 (0.06; 95% CI: -0.13 to 0.25) ¹
Type of therapy	Thrombolysis 87% (n = 54) Thrombectomy 6.4% (n = 4) Combined 6.4% (n = 4)	Thrombolysis 97.6% (n = 41) Thrombectomy 2.3% (n = 1) Combined 0% (n = 0)	0.14
Start-door time	124.1 ± 102.7	98.3 ± 58.7	0.14 (25.77; 95% CI: -9.02 to 60.56) ²
Door-CT time	24.3 ± 13.8	30.2 ± 20	0.08 (-5.86; 95% CI: -12.46 to 0.73) ²
Door-to-Needle time	58.5 ± 30.4	68.4 ± 35.1	0.13 (-9.80; 95% CI -22.64 to 3) ²
Start-needle time	173.4 ± 111.9	166.5 ± 67.3	0.71 (6.94; 95% CI: -31.33 to 45.21) ²

MCA: Middle cerebral artery. ICA: Internal carotide artery. BA: Basilar artery. NIHSS: National Institutes of Health Stroke Scale. CT : computed tomography.

¹ 95% confidence interval for the difference in proportions. ² 95% confidence interval for the mean difference.

Results in proportions and averages ± standard deviation. Student's t and Chi-square were used for the comparison of means and proportions, respectively.

Source: Prepared by the authors based on data from the study.

Table 4. Variable correlation matrix.

	1	2	3	4	5	6
Age						
NIHSS	0.13					
Start-door time	0.06	0.07				
Door-CT time	0.03	-0.18	-0.02			
Door-to-Needle time	0.09	-0.12	-0.10	0.57¹		
Start-needle time	0.13	-0.01	0.84¹	0.16	0.34¹	

NIHSS, *National Institutes of Health Stroke Scale*; CT: Computed tomography.

¹ p-value < 0.001.

Values expressed in correlation coefficients (r).

Source: Prepared by the authors of this study.

nor differences in the metrics of treatment time for endovascular thrombolysis [14]. This suggests that the standard of care was maintained during the critical period of the pandemic. However, increased severity of ischemic stroke and associated mortality has been described [16,17]. In this investigation, a temporal analysis of the administration of encephalic reperfusion therapies during the pre-pandemic period compared to those treated in the critical period of the COVID-19 pandemic was performed, which revealed no significant differences. This fact could suggest that the standard of care for ischemic stroke

in the study hospital was maintained, consistent with national experience [8,14].

On the other hand, a non-significant trend of door-needle time delay was observed. This medical assistance could have been threatened by the reorganization in the emergency departments imposed by the management of potentially infected patients, as well as by the disinfection processes in the imaging equipment [8,10,11]. This is reflected in the increased door-to-computed tomography time observed. Although this result is not significant, it may indicate internal management and quality of cerebral infarction care. There was a significant,

positive and high correlation between onset-door and onset-needle time ($r = 0.84$). This could be associated with the implementation of social isolation measures and sanitary controls throughout the city, which restricted free transit and, from some point of view, favored a more expeditious arrival at the emergency department from the onset of symptoms. Likewise, the hospital maintained ambulance services and on-call neurologist care during the health crisis, which favored timely care for patients eligible for reperfusion therapies.

Our center reported a 21% reduction in hospitalizations for ischemic stroke (548 versus 432) during the pandemic period, similar to that observed worldwide [5,6]. It is likely that this decrease is associated with a lower number of hospital visits, for reasons such as fear of contagion, social distancing barriers, and confinement, similar to what occurred in international reports [5]. Despite this, there was no significant reduction in the number of thrombolyses performed ($p = 0.14$), nor in the overall reperfusion rate (11.7% versus 9.7, $p = 0.23$), consistent with national studies that show no significant changes in thrombolysis time metrics [8,14]. Furthermore, our center did not exhibit significant changes in clinical severity compared to the pre-pandemic period. The findings are consistent with the fact that the large population of Valparaíso has a high morbidity and mortality rate for stroke in Chile [12]. This differs from the national experience, as reported by Silva-Pozo et al [14,17] in a hospital in the southern zone of Santiago, where they observed increased severity in NIHSS (7.23 versus 8.78) and mortality (5.2% versus 12.4%).

On the other hand, the main contributing factor to the increase in hospital mortality would be the admission NIHSS [14], a result consistent with that reported in international studies [7]. Our work did not conclude a significant difference in the number of patients with major vessel occlusion when comparing both periods ($p = 0.5$), similar to that described by Rivera et al [15] in a national referral hospital for mechanical thrombectomy. Unlike them, we did not evidence significant changes in the distribution of occlusion site. Recently, the systematic review with meta-analysis by Burton et al [18] concluded, from 52 primary studies, that there was a delay in prehospital stroke care during the COVID-19 pandemic, as well as a lower volume of emergency consultations.

Among the limitations of this study, the low sample size considered may have limited the conclusions drawn from the hypothesis testing. It is essential to keep this consideration in mind when interpreting the results. Likewise, the low number of thrombectomies performed due to the low availability of endovascular therapy in that period did not allow more robust conclusions to be drawn in this respect. Unlike other studies, we evaluated stroke severity in the subgroup of patients undergoing encephalic reperfusion therapy and not in the total number of patients admitted for ischemic stroke. We also did not evaluate variations in stroke consultations, personal history including COVID-19 infection or whether there was a relationship between this and the clinical severity studied, as well as

functional clinical follow-up at discharge and patient mortality. This would have allowed a more in-depth analysis of the impact of the pandemic on clinical prognosis. Finally, it is interesting to evaluate the results obtained from the perspective of secular bias [19], which points out that there are intervention-outcome associations that can be misinterpreted due to changes in clinical practices, which introduces a bias. In the case of this study, we assume that the COVID-19 pandemic and socio-sanitary restrictions imposed a series of changes in clinical practice that hindered a more accurate analysis of thrombolytic therapy and its outcomes.

CONCLUSIONS

Our results indicate that no statistically significant differences were observed in the administration times of encephalic reperfusion therapies between the pre-pandemic period and the critical period of the COVID-19 pandemic. This finding coincides with that reported in other Chilean and Latin American series and highlights the adaptive capacity of the health system in the face of an unprecedented health crisis. However, there was a non-significant trend towards a delay in institutional time metrics and a decrease in the number of patients treated. This trend could be associated with delays in neuroimaging acquisition, highlighting the need to review and optimize local protocols in stroke centers. Efficient management to reduce these times is crucial to ensure timely access to reperfusion therapies, given their direct impact on neurological and functional prognosis. In this sense, the results of this study could guide the development of response protocols for future health emergencies, focusing on maintaining the continuity and efficiency of acute stroke care, even in contexts of high demand for care.

Contributor roles KZ: conceptualization, methodology, research, resources, writing the original draft, reviewing and editing, project management; MA: formal analysis, methodology, writing the original draft, reviewing and editing; CS: research, resources, writing the original draft, reviewing and editing; JR: conceptualization, methodology, research, resources, writing the original draft, reviewing and editing, project management.

Competing interests The authors completed the ICMJE conflict of interest statement and declared that they received no funds for the realization of this article; they have no financial relationships with organizations that may have an interest in the published article in the last three years and have no other relationships or activities that may influence the publication of the article. Forms can be requested by contacting the responsible author or the Editorial Committee of the Journal.

Financiamiento The authors state that there were no external sources of funding.

Language of submission Spanish.

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Análisis temporal de administración de terapias de reperfusión encefálica durante la pandemia de COVID-19 en un hospital chileno: estudio transversal analítico

RESUMEN

INTRODUCCIÓN La pandemia de COVID-19 generó un gran impacto en los servicios de urgencia, incluyendo la atención del ataque cerebrovascular. Los cambios en los tiempos de administración de terapias de reperfusión encefálica del ataque cerebrovascular han sido poco explorados en Chile. El objetivo de este trabajo fue analizar el impacto que tuvo la pandemia en los tiempos críticos de tratamiento del ataque cerebrovascular, el número de pacientes tratados, la severidad clínica y la presencia de oclusión de vaso mayor.

MÉTODOS Se realizó un análisis retrospectivo de los pacientes sometidos a terapia de reperfusión encefálica en un hospital de Valparaíso, Chile. Se compararon dos grupos de pacientes atendidos un año antes (grupo prepandemia) y un año después (grupo pandemia) del inicio de las restricciones sanitarias.

RESULTADOS Se incluyeron 104 pacientes, con una edad promedio de $67,4 \pm 13$ años y una severidad clínica de $13,5 \pm 6,5$ en la escala NIHSS. Un 91,5% recibió terapia trombolítica. No se encontraron diferencias significativas intergrupales en las métricas de tiempo de tratamiento, número de pacientes tratados, severidad clínica, ni presencia de oclusión de vaso mayor. Aunque hubo una tendencia no significativa de retraso en los tiempos terapéuticos institucionales, se encontró una correlación significativa que sugiere que, a menor tiempo desde el inicio de los síntomas a puerta, menor tiempo de acceso a terapia ($r = 0,84$).

CONCLUSIONES No hubo diferencias en los tiempos terapéuticos del ataque cerebrovascular en el periodo previo a la pandemia y en el periodo pandémico, mostrando similitudes con la experiencia reportada en Chile y resaltando la adaptación del sistema de salud durante la crisis sanitaria. Estudios con diseños epidemiológicos más complejos y muestras mayores complementarán estos resultados.



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