

Thrombolysis in ischemic cerebrovascular accidents

The experience in Boyacá

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Abstract

Introduction: the experience of a thrombolysis program for ischemic cerebrovascular accidents in a Colombian public tertiary care hospital is described.

Objectives: to characterize patients who received intravenous thrombolysis due to an ischemic cerebrovascular accident in this hospital between January 2014 and June 2019.

Materials and methods: a retrospective observational study based on a chart review.

Results: 156 patients were included. The average age was 66.1 years, and 50.6% were women. Only 28.8% were from Tunja. Arterial hypertension was the most prevalent risk factor. The average length of stay was eight days (SD 7.7), and the average window period was 2.8 hours (SD 1.29). The average NIHSS score on admission was 12.4 (SD 5) and at discharge was 4.8 (SD 4.48). The inpatient mortality rate was 14.7%, and the rate of hemorrhagic transformation was 10.9%. The average door-to-needle time was 62.8 minutes (SD 42.95), and the average door-to-imaging time was 23.5 minutes (SD 27.42).

Conclusions: The results obtained contribute to strengthening the epidemiological data on thrombolysis programs for ischemic cerebrovascular accidents in Colombia and Latin America. The geographical distribution of the study population highlights the importance of constructing thrombolysis networks and using tools like telemedicine. (*Acta Med Colomb* 2021; 46. DOI: <https://doi.org/10.36104/amc.2021.1862>)

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Introduction

Cerebrovascular disease (CVD) entails a significant burden of morbidity and mortality today (1-3). According to data from the 2013 global burden of disease study (1), cerebrovascular accidents (CVAs) were the second cause of mortality worldwide (11.8% of deaths) after acute myocardial infarction, and the third cause of disability (4.5% of disability-adjusted life years for all causes). Cerebrovascular disease is also the second cause of death in Colombia (2), with a 2016 mortality rate of 31.99 per 100,000 inhabitants (3).

A CVA is defined by the American Heart Association (AHA) as a demonstrable neurological deficit attributed to focal damage of the central nervous system and due to a vascular cause (4). Within the treatment of acute ischemic CVA, reperfusion therapies play a key role as the most effective alternatives for rapidly re-establishing oxygen supply to the tissues, thus seeking the patient's functional recovery (5, 6).

The need to shorten the time between the onset of symptoms and reperfusion therapy has led to the design of thrombolysis networks, programs and protocols in the institutions which care for patients with acute ischemic CVA.

In this context, some parameters have been established to measure the proper functioning of these programs, including door-to-needle time and door-to-imaging time (6).

The E.S.E. Hospital San Rafael de Tunja is a public tertiary care institution which is a reference center for Boyacá Department and neighboring departments, thus covering a broad geographic area. The institution has a cerebral thrombolysis program which began to function in 2012.

This paper describes the sociodemographic and clinical characteristics, inpatient outcomes and rate of complications of the population of patients who have received intravenous thrombolysis due to ischemic CVA at the E.S.E. Hospital San Rafael de Tunja in the last six years. In addition, the door-to-needle and door-to-imaging times are reported, as some of the care quality indicators listed for thrombolysis programs.

Materials and methods

This is a retrospective observational study carried out in a population of patients who received intravenous thrombolysis due to a diagnosis of ischemic CVA at E.S.E. Hospital San Rafael de Tunja, Boyacá between January 1, 2014 and June 30, 2019.

First, the physical thrombolysis register in the institution's resuscitation room was reviewed to identify the total number of patients. With the approval of the institutional research and bioethics committee, the clinical charts were reviewed, and a database constructed based on this review. This study is aligned with the ethical principles for human research stated in the Declaration of Helsinki (7). Due to its retrospective nature, informed consent was not required.

The inclusion criteria were: patients over the age of 18, a diagnosis of ischemic CVA as proposed by AHA in 2013 (4), and intravenous thrombolysis using recombinant tissue plasminogen activator performed at the E.S.E Hospital San Rafael de Tunja. The exclusion criteria were: telemedicine-directed thrombolysis, hemorrhagic CVA and incomplete clinical charts or those that were not found in the institution's statistics and archive office.

The population's main sociodemographic characteristics were taken, along with the prevalence of premorbid cardiovascular risk factors, clinical variables associated with the CVA event [vascular territory of the CVA, length of hospital stay, time elapsed from the onset of symptoms-arrival at the hospital, time elapsed to assessment by physical therapy, National Institutes of Health Stroke Scale (NIHSS) (8) score on admission], inpatient outcomes (inpatient mortality and NIHSS score at discharge), most relevant inpatient complications (hemorrhagic transformation, aspiration pneumonia, and pressure sores) and quality indicators of the thrombolysis program (door-to-needle and door-to-imaging times).

The NIHSS score was determined by the neurologist on duty both at patient admission as well as discharge. This was further categorized according to Muchada et al.'s proposal in 2014 (9) as follows: mild ≤ 8 points, moderate 9-15 points and severe ≥ 16 points. For hemorrhagic transformation, the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) was used, which conceptualizes it as a parenchymal space-occupying hemorrhage which covers more than 30% of the infarcted area, as seen on imaging 22-36 hours after thrombolytic treatment (10). We also analyzed whether the hemorrhagic transformation was associated with neurological deterioration quantified using the NIHSS score. For the pressure sores variable, the diagnosis was tracked in the clinical charts, and an active search was performed comparing this study's database with the institution's healthy skin service and wound clinic databases.

The statistical analysis was performed using Microsoft® Excel®, Mac Version 14.4.3 -140616-, 2011. Frequency distributions and proportions were calculated for categorical variables, and measures of central tendency with their respective measures of dispersion were calculated for continuous variables.

Various biases could be present in this study, including selection bias. To avoid this, inclusion and exclusion criteria were specified. Another possible bias is information bias, which was controlled for by specifying a list of variables to be analyzed from the beginning; in addition,

those in charge of collecting data were aware of how to complete the database.

Results

A total of 166 patients were identified in the physical register as having received thrombolysis due to a diagnosis of ischemic CVA at the E.S.E. Hospital San Rafael de Tunja between January 1, 2014 and June 30, 2019. Three patients were excluded due to having been thrombolized by telemedicine, two due to incomplete medical charts, and five because their clinical charts were not available in the institution's office of statistics and archives. The final included population was 156 patients: 24 from 2014, 30 from 2015, 35 from 2016, 29 from 2017, 22 from 2018 and 16 from 2019.

The population's average age was 66.1 years, with a range from 30 to 92 years. The sociodemographic characteristics are shown in Table 1. The clinical variables, outcomes, complications and inpatient mortality are shown in Table 2.

Altogether, 48.72% of the patients were admitted with a moderate NIHSS score (between 9 and 15 points), while 69.9% of the patients were discharged with a mild score or with no deficit (between 0 and 8 points). Of the patients who survived, 92.5% improved their NIHSS score during hospitalization, with an average 6.9 point decrease (SD 4.9). The rate of hemorrhagic transformation after thrombolysis was 10.9%, and only five patients (3.2% of the total) had neurological deterioration related to the hemorrhagic transformation. The admission and discharge NIHSS scores are found in Table 3 and are diagrammed by severity category in Figures 1 and 2.

The key times for programs caring for patients with acute ischemic CVA are shown in Table 4. In 59% of the cases, the door-to-needle time was less than 60 minutes and in 43.6% it was less than 45 minutes. Furthermore, in 63.7% of the patients, the door-to-imaging time was less than 20 minutes.

Discussion

Worldwide, only 2-10% of patients with ischemic CVA are thrombolized (10). This study describes the largest population of patients receiving thrombolysis for ischemic CVA to date in Colombia (156), compared to studies from the Hospital Universitario San Ignacio (24 patients) (12), Hospital Universitario Fundación Santa Fe de Bogotá (70 patients) (13) and Fundación Hospital Universidad del Norte (27 patients) (14).

The benefit of intravenous thrombolysis in terms of mortality and dependence for patients with ischemic CVA is widely recognized in the literature (OR 0.85 three to six months after the event, according to a recent meta-analysis) (15), especially with the implementation of multidimensional programs which extend the intervention's reach (6, 16-18). The results of our program show an improvement in the NIHSS score in most thrombolized patients, with a mean decrease of more than 4 points, which favors the

clinical effectiveness of this treatment. The average discharge NIHSS score found (4.8) is lower than that reported in the Colombian studies from the Hospital Universitario Fundación Santa Fe de Bogotá (7, 13) and the Fundación Hospital Universidad del Norte (9, 14).

The main adverse event related to thrombolysis in ischemic CVA is symptomatic intracranial hemorrhage (15). The total hemorrhagic transformation rate at our institution (10.9%) is higher than that reported in the Colombian Hospital Universitario Fundación Santa Fe de Bogotá study (4%) (13), and Tosta et al.'s study in Brazil (6%) (19). The rate of hemorrhagic transformation with neurological deterioration (3.2%) is lower than reported in Khan et al.'s study in Dubai (6.8%) (20), but slightly higher than that of the Hospital Universitario Fundación Santa Fe de Bogotá (2.8%) (13) and the SITS-MOST study (1.7%) (21). The inpatient mortality rate (14.7%) is higher than that reported in the Hospital Universitario San Ignacio (12.5%) (12) and the Hospital Universitario Fundación Santa Fe de Bogotá (9%) (13) studies, and very similar to the rate reported in the Chilean study by Guevara et al. (14.8%) (22), also carried out in a public hospital. Altogether, 2.6% of the study patients died from hemorrhagic transformation related to the thrombolytic procedure.

With regard to inpatient complications, the rate of aspiration pneumonia found (5.1%) is lower than what was reported in Licona et al.'s study in 2009 (12.5%) (23), Wilson's

study in 2012 (8.1%) (24), and the rate of chest infections reported by Langhorne in 2000 (22%) (25). Moreover, the rate of pressure sores (0.6%) is lower than that reported by Amir et al. in 2013 (22%) (26) and by Langhorne (21%) (25), but higher than that reported by Bilir in 2019 (0%) (27). The data supplied by the other Colombian studies (12-14)

Table 2. Clinical variables, outcomes and inpatient complications associated with the CVA event.

Variable		Frequency (N) %
Vascular territory of the CVA (n= 156)	Left middle cerebral artery	46.2 (72)
	Right middle cerebral artery	44.9 (70)
	Posterior circulation	3.9 (6)
	Lacunar	2.6 (4)
	Multitopographic	1.9 (3)
	Anterior cerebral artery	0.6 (1)
Pre-morbid risk factors associated with CVA (n= 156)	Arterial hypertension	66 (103)
	Diabetes mellitus	16.7 (26)
	History of prior CVA	14.7 (23)
	Smoking	10.9 (17)
	Atrial fibrillation	10.3 (16)
	Coronary disease	10.3 (16)
	Dyslipidemia	2.6 (4)
Inpatient mortality (n= 156)	Total	14.7 (23)
	Due to hemorrhagic transformation after thrombolysis	2.6 (4)
	Due to edema associated with ischemic CVA	7.1 (11)
	Due to aspiration pneumonia	2.6 (4)
	Due to other causes	2.6 (4)
Hemorrhagic transformation after thrombolysis (n= 156)	Total	10.9 (17)
	With neurological deterioration	3.2 (5)
	Without neurological deterioration	7.7 (12)
Aspiration pneumonia during hospitalization (n= 156)		5.1 (8)
Pressure sores during hospitalization (n= 156)		0.6 (1)
<i>Source: Authors.</i>		

Table 1. Sociodemographic characteristics of the population.

Variable		Frequency (N) (%)	
Age group (n= 156)	Under 65 years	37.2 (58)	
	Between 65 and 79 years	51.9 (81)	
	80 years or older	10.9 (17)	
Sex (n= 156)	Male	49.4 (77)	
	Female	50.6 (79)	
Place of origin (n= 156)	Boyacá	91.7 (143)	
		Tunja	Other towns
		31.5 (45)	68.5 (98)
	Santander	6.41 (10)	
Others	1.9 (3)		
Zone of origin (n= 156)	Urban/county seat	62.8 (98)	
	Rural	37.2 (58)	
Type of health insurance (N= 156)	Contributory	37.8 (59)	
	Subsidized	57.7 (90)	
	Special	4.5 (7)	
<i>Source: Authors.</i>			

Table 3. Admission and discharge NIHSS scores.

Variable	Mean	Standard deviation (SD)	Median	Interquartile range (IQR)
Admission NIHSS score (N= 156)	12.4	5	12	7
Discharge NIHSS score (N= 133)	4.8	4.48	4	7
<i>Source: Authors.</i>				

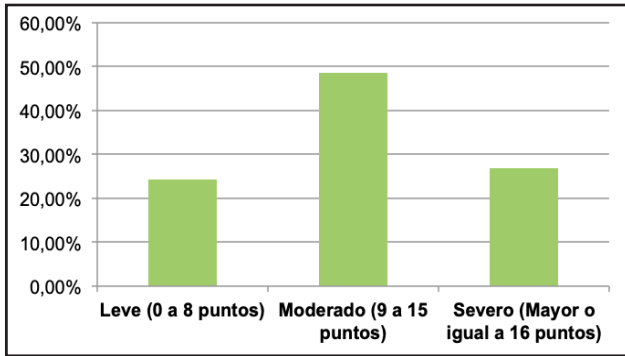


Figure 1. NIHSS score on admission, according to severity categories. Source: Authors.

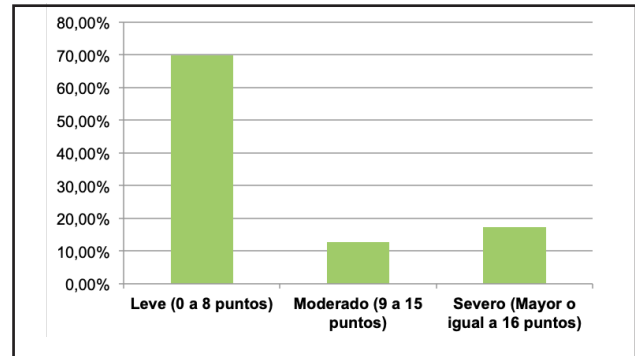


Figure 2. NIHSS score at discharge, according to severity categories. Source: Authors.

Table 4. Key times for acute ischemic CVA care programs.

Variable	Mean	Standard deviation (SD)	Median	Interquartile range (IQR)
Length of hospital stay (days)	8	7.7	6	5
Time elapsed from onset of symptoms to arrival at the hospital (hours)	2.7	1.29	3	1.5
Door-to-imaging time (minutes)	23.5	27.42	16	25.5
Door-to-needle time (minutes)	62.8	42.95	50	52.5
Time elapsed to assessment by physical therapy (hours)	47.5	51.6	24	48

Source: Authors.

do not allow a comparison with the rate of complications found in our institution.

The average length of hospital stay found in this study (eight days) is lower than that reported in the other Colombian studies (10.8 days and 10.4 days) (12, 13) and in Canada (34-47 days), but higher than what is reported in the United States (six days) (28). The time elapsed from the onset of symptoms to arrival at the hospital was greater than that reported in national and international studies (13, 14, 19, 20-31), which could be related to the broad geographical area from which our population was derived, together with the delays in the region’s ambulance system, a problem which has already been discussed in other Colombian departments (32).

On the other hand, the door-to-needle and door-to-imaging times were lower than those in the other Colombian studies (13, 14) and most of the international studies (19, 22, 30, 33). Although some of these studies included data from before 2014, these lower times could be related to continuous communication of the thrombolysis program in our area of influence, which leads to early activation of the CVA code by the referral site and expedites care at the receiving center. In 2018, AHA established a primary ob-

jective for the door-to-needle time of 60 minutes in $\geq 50\%$ of thrombolized patients and a secondary objective of less than 45 minutes in $\geq 50\%$ of thrombolized patients (6). With regard to door-to-imaging time, a goal was set of less than 20 minutes in at least 50% of the patients who may be candidates for reperfusion therapy (6). The data confirm that E.S.E. Hospital San Rafael de Tunja meets the primary door-to-needle time objective and the door-to-imaging time objective proposed by the AHA (6).

In this study, it is noteworthy that most of the population came from towns other than Tunja, the city in which the institution is located. This supports the usefulness of establishing regional networks for managing CVA, as has been proposed in the recent evidence (6, 16-18). In addition, it should be highlighted that the Boyacá thrombolysis network has been complemented since 2019 with telemedicine, as a recognized strategy for optimizing reperfusion therapy times and thus improving patient outcomes (34, 35). E.S.E. Hospital San Rafael de Tunja implemented the first telethrombolysis experience in Colombia together with E.S.E. Hospital Regional de Duitama, and will soon do so with four more institutions in four other cities in the department of Boyacá.

Conclusion

Cerebrovascular disease incurs a significant burden of morbidity, mortality and disability (1-3). Reperfusion strategies are recognized as the fundamental pillar of treatment, and therefore should be improved through the implementation of programs, construction of care networks and use of tools such as telemedicine (5, 6, 17, 18, 34, 35). The results obtained contribute to strengthening the epidemiological data on ischemic CVA and thrombolysis programs in Colombia and Latin America.

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