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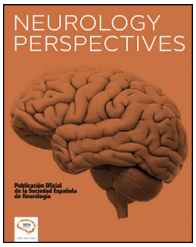

ORIGINAL

Comparison between telestroke versus face-to-face thrombolysis models in stroke management in Colombia

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Abstract Introduction: The incidence of stroke continues to rise globally, as it remains an important cause in overall mortality and disability. Given the fact that several patients cannot access thrombolytic therapy due to neurologist unavailability or because of geographic barriers, Teleictus and Telestroke have become reasonable alternatives for providing treatment. Objective: The Teleictus network in Colombia was first implemented in 2018 in Boyacá; Our main goal was to compare the results of two models approaching patient care in stroke: Telestroke versus Face-to-face thrombolysis. Materials and Methods: This was an observational, analytic study using a retrospective cohort. Sociodemographic, clinical, protocol thrombolysis related and clinical evolution variables were considered into the study. Results 65 patients were allocated to the Face-to-face thrombolysis model and 35 were set into the Telestroke model. Median age was 69 and 67 years respectively; both groups had a higher proportion of women than men. Median symptom-onset-to-door time was 136 min in the Face-to-face thrombolysis and 81 min in the Telestroke model p = 0.0083. Median start NIHSS was eleven points for the former and twelve for the latter. At discharge, both groups had a median NIHSS score of 4. Conclusions: Thrombolytic therapy showed safety and efficacy. First and second level institutions are key in the setup of the Telestroke and Teleictus algorithms. More studies are needed to further evaluate this intervention.

Abbreviations: IV-tPA, Intravenous Tissue Plasminogen Activator; HUSRT, San Rafael de Tunja University Hospital; NIHSS, National Institutes of Health Stroke Scale; NCCT, non contrast CT scan; AHA, American Heart Association; sICH, Symptomatic Intracerebral Hemorrhage

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PALABRAS CLAVE
Ataque Cerebrovascular Agudo;
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Telemedicina;
Modelo de atención

Comparación del modelo de teletrombólisis versus trombólisis presencial en el manejo del ataque cerebrovascular isquémico en Colombia

Resumen Introducción: el ataque cerebrovascular (ACV) ha aumentado su incidencia global en los últimos años, asociado constituye causa importante de mortalidad y una de las primeras causas de años perdidos por discapacidad. Por ende, es necesario contar con tratamientos que modifiquen el habitual desarrollo natural de la enfermedad. La trombólisis intravenosa con activador tisular del plasminógeno (tPA) es el principal tratamiento de reperfusión sistémica. Los pacientes no pueden acceder a esta terapia por falta de neurólogos y barreras geográficas, siendo el teleictus o telestroke una opción para que los pacientes no pierdan la ventana terapéutica. Objetivo: la primera red de teleictus en Colombia fue implementada en el año 2018 en Boyacá, nuestro objetivo fue comparar los resultados de dos modelos de atención del ACV: teleictus versus trombólisis presencial. Materiales y Métodos: estudio observacional analítico de cohorte retrospectiva, se tomó como cohorte no expuesta las historias clínicas de población adulta que se le realizó trombólisis presencial y la cohorte expuesta aquellas en las que se realizó mediante teleictus en el periodo comprendido entre junio de 2019 y abril 2021. Se tuvieron en cuenta variables sociodemográficas: edad, sexo; variables clínicas como NIHSS de ingreso, territorio del ACV; variables relacionadas con los protocolos de Trombólisis como tiempos inicio-puerta, puerta-TC, puerta- aguja; variables de evolución: NIHSS de egreso, complicación hemorrágica, presencia de fibrilación auricular, porcentaje de estenosis carotidea, fracción de eyección (%), días de estancia hospitalaria, mortalidad al egreso y a los 3 meses. Resultados: se identificaron 65 pacientes con ACV manejados con el modelo de trombólisis presencial y 35 con teleictus. La mediana de edad de los pacientes fue de 69 y 67 años en los grupos respectivamente; con mayor frecuencia del sexo femenino en ambos grupos. Se observó una mediana de tiempo inicio – puerta de 136 minutos (RIC): 81–180 en el grupo presencial y de 81 minutos (RIC): 44–51 en el grupo de teleictus, p = 0,0083. Los tiempos puerta-TC y puerta-aguja mostraron respectivamente medianas de 4,6 y 49,50 respectivamente con una p > 0,05. La mediana del NIHSS de ingreso fue de 11 en el presencial y 12 en teleictus y la mediana del NIHSS de egreso fue de 4 en ambos grupos. Hubo hematoma parenquimatoso tipo 2 (PH2) a las 24 horas después de la aplicación de tPA en 6.1% de los pacientes en trombólisis presencial y 5,7% del teleictus, sin encontrarse diferencias significativas en los 2 grupos. No existieron diferencias significativas con respecto a la estancia hospitalaria, vivo al egreso y a los 90 días y en los fallecidos totales en los grupos comparados. El análisis de asociación ajustada mostró que el modelo de atención por telestroke tiene un OR de 3,49 (IC 95%: 1,45 – 8,42) para obtener un tiempo inicio puerta menor o igual a 81 minutos, comparado con el modelo presencial. Conclusiones: La terapia trombolítica es segura y eficaz demostrado por las medianas del NIHSS al egreso, la incidencia de PH2 y la mortalidad al egreso y a los 3 meses. Nuestros datos soportan que los pacientes que se encuentran distantes de un centro primario de atención del ACV pueden acceder a la terapia trombolítica acortando una brecha geográfica. Se reconoce la importancia de los hospitales de primer y segundo nivel de complejidad en el algoritmo telestroke o teleictus. Es necesario que esta experiencia se pueda replicar en diferentes instituciones del país ya que se necesitan más estudios prospectivos.

Introduction

The global incidence of stroke keeps rising. In Colombia, the stroke incidence lays between 85–87 cases per 100,000 people.[1,2] It represents one of the most important causes of overall mortality and disability.[3,4] Further treatments are needed to modify the natural course of the disease.

Tissue plasminogen activator thrombolysis (IV-tPA) is the most important treatment for systemic reperfusion approved for stroke patients.[5] Its administration should be

supervised by a vascular neurologist or a stroke specialist. Nonetheless, the lack of neurologists and the geographic barriers pose an important challenge that precludes rural areas from receiving adequate stroke care.[5,6] Considering this, the American Heart Association (AHA) has endorsed the use of telemedicine for Stroke workup and treatment; such strategy is also known as Teleictus or Telestroke.[7]

While some centers are able to perform thrombolysis and keep these patients in observation after receiving tPA (on-site thrombolysis or Face-to-face thrombolysis), others need the advice and expertise from a specialized team that remotely directs and sets up IV thrombolysis and then sends the patients to a concentration stroke center (Telestroke strategy). In our study, we used the experience from the San Rafael Tunja University Hospital (HUSRT), which works as a regional reference center (face-to-face thrombolysis center).

Considering this, we decided to conduct a study with the aim of comparing the outcomes of stroke treatment using the Telestroke versus the Face-to-face thrombolysis models of care.

Materials and methods

We performed a retrospective, analytic, observational study using 2 cohort groups comparing the clinical evolution and outcomes of adult patients that underwent stroke treatment using either the Face-to-face thrombolysis or the Telestroke strategies between June 2019 and April 2021. Socio-demographic, clinical, protocol thrombolysis related and clinical evolution variables were analyzed in all patients.

Our main goal was to evaluate the National Instituted of Health Stroke Scale (NIHSS) score at discharge. Other secondary outcomes that were studied were hospital length of stay, in-hospital mortality, and mortality after 3 months. We also studied the intracerebral hemorrhage (ICH) incidence during the first 24 h after thrombolysis, using non contrast CT scan (NCCT), as a variable to assess the safety of the thrombolytic therapy in both scenarios. CT scan studies were evaluated using appropriate classifications[8] by two members of the research team. This study was approved by the ethics committee of the HUSRT.

Statistical analysis

Qualitative variables were processed using absolute and relative frequency calculations, and quantitative variables were analyzed using median(Me) as measures of central tendency, with their respective measure of dispersion: interquartile range (IQR) and the Shapiro–Wilk test to stablish nonparametric behavior.

In order to compare the qualitative demographic and clinical characteristics between the Face-to-face thrombolysis and Telestroke model groups, Chi-squared and Fisher exact test were used when indicated. Qualitative variables were studied using the T test or the Mann Whitney U Test. A p level under 0.05 was set as statistically significant. Association analysis was conducted using the crude and adjusted odds ratio (OR) using logistical regression with a 95% confidence interval (95% CI).

We considered the patients in the experimental groups as independent variables and primary and secondary outcomes as dependent variables. Sociodemographic, clinical, thrombolysis specific and evolution variables were adjusted for confounders.

Results

During the study period, 65 stroke patients were treated using the Face-to-face thrombolysis model and 35 were intervened using the Telestroke model in the HUSRT. Median age was 69 and 67 for each group. Women outnumbered men in both groups; 52.3% were women in the Face-to-face thrombolysis group and 62.8% in the Telestroke group.

Regarding attention times, a median onset-of-symptoms to door time was calculated at 136 min (IQR 81–180) for the Face-to-face thrombolysis group and 81 min (IQR 44–155) for the Telestroke group $p = 0.0083$. In the case of the door-to-CT and door-to-needle times, their respective median was 4, 6 and 49, 50 min; neither were statistically significant between both groups ($p > 0.05$) Table 1.

When comparing clinical characteristics of the stroke patients in the face-to-face thrombolysis and telestroke groups, we found an initial NIHSS score of 11 and 12 points respectively. 80% of the patients had an anterior circulation stroke and more than 50% of patients had a left stroke, slightly higher than right stroke. The most compromised arteries were the Middle Cerebral Artery (MCA) (76.9% for the Face-to-face thrombolysis group and 82.8% for the Telestroke group), followed by the Posterior Cerebral Artery (PCA) (13.8% in the Face-to-face thrombolysis group) and the Anterior Cerebral Artery (5.7% in the Telestroke group). No statistically significant differences were observed between the NIHSS scores, stroke territories, side and affected arteries of the study groups Table 2.

When analyzing the etiologies of the strokes included in the study, we found an auricular fibrillation frequency of 21.5% in the Face-to-face thrombolysis group and 40% in the Telestroke group ($p = 0.04986$). The percentage of carotid stenosis lower than 50% was 93.8% for the Face-to-face thrombolysis group and 88.5% for the Telestroke group. The Left Ventricle Ejection Fractions (LVEFs) reported for the

Table 1 General characteristics and comparison between the attention timeframes of stroke patients in the Face-to-face thrombolysis and Telestroke models.

	Face-to-face thrombolysis N = 65 n (%)	Telestroke N = 35 n (%)	*p* value
Median Age (IQR)	69 (57–79)	67 (55–80)	0.7835
Sex			
Female	34 (52.3)	22 (62.8)	0.3107
Male	31 (47.7)	13 (37.1)	
Median Attention timeframes (IQR)			
Onset-to-door	136 (81–180)	81 (44–151)	0.0083
Door-to-CT	4 (3–16)	6 (4–9)	0.7869
Door-to-needle	49 (32–64)	50 (40–67)	0.1685

Table 2 Comparison between the clinical characteristics of stroke patients in the Face-to-face thrombolysis and Telestroke models.

	Face-to-face thrombolysis N = 65 n (%)	Telestroke N = 35 n (%)	*p* value
Stroke Characteristics			
Initial NIHSS	11 (6–15)	12 (8–16)	0,6071
Stroke circulation			
Anterior	55 (84.6)	32 (91.4)	0,5341
Posterior	11 (16.9)	3 (8,5)	0,3676
Anterior–Posterior	1 (1.5)	0 (0.0)	0,9998
Side			
Bilateral	2 (3.0)	0 (0.0)	0,5404
Right	18 (27.6)	16 (45.7)	0,0695
Left	36 (55.3)	18 (51.4)	0,7049
Posterior	9 (13.8)	1 (2.8)	0,1585
Compromised artery			
MCA	50 (76.9)	29 (82.8)	0,4871
ACA	1 (1.5)	2 (5.7)	0,2796
AICA	1 (1.5)	1 (2.8)	0,9999
PICA	0 (0.0)	1 (2.8)	0,3500
PCA	9 (13.8)	1 (2.8)	0,1585
Lacunar	3 (4.6)	1 (2.8)	0,9997
Multiple vessels	1 (1.5)	0 (0.0)	0,9998
No infarction	1 (1.5)	0 (0.0)	0,9998

NIHSS: National Institutes of Health Stroke Scale.
MCA: Middle Cerebral Artery.
ACA: Anterior Cerebral Artery.
AICA: Anterior Inferior Cerebellar Artery.
PICA: Posterior Inferior Cerebellar Artery.
PCA: Posterior Cerebellar Artery.

patients were non-significant between the groups. The most common hemorrhagic complications were the Hemorrhagic Infarction type 1 and the Hemorrhagic Infarction type 2; intraparenchymal hemorrhage was observed at a lower percentage.

When comparing the evolution data of the patients, both groups had a discharge NIHSS score of 4 $p = 0.9091$. Hospital length of stay show a median of 4 in both groups. At discharge, 89.2% of patients in the Face-to-face thrombolysis model were alive, compared to 77.1% in the Telestroke model. 3-month survival rate was calculated at 81.5% and 65.7% for the Face-to-face thrombolysis and Telestroke models respectively. Total of deceased patients was 13.8% in the Face-to-face thrombolysis group and 28.5% in the Telestroke model. No statistically relevant data was found for the hospital length of stay, survival at discharge and 3-month survival variables Table 3.

The adjusted association analysis showed that the Telestroke model has a OR of 3.49 (95% CI; 1.45–8.42) of having an onset-of-symptoms to door time equal or less than 81 min comparted to the Face-to-face thrombolysis model. Associations between survival at discharge, 3-month survival and mortality did not yield statistically significant differences.

Discussion

The San Rafael Tunja University Hospital successfully performed the first telethrombolysis strategy in Colombia as an answer to the need to provide adequate care and thrombolysis to stroke patients from other counties away from Tunja, where the hospital is located.[9] Stroke patients coming from up to 56.6 km away from our main institution were successfully treated, lowering the geographic coverage gap[10] and allowing the creation of a virtual network covering the main hospitals in the region.

The clinical characteristics of the patients who underwent thrombolysis in both groups were similar.

Our study found that the age of presentation of stroke was similar in both groups, with a discrete higher prevalence in female patients; this is different from the findings published in the TEMPis and NINDS studies,[11] as well as the Chilean experience,[6] where the majority of patients were men, aged 68, 67 and 65.6 years respectively. A systematic analysis of the stroke burden of disease found that, when classified into age groups, stroke incidence is similar between men and women under 55 years, but significantly higher in men for ages between 55 and 75.[1] Furthermore, some Colombian epidemiology studies report a higher incidence for men as well.[12]

Average initial NIHSS score was marginally lower than the ones reported in TEMPis and NINDS (13 and 14 points each)[11] and in the Chilean study (8 points),[6] but it still was higher than some studies that reported an average of 5 points.[13] Compared to a previous systematic review published in Colombia, the initial NIHSS scores were similar to the ones observed in Bogotá (average 11.7 points), but higher than the ones found in an article in Barranquilla in

Table 3 Comparison between the complementary studies, complications and evolution of stroke patients in the Face-to-face thrombolysis and Telestroke models.

	Face-to-face thrombolysis N = 65 n (%)	Telestroke N = 35 n (%)	Valor P
Complementary studies			
AF	14 (21.5)	14 (40.0)	0,04986
Internal Carotid Artery Stenois %			
<50%	61 (93.8)	31 (88.5)	0,4453
≥50%–99%	1 (1.54)	1 (2.8)	0,9999
100%	1 (1.54)	0 (0.0)	0,9998
NA	1 (1.54)	2 (5.7)	0,2796
Thrombus	1 (1.54)	1 (2.8)	0,9999
LVEF	58 (53–62)	57 (52–62)	0,9781
Hemorrhagic complications			
HI1	10 (15.3)	4 (11.4)	0,7651
HI2	6 (9.2)	3 (8.5)	0,9129
No	41 (63.0)	26 (74.2)	0,2555
PH1	3 (4.6)	0 (0.0)	0,2355
PH2	4 (6.1)	2 (5.7)	0,9300
NA	1 (1.5)	0 (0.0)	0,9998
Evolution data			
Discharge NIHSS	4 (2–9)	4.5 (1–10)	0,9091
HL	4 (2–7)	4 (3–6)	0,7593
Survival at discharge	58 (89.2)	27 (77.1)	0,1427
3 month survival	53 (81.5)	23 (65.7)	0,0771
Total deceased	9 (13.8)	10 (28.5)	0,0733

AF: Atrial Fibrillation; LVEF: Left Ventricular Ejection Fraction; HI 1: Type 1 Intracerebral Hemorrhage; HI 2: Type 2 Intracerebral Hemorrhage; PH1: Type 1 Parenchymal hematoma; PH2: Type 2 Parenchymal hematoma; NA: Not available; HL: Hospital length of stay(days).

2017 (9 points) and lower than those in Cali in 2014 (12.9 points).[14]

The reported median onset-of symptoms-to-door, door-to-CT and door-to-needle times in our study were within the internationally standardized time frames according to the latest update in the Guidelines for the Early Management of Patients with Acute Ischemic Stroke by the AHA.[15] In this guidelines and other documents, a shorter door-to-needle time is heavily emphasized, as stated in the phrase <<time is brain>>.[16]

Among the comparison between the timeframes reported in our study and those reported externally, we observed a lower door-to-CT than the Chilean study (14 min),[6] and a lower average door-to-needle time than what was reported in the TEMPis study in Bavaria (76 ± 24 min),[11] as well as in the Sami Al Kasab cohort (57 min),[13] the Mansilla et al. group (56.5 min)[6] and the study in Catalonia (55 min).[17]

Our median door-to-needle time is remarkably lower than what was reported from on-site thrombolysis studies in Bogotá, Barranquilla, and Pasto (2017), each showing a median time of 98, 175 and 128.6 min respectively.[14] Such reduction in time becomes crucial for countries and regions like ours, where geographic characteristics like mountain ranges become a burden for treatment and where the use of new technological tools can improve attention timeframes to access reperfusion therapies. Thus, telestroke becomes a major strategy to improve door-to-needle time in stroke patients.[18]

Regarding clinical characteristics, stroke was more common in anterior circulation than posterior, with a higher prevalence in the left side. The most affected arteries were the MCA, the PCA and the ACA. We found a patient in the Face-to-face thrombolysis group that did not show arterial occlusion in brain imaging and was then reclassified as a stroke mimic which represents from 5 to 30% of all patients who present cerebral ischemic symptoms in the emergency department. Even in stroke mimics, the thrombolysis safety profile is excellent, and the incidence of ICH is rare. Some of these cases may be ruled out using Magnetic Resonance Imaging (MRI).[19,20]

Median hospital length of stay was 4 days for both groups (Face-to-face thrombolysis and Telestroke). This value was lower than what was found in a previous publication from our own institution there we reported a median of 8 days,[9] something still lower than what was reported in 2 Colombian articles that studied this variable (average of 10.6 days) (Bogotá 2017 and Bogotá 2014).[14] After discharge, all patients were studied for stroke causes using Duplex Carotid Ultrasound, Echocardiogram and Holter electrocardiogram; this protocol marks an improvement in stroke care in our institution and has become an important intervention for secondary stroke prevention.

We found no statistically significant differences in discharge and 3-month mortality. We should stress that external studies have not reported relevant differences in the 90-day mortality rate between the 2 groups.[21] We can then infer that the safety of tPA treatment does not change between on-site thrombolysis and telemedicine.

It should be stated that we could not identify whether the patients' primary cause of death was related to stroke, mostly because patient follow up is considerably hard in our health system, thus becoming a limitation in our study.

Our study had other limitations. Even though the telethrombolysis leg (telestroke) of the study was carried out prospectively, some of the data had to be gathered retrospectively. This is because initially we only used radiologic criteria to diagnose hemorrhagic transformation, without reporting clinical neurologic deterioration, as in the ECAS 1 study.[8,22] However, we considered these data to be important since Type 2 parenchymal hematoma (PH2) has been associated to a devastating effect in early neurologic damage and 3-month mortality.[22]

Despite this, when compared to other relevant thrombolysis studies, we found these associations to be an expected result, given that the ECAS II reported a sICH incidence of 8.1%,[23] TEMPis reported 8.5%[11] and the Elena Lopez-Cacio group reported 4.1% for in-person thrombolysis and 6.1% for telethrombolysis patients.[17] A recent metanalysis did not find significant differences in the thrombolysis safety data (sICH) between the telestroke patients in the Drip and Stay model and those in the Telestroke or Hub models ($p = 0.942$)[24]; furthermore, in a 2 year prospective telestroke experience, symptomatic intracranial hemorrhage was calculated at 6.7%,[25] and a 2016 metanalysis from the American Academy of Neurology also found the sICH rate between the 2 previously stated groups to be similar ($RR = 1.01$, 95% IC 0.37—2.80; $p = 0.978$), effectively confirming the findings from the telestroke experience.

A final limitation was that we couldn't compare the disability in our patients against what is reported in other studies because the modified Rankin Scale assessment was not performed in our patients at discharge.

Conclusions

- There are no statistically significant differences in the discharge NIHSS, the hospital length of stay, discharge mortality and 3-moth mortality between the Telestroke (telehealth) and the Face-to-face thrombolysis (on-site thrombolysis) models.
- Thrombolytic therapy performed by a general practitioner guided by a certified neurologist from a telestroke team is as safe as those performed in a stroke center.
- Our data show that patients who are distant from a stroke center may access thrombolytic therapy through the telestroke model, bypassing the geographic burdens and shortening the timeframes for acute stroke care.
- First and second level institutions are vital to the telestroke and teleictus approach.
- This experience ought to be replicated in other institutions around the country to further confirm the evidence the findings concerning these two approaches to stroke care.

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Patient consent

Does not apply.

Protection of human and animal subjects

The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent

The authors declare that no patient data appear in this article.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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