

# Hospital service for ischemic stroke patients in Brazilian countryside: are we still in the '80s?

## *Tratamento hospitalar a vítimas de acidente vascular cerebral isquêmico no interior do Brasil: ainda estamos na década de 80?*

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Arq. Neuropsiquiatr. 2022;80(8):770–778.

### Abstract

**Background** Stroke is one of the most common causes of death and incapacity in the world. The benefits of reperfusion therapies and hospitalization in neurologic intensive care units (ICUs) are undeniable. However, these treatments are not widely available in a continental-sized country like Brazil.

**Objective** To describe the treatment for ischemic stroke and the functional outcome 90 days after the hospitalization of patients in the Brazilian countryside.

**Methods** Observational, prospective case series study design. The data collected refer to randomly selected patients hospitalized in 3 hospitals in the south region of the state of Bahia between December 2018 and December 2019.

**Results** The population consisted of 61 consecutive patients. They were elderly (median age: 62 years old); with a predominance of hypertension (82%); and were light to moderate stroke cases (National Institute of Health Stroke Scale [NIHSS] median: 7). A total of 37.7% of the cases arrived at the hospital in a < 4.5-hour window but received no reperfusion therapy. Of these, 94.3% were discharged from the hospital with a prescription for antiplatelets or anticoagulant. A total of 64.1% of the patients received a statin prescription. At the end of the follow-up period, the general mortality was 21%. Almost half of the population (47.9%) evolved to an unfavored outcome (modified Rankin scale [mRs]: 3 to 6).

**Conclusion** Our population presented sociodemographic and comorbidities characteristics similar to those of other national samples. No reperfusion therapy was used and the treatment was basically secondary and prophylaxis-oriented, and almost half of the population evolved with incapacities and a high mortality rate, despite the initial low clinical gravity.

### Keywords

- ▶ Stroke
- ▶ Risk Factors
- ▶ Hospitalization
- ▶ Prognosis

received  
April 30, 2021  
accepted  
October 11, 2021

DOI <https://doi.org/10.1055/s-0042-1755228>.  
ISSN 0004-282X.

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Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

## Resumo

**Antecedentes** Acidente vascular cerebral (AVC) é uma das principais causas de morte e incapacidade no mundo. Os benefícios das terapias de reperfusão e hospitalização em unidade intensiva neurológica são inegáveis. Porém, estes tratamentos não estão largamente disponíveis em um país de dimensões continentais como o Brasil.

**Objetivos** Descrever o tratamento do AVC isquêmico agudo e a funcionalidade, 90 dias após o evento, de pacientes hospitalizados no interior do Brasil.

**Métodos** Estudo observacional, prospectivo, tipo série de casos. Os dados foram coletados de pacientes consecutivos, aleatoriamente selecionados, internados em 3 hospitais da região Sul da Bahia entre dezembro de 2018 e dezembro de 2019.

**Resultados** A população amostral consistiu de 61 pacientes. Houve predomínio de idosos (mediana de idade: 62 anos), hipertensos (82%), com AVC leve a moderado (mediana do National Institute of Health Stroke Scale [NIHSS, na sigla em inglês]: 7), dos quais 37,7% chegaram ao hospital com <4,5 horas de sintomas, mas não receberam terapias de reperfusão. Um total de 94,3% dos pacientes recebeu alta com prescrição de antiagregante plaquetário ou anticoagulante e 64,1% receberam prescrição de estatina. Ao final do período de seguimento, a mortalidade geral foi de 21% e quase metade da população amostral (47,9%) evoluiu com desfecho desfavorável (escala de Rankin modificada: 3 a 6).

**Conclusão** A população amostral apresentou características sociodemográficas e comorbidades semelhantes às de outros recortes nacionais. Terapias de reperfusão não foram realizadas e o tratamento foi basicamente orientado para profilaxia secundária. Quase metade da população evoluiu com incapacidade ou morte, apesar da baixa gravidade clínica à admissão.

## Palavras-chave

- ▶ Acidente Vascular Cerebral
- ▶ Fatores de Risco
- ▶ Hospitalização
- ▶ Prognóstico

## INTRODUCTION

Stroke is one of the main causes of death and incapacity in the world.<sup>1</sup> This disease has a high percentage (90%) of potentially preventable cases when controlled for 10 risk factors pointed out by O'Donnell et al.<sup>2</sup> Still, the event remains prevalent in Brazil and is responsible for > 100,000 annual deaths, accounting for 1,437.74 years of healthy lives lost in 2016.<sup>3</sup>

The suitable treatment for ischemic stroke involves controlling for risk factors to prevent new events, preventing associated complications, treating specific pathophysiologic processes, facilitating recovery, and lowering incapacities.<sup>4</sup>

Reperfusion therapy for ischemic stroke has become a milestone of stroke treatment since 1995, having its benefit documented when performed up to 4.5 hours after the first symptoms.<sup>5</sup> The second significant milestone happened in 2015 when the benefits of mechanical thrombectomy were established as a fundamental part of ischemic stroke treatment up to 6 hours after the onset of symptoms,<sup>6</sup> and, more recently, its efficacy was endorsed for selected patients treated 6 to 24 hours after the onset of symptoms.<sup>7</sup>

Many of these advances are not consolidated or available in Brazilian hospitals, despite being regimented by the Brazilian Unified Health System (SUS, in the Portuguese acronym), especially in the least favored areas away from the big cities. A study by the Federal Medicine Board indicated that 76% of Brazilian hospitals did not have an adequate

stroke treatment structure, according to doctors interviewed in 2017.

Understanding medical assistance conditions in small centers allow better-adequate planning in the application of resources of the SUS. Therefore, the present study aimed to describe the characteristics medical assistance for ischemic stroke patients in the countryside of the state of Bahia.

## METHODS

### Study design

The present study is prospective, observational, with randomly selected consecutive patients hospitalized for acute ischemic stroke in 3 hospital units in the macroregion of the South of Bahia.

### Site of investigation

The microregion of the South of Bahia consists of 68 municipalities and 1,691,844 inhabitants, subdivided into the Health Regions of Ilhéus, Itabuna, Jequié, and Valença. Ilhéus and Itabuna are the most populated ones, and Ilhéus is the primary reference municipality<sup>8</sup> and headquarter of the higher educational institution that fomented the present research.

Epidemiologic regional data from 2007 to 2017 show cerebrovascular diseases as responsible for the highest mortality rate (44/100,000 inhabitants), surpassing cardiac

ischemic disease (35.37/100,000 inhabitants in the same year).<sup>9</sup>

Ilhéus has four hospital units for the admission of adult patients. Itabuna only has two. This data considers tertiary hospitals that can potentially have full care for adults with ischemic stroke, which must fulfill the following criteria (defined by the authors): to be part of the SUS; to have minimal physical structure (24-hour emergency room [ER], tomography, intensive care unit [ICU], and surgery center); and to have a medical team with a neurologist and a neurosurgeon. The following units fulfilled the criteria: Hospital Regional Costa do Cacao (HRCC, in the Portuguese acronym) (public hospital, 180 beds, integrating the state bed regulation system), Hospital São José (HSJ, in the Portuguese acronym) (philanthropic, 100 beds, working both with the SUS and private healthcare), and Hospital Calixto Midlej Filho (HCMF, in the Portuguese acronym) (philanthropic, 179 beds, working both with the SUS and private healthcare).

### Procedures

We visited the HSJ and HCMF units weekly during the present study. Data collection in the HRCC took place only in part of this period due to administration changes. All cases consisted of hospitalized patients under suspicion of ischemic stroke within < 7 of the onset of symptoms. All participants were > 18 years old and agreed to take part in the study.

### Exclusion criteria

Intracranial hemorrhage present on imaging exam.

Patients were followed-up during hospitalization until medical discharge and after 2 moments: 30 and 90 days after the stroke.

We investigated demographic characteristics, stroke risk factors, prehospitalization information, hospital admission information, first symptoms and hospital arrival timeframe (delta T), vital signs, and the National Institute of Health Stroke Scale (NIHSS).

We also considered other factors, such as the frequency of reperfusion therapies, their nonapplication associated factors, hospitalization in ICU or wards, frequency of complications (related infections, venous thromboembolism, and reoccurrence), intrahospital rehabilitation, medication prescriptions, hospitalization period, results of etiologic investigation exams, stroke subtype according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria, and intrahospital mortality.

We considered the modified Rankin scale (mRs) graduation within 30 and 90 days after the event, an automatized version of the SSS-TOAST application,<sup>10</sup> and the Causative Classification of Stroke (CCS). The CCS concerned the last evaluation with all intrahospital and postdischarge examinations, until the end of the segment, for a better discrimination of the etiologic subtypes.<sup>11</sup>

### Ethical aspects

The present study was submitted to the Ethical Research Committee at the Universidade Estadual de Santa Cruz (UESC, in the Portuguese acronym), Ilhéus, state of Bahia,

Brazil, taking place after being approved by the Committee under the statement CAAE 03669118.7.0000.5526, issued on December 17<sup>th</sup>, 2018.

### Statistical analysis

We calculated the mean, median, standard deviation (SD), and interquartile range (IQR) for continuous variables and for proportions of categorical and ordinal variables and proportions for the descriptive statistical analysis.

The initially planned exploratory analyses were not carried out due to the sample size, below our target of 100 patients. The statistical tests were performed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA).

## RESULTS

### Population

As shown in ►Table 1, 61 patients were included in the present study, with a median age of 62 years old (39 to 98 years old), brown skin (63.9%), and male (59%) predominance. The median for *per capita* income was R\$ 954,00/month, while education had a median of 6.5 years.

### Prior pathological history

►Table 1 also shows the most common comorbidities: systemic arterial hypertension (82%), diabetes mellitus (34.4%), dyslipidemia (16.4%), and atrial fibrillation (13.1%). Also, 11.1% of the patients declared to be active smokers (last 12 months), and 9.8% declared heavy alcohol consumption (> 5 consecutive alcoholic doses/previous month or > 14 doses/week for women and 21 for men). Although a prior stroke was reported by 19.7% of the patients, none had a disability (mRs ≤ 2).

### Clinical presentation

Most patients (73.8%) were at home when the first symptoms occurred, as seen in ►Table 2. Only 16.4% called the ambulance of the Emergency Mobile Care Service of the SUS (SAMU, in the Portuguese acronym). First care took place at a local care unit (Unidade de Atendimento [UPA, in the Portuguese acronym]) or at a small hospital in 24.6% of the cases. The median time from the onset of the first symptoms until arrival at the hospital was 8 hours. All patients had a cranial tomography within a median of 4 hours. The majority was hospitalized directly in a ward.

►Table 2 also refers to the graduation of symptoms applied until the 7<sup>th</sup> day after the stroke. According to the NIHSS scale, 62.3% presented an NIHSS between 0 and 9; of these, 22 (36.1%) were patients with light symptoms (NIHSS between 0 and 4). On the other hand, only 10 (or 16.4%) had severe symptoms (NIHSS ≥ 15). Admission glycemia and blood pressure factors were only present in 9 records, with a median blood glucose of 115.5 mg/dL (77 to 205 mg/dL). The median blood pressure was 140 × 80 mmHg (120 × 60 to 190 × 110 mmHg).

### Hospital care

None of the patients were submitted to reperfusion therapies. However, 23 patients (37.7%) were hospitalized in a

**Table 1** Sociodemographic characteristics and comorbidities

Characteristics		All patients (n = 61)
Sociodemographic data	Age, years old (median, IQR*)	62 (56–77.5)
	Male	36 (59%)
Ethnicity	Brown	39 (63.9%)
	White	13 (21.3%)
	Black	9 (14.8%)
Public health system		43 (70.5%)
City of origin	Ilhéus	39 (63.9%)
	Itabuna	9 (14.8%)
	Others	13 (21.3%)
Retirees		30 (49.2%)
Education, years (median, IQR)		6.5 (3–12)
< 1 year (illiterate)		11 (18%)
1–9 years (elementary school)		28 (45.9%)
10–12 years (high school)		12 (19.7%)
> 12 years (university degree)		10 (16.4%)
Per capita income in Reais (median, IQR)		954 (500–2000)
up to half of the minimum wage		11 of 58 (19%)
half to one minimum wage		20 of 58 (34.5%)
one to two minimum wages		12 of 58 (20.7%)
> 2 minimum wages		15 of 58 (25.9%)
Comorbidities and risk factors	Systemic arterial hypertension	50 (82.0%)
	Diabetes mellitus	21 (34.4%)
	Dyslipidemia	10 (16.4%)
	Atrial fibrillation	8 (13.1%)
	Prior stroke	12 (19.7%)
	Active smoking	7 (11.5%)
	Alcoholism	6 (9.8%)
	Overweight (BMI $\geq$ 25 and $<$ 30 kg/m <sup>2</sup> )	22/56 (39.3%)
	Obesity (BMI $\geq$ 30 kg/m <sup>2</sup> )	13/56 (23.2%)
	Sedentary lifestyle	54 (88.5%)
Good previous functionality (mRs $\leq$ 2)		61 (100%)

Abbreviation: BMI, body mass index; IQR interquartile range; mRs, modified Rankin scale.  
\*IQR: interquartile range 1<sup>st</sup>–3<sup>rd</sup>.

high-complexity unit in a feasible time window for venous thrombolytic treatment (delta T < 4.5 hours).

None of the patients were submitted to a contrasted vessel study during admission, even at the units with available computed tomography (CT) angiography and digital arteriography equipment available. At least 1 evaluation for dysphagia was noted in 42.6% of the cases, and physiotherapy care treatment was identified in 49.2%.

Sixteen patients (26.2%) experienced infections, especially in the respiratory (62.5%) tract. Carotid revascularization was not performed in any case. Electrocardiogram, echocardiogram, as well as carotid and vertebral duplex scans, were present in, respectively, 80.3, 32.8, and 31.1 of the records of

the patients. We also identified lipidic profile (42.6%) and blood glucose (67.2%) results in the sample.

According to the TOAST etiologic classification, 78.7% of the patients were classified as being of the undetermined etiologic subtype (UN). During discharge (patients alive: 53), 79.3% received an antiaggregative (acetylsalicylic acid or clopidogrel) prescription. Anticoagulants were prescribed to 15.1% of the patients, while statin was prescribed to 64.1%.

### Mortality and recurrence

The intrahospital mortality was 13.1%, while the median hospitalization time was 10.5 days (minimum of 1 and maximum of 59 days). Hospitalization extended to 2 weeks

**Table 2** Clinical characteristics, hospital management, and complications

Characteristics		All patients (n = 61)
<i>Treatments and Outcomes</i>		
Prehospital data	Wake-up stroke	15 (24.6%)
	Symptoms at home	45 (73.8%)
	Use of SAMU	10 (16.4%)
	Delta T in minutes, median (IQR*)	480 (90–885)
	Tertiary hospital entrance door	46 (75.4%)
	Transfer from UPA or a smaller hospital	15 (24.6%)
Hospital data	Delta T < 4.5 hours	23 (37.7%)
	Delta CT in minutes, median (IQR*)	240 (126.5–532.5)
	ICU admission	6 (9.8%)
Clinical characteristics	NIHSS, median (IQR*)	7 (3–12.5)
	NIHSS < 5	22 (36.1%)
	NIHSS 5–14	29 (47.5%)
	NIHSS ≥ 15	10 (16.4%)
	Capilar glicemia at admission in mg/dL, median, (IQR*)	115.5 (90.2–191)
	Systolic arterial hypertension in mmHg, median (IQR*)	140 (130–172.5)
	Diastolic arterial hypertension in mmHg, median (IQR*)	80 (80–90.5)
Treatments	Hiperacute treatment (rt-PA or thrombectomy)	–
	Eligible by the time window < 4.5 hours for rt-PA usage	23 (37.7%)
	Lost window due to delay in transfer (n)	6
	Lost window due to delay in performing CT (n)	6
	Exclusion criteria for the use of thrombolytic agents (n)	3
	Not performed for unknown reason (n)	8
Simple antiaggregation prescription (AAS or clopidogrel) at discharge		33 of 53 (62.3%)
Double antiaggregation prescription (AAS and clopidogrel) at discharge		9 of 53 (17%)
Statin prescription at discharge		34 of 53 (64.1%)
Anticoagulant prescription at discharge		8 of 53 (15.1%)
Endarterectomy or carotid angioplasty		–
At least one consultation with speech therapist and assessment for dysphagia		26 (42.6%)
Evaluation and monitoring with physiotherapy		31 (50.8%)
Complications	Need for neurosurgical intervention (craniectomy or EVD ±)	3 (4.9%)
	Venous thromboembolism	1 (1.7%)
	Infection	16 (26.2%)
	Stroke recurrence*	3 (4.9%)
	Length of stay in days, median (IQR*)	10.5 (5–16)
	Length of stay > 14 days (n)	20/60 (33.3%)
	Hospitalar mortality	8 (13.1%)

Abbreviations: AAS, acetylsalicylic acid; Delta CT, the time between arrival at the hospital and cranial tomography; Delta T, time between the onset of symptoms and arrival at the health service; EVD ±, external ventricular drain; ICU, intensive care unit; IQR, interquartile range; NIHSS, National Institute of Health Stroke Scale (severity score in stroke); Wake-up stroke, stroke symptoms upon awakening.

\*IQR: interquartile range 1<sup>st</sup>–3<sup>rd</sup>.

in 33.3% of the cases. Considering a 3-month period, 3 patients (4.9%) had a stroke recurrence – 2 intrahospital and 1 between discharge and the 30<sup>th</sup> day evaluation.

#### Complementary examinations

As shown in – **Table 3**, all patients had a cranial tomography. At the last evaluation, 88.5% also had an electrocardiogram,

**Table 3** Neuroimaging and etiological investigations

Characteristics		All patients (n = 61)
<i>Exams performed during the study period</i>		
Neuroimaging	Computed tomography	61 (100%)
	Nuclear magnetic resonance	12 (19.7%)
Stroke etiologic investigation	Electrocardiogram	54 (88.5%)
	Echocardiogram	34 (55.7%)
	Duplex arterial scan of carotid and vertebral	29 (47.5%)
	Arterial cranial and/or cervical angiotomography	7 (11.4%)
	Arterial cranial and/or cervical angioressonance	6 (9.8%)
	Minimal etiological investigation	28 (45.9%)
Neuroimaging exam findings	Cortical ischemia/subcortical location (nonlacunar)	38 (63.3%)
	Deep-located ischemia (lacunar)	22 (36.7%)
	Ischemia in anterior circulation territory	45 (75%)
	Ischemia in posterior circulation territory	15 (25%)
Etiological subtype according to TOAST at discharge	Undetermined (incomplete investigation or > 1 mechanism)	48 (78.7%)
	Cardioembolic	4 (6.6%)
	Large artery atherosclerosis	4 (6.6%)
	Undetermined (cryptogenic)	3 (4.9%)
	Small vessel disease	2 (3.3%)
Laboratory tests (n = 30)	Total cholesterol in mg/dl (median, IQR)	194 (179–218)
	HDL in mg/dl (median, IQR)	40.5 (36–47)
	LDL in mg/dl (median, IQR)	116.5 (104–139)
	Triglycerides in mg/dl (median, IQR)	145 (110–214)
	Fasting blood glucose in mg/dl ± (median, IQR)	128 (102–194)

Abbreviations: HDL, high-density lipoprotein cholesterol; IQR, interquartile range; LDL, low-density lipoprotein cholesterol.

Ischemia of cortical/subcortical location denotes any ischemia > 2 cm in diameter. Ischemia in posterior circulation territory indicates any ischemia in the vertebrobasilar territory (including the posterior cerebral artery territory, in the absence of documentation of fetal standard anatomical variation).

\* IQR: interquartile range 1<sup>st</sup>–3<sup>rd</sup>; ±: Result identified in the medical records of 41 patients.

55.7% an echocardiogram, 47.5% a carotid and vertebral duplex scan, and ~ 22% had an angiotomography or angioresonance (in addition to ultrasound study). The final data of the aftercare evaluation showed that only 45.9% of the patients received a complete etiologic investigation (electrocardiogram, echocardiogram, and vessel studies).

► **Table 3** also shows the aftercare evaluation performed 30 and 90 days after the stroke. We identified an improvement in the discrimination of etiologic subtypes. According to the TOAST, 78.7% of the patients fell into the UN etiology (incomplete investigation or > 1 mechanism) by the time of medical discharge. The CCS classification, considering all exams 90 days after the stroke, showed 32.8% of UN cases (cryptogenic, incomplete investigation, or unclassified), the most prevalent subtype, followed by cardioembolic (29.5%), and small vessel occlusion (27.9%).

► **Table 4** presents the functional outcome data. In a 30-day evaluation, 59 out of 61 patients were accessible, 59.3% presented some degree of incapacitation (mRs ≥ 3), and the mortality was 11.9%. A total of 57 patients were accessible in the 90-day evaluation, and 47.4% evolved to a poor

outcome (mRs ≥ 3). From those, 7% had moderate dysfunction and incapacitation (mRs = 3), 8.8% had wheelchair dependency (mRs = 4), and 10.5% were confined to bed (mRs = 5). The excellent outcome (independent patient: mRs 0 to 1) rate was 31.6%, and the general mortality was 21.1%.

## DISCUSSION

### Risk factors

We identified that the prevalence of risk factors and comorbidities was similar to those of other national regions, like Joinville,<sup>12</sup> Matão,<sup>13</sup> and Fortaleza.<sup>14</sup> However, the population of the present study differs ethnically from them, being more similar to the population of Fortaleza, where white skin patients represented only 28%.

The INTERSTROKE study<sup>2</sup> identified 10 modifiable risk factors related to 90% of the population attributable risk of stroke. The prevalence of these risk factors was higher in our sample than in the general population,<sup>15</sup> notably arterial hypertension, diabetes mellitus, and dyslipidemia.

**Table 4** Functional outcome and etiological classification of stroke

Characteristics		Results	
Outcomes		1 month (n = 59)	3 months (n = 57)
Functional outcome	mRs (median, IQR*)	3.2–4	2.1–5
	mRs 0	3 (5.1%)	5 (8.8%)
	mRs 1	6 (10.2%)	13 (22.8%)
	mRs 2	15 (25.4%)	12 (21.1%)
	mRs 3	13 (22%)	4 (7%)
	mRs 4	8 (13.6%)	5 (8.8%)
	mRs 5	7 (11.9%)	6 (10.5%)
	mRs 6	7 (11.9%)	12 (21.1%)
Categorized functional outcome	Excellent outcome (mRS 0–1: independent patient)		18 (31.6%)
	Good outcome (mRS 0–2: patient without disability)		30 (52.6%)
	Bad outcome (mRS 3–6: disability or death)		27 (47.4%)
Etiological classification of stroke by CCS	Cardio-aortic embolism		18 (29.5%)
	Supra-aortic large artery atherosclerosis		5 (8.2%)
	Small artery occlusion		17 (27.9%)
	Other causes		1 (1.6%)
	Undetermined causes		20 (32.8%)
Mortality			12 of 57 (21.1%)

Abbreviation: CCS, Causative Classification of Stroke; IQR, interquartile range; mRs, modified Rankin scale.

\*IQR: interquartile range 1<sup>st</sup>–3<sup>rd</sup>.

### Initial treatment

A determinant factor in improving the outcomes of patients are reperfusion treatments,<sup>16</sup> which are time-dependent. The higher the timeframe in ischemia, the lower the number of "healthy" neurons. Saver et al. quantified time dependency identifying that, with each minute in ischemia, a cerebral area loses approximately two million neurons.<sup>17</sup> In our sample, the median time between the first symptoms and hospital arrival was 8 hours, which limited the possibilities of thrombolytic therapy.

A study in populous Brazilian cities in 2008 showed that 22.2% of the interviewed individuals could not identify stroke signs by a typical occurrence description.<sup>18</sup> Ten years later, with audiovisual resources, Meira et al.<sup>19</sup> analyzed stroke knowledge in a similar population, 44% of which could not recognize the disease. Our study examined the knowledge of family members (or caregivers) on stroke during hospitalization, 44.3% of whom did not recognize the event of the patient a stroke; 90.2% were unaware of a treatment capable of reversing stroke symptoms when done quickly; and 32.8% did not know any risk factors. In aforementioned studies,<sup>18,19</sup> more than half of the interviewees stated that they would call SAMU if a family member showed the presented symptoms. The results of our populations showed that only 16.4% used SAMU as a resource, a factor perhaps influenced by lack of knowledge about the service, insufficient ambulances to attend all calls, living in a rural area, living in a city without the service, urban mobility, and access to the hospitals.

Studies point out that ~ 25% of ischemic stroke patients are eligible to receive thrombolytic treatment.<sup>20</sup> Regardless, national studies show low use percentages, varying from 4.6%<sup>21</sup> to 8.9%<sup>22</sup> in the Southeast to 1.1%<sup>14</sup> in the Northeast. Many factors influence this, from the lack of knowledge of the population regarding emergency care, leading to late arrival of patients, until intrahospital immediate care, mainly fear of the risk of complications of thrombolysis.<sup>23</sup> The hospitals included in our study have similar physical structures and handling characteristics: "open doors", ER for adult patients, spontaneous demand care, tomography, ICUs, and backend neurosurgery. Despite these, there is no neurologist on duty, neither a stroke unit nor a formally established patient assistance protocol. The Academia Brasileira de Neurologia recommends<sup>23</sup> handling systematization for fast stroke identification and prioritizing to guarantee therapy infusion up to 60 minutes after admission. The present study observed that 37.7% of the patients arrived in a health service in < 4.5 hours, but transfer and cranium TC scan delays were responsible for the majority of losses of therapeutic window for patients. However, considering that patients arrived at the hospital in an adequate delta T and did a head CT scan in < 4.5 hours, the reason for the nonprescription of the therapy was not clear from the medical record data in ~ 13% of all cases, as r-TPa was available in 2 of the 3 hospitals, and the assistant physician was not interviewed. The hypotheses for nonprescription are unavailability of medication, lack of experience of the team with the therapy, lack of knowledge regarding the efficiency

of the therapy, fear of associated complications, or light stroke symptoms.<sup>24</sup>

The NIHSS is a predictor regardless of ICU requirement and, the higher it is, the higher the chance of an unfavorable evolution.<sup>25</sup> In our study, only 6 (9.8%) cases were admitted in an ICU, despite 10 (16.4%) patients having scored  $\geq 15$  in the NIHSS. The data does not allow clarification of further determinants and possible avoidable death implications. However, the lack of ICU beds and of recognition for potential clinical gravity require subsequent analysis.

The most prescribed medication for secondary cerebrovascular prophylaxis were antiplatelets (79.3%), followed by statins (64.1%) and anticoagulants (15.1%) – not taking into consideration the prescription of antihypertensives and hypoglycemics drugs. All patients should receive antiaggregatives in the first 48 hours and anticoagulants in cardioembolic etiology cases.<sup>16</sup> In a combined analysis, 95% of the patients essentially received secondary prophylaxis. Regarding statin prescription, simvastatin was prescribed in 3 out of 4 cases, possibly due to the price of the medication. Strong statins are costly and only available as special medication, requiring forms, medical history, and SUS registration. Another data that drew our attention was that 8 (15.1%) of the 53 medically discharged patients were prescribed anticoagulants. However, 18 (29.5%) had a cardioembolic etiology by the end of the study. This hospitalization rate was undoubtedly influenced by low etiologic investigation, which was incomplete in 78.7% of the cases. No anticoagulant was prescribed during hospitalization for 10 patients classified as cardioembolic (CE) 90 days after. Further understanding and exploration of the impact of "subprescription" are necessary.

### Functionality of the patients

The functionality after stroke is influenced by age, stroke gravity level, hyperacute therapies implemented, stroke subtype, multidisciplinary care, etc. The present research identified an excellent outcome in only 31.6% of the patients, with a general mortality of 21.1%. This proportion was considerably worse compared with that observed by Thomalla et al., who had a population median NIHSS of 6 when measuring outcomes differences between cranial magnetic resonance imaging (MRI)-guided alteplase within an unknown time window versus standard treatment identified that in treatment group patients had 53.3% excellent outcomes and 2.6% general mortality. The treatment group population had 53.3% excellent outcomes and 2.6% general mortality.<sup>26</sup> Similarly, in the ECASS III study, which measured the differences in outcome with the use of alteplase within a 3- to 4.5- hour therapeutic window, the median NIHSS was 10, and in the treatment group, an excellent outcome occurred in 52.4%, and the general mortality was 8%.<sup>4</sup> Furthermore, in these 2 studies, conducted in stroke excellence units without thrombolytic therapy and with multidisciplinary care, the control groups had  $> 40\%$  excellent outcomes, confirming that other variables are fundamental to patient care. However, our small sample does not allow an in-depth evolution analysis for independent and determinant factors.

### Limitations

The observational design of the present study limits us to infer associations and only describe the studied population regarding stroke occurrence, treatment conduction, and generate hypotheses related to functional outcome determinants for further analysis in poststudies. The convenience sample might generate a biased patient selection for those hospitalized longer and in the least favorable conditions. Access to rehabilitation, physiotherapy, medication, and neurological care between medical discharge and the 90-days evaluation were not measured.

We experienced difficulties finding data on the patients in hospital records to confront them with self-provided information. Despite having an electronic data system, the hospitals do not have electronic records. There is no interface integration for emergency files, with some of them being registered only manually. Absence of protocols and the consequent standard care allowed the experience of individual general practitioners to affect the quantity and quality of the medical record data.

### Final considerations

In conclusion, we did not find any other study in the literature conducted after the thrombectomy era describing acute stroke treatment in one of the less favored regions of Brazil. Thrombolytic use for acute ischemic stroke and stroke unities organization, are standardized by the Brazilian Ministry of Health, in ordinances published in the Diário Oficial da União in 2012 (Portarias n° 664/GM/MS and n° 665/GM/MS) and 2015 (Portaria n° 800/GM/MS); however, in the studied area, there are no stroke units.

Our population presented sociodemographic and comorbidities characteristics similar to those of other national samples. The patients took a long time to arrive at the hospital. Many of them did not use SAMU as a transportation and care option. The patients were handled mainly in general wards, without reperfusion therapies. Infection was the most frequent clinical complication, and the most prevalent stroke subtype was UN, influenced by the low frequency of etiologic investigation. Rehabilitation was not regular, and there was a considerable secondary cerebrovascular prophylaxis prescription. Almost half of the population evolved with incapacities and a high mortality rate regarding patient functionality, despite the initial low clinical gravity.

Without stroke units and an institutional protocol, there is a denial related to therapeutic advances and comprehensive care, and we believe this to be representative of most of the country. The treatment received is still similar to the one provided during the 1980s: A secondary prevention-oriented treatment. In the excellence centers, is celebrated the Randomization of Endovascular Treatment with Stent-retriever and/or Thromboaspiration versus Best Medical Therapy in Acute Ischemic Stroke due to Large Vessel Occlusion Trial (RESILIENT) results,<sup>27</sup> while in the countryside we are still stuck in the past. The present research hopes to alert for technological duality. We believe there is a national effort in this regard; nevertheless, we are far from spreading the technology throughout the country. We need urgently to

make it more accessible for the population outside of developed cities. Doing so can reduce the distance between the countryside and the big centers and the impact of stroke in our community.

#### Authors' contributions

AFRSJ: conception, data collection, formal analysis, project management, resources, draft writing, reviewing, and writing editing; GCS: data collection, project management; CMK: data collection, formal analysis, methodology, reviewing and writing editing; PAPJ: conception, formal analysis, supervision, reviewing and writing editing; PRSM: conception, formal analysis, supervision, methodology, reviewing and writing editing.

#### Conflict of Interest

The authors have no conflict of interests to declare.

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