



Research Article

Pre-hospitalar Factors Associated with Delayed Arrival of Stroke Patients in Emergency Room in Brazil

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Abstract

Background: Late hospital presentation after acute stroke is one of the main reasons for low rates of intravenous thrombolysis. This study aimed to investigate the factors associated with presentation delays after an acute stroke. **Methods:** A cross-sectional study with consecutive stroke patients from a Brazilian public university Stroke Center assisted from May 2018 to August 2019. Patients were interviewed from a structured questionnaire involving sociodemographic data, clinical history, the context in which the stroke occurred and knowledge about the disease. **Results:** Of the 154 patients interviewed, 78% had ischemic stroke and 14% hemorrhagic stroke. The mean age was 64.4±14, 53% were men and 43% patients arrived before 4.5h. Knowledge about the therapeutic window was low (59% of all patients). Decreased level of consciousness, concomitant psychiatric disease, transferred patients and not seeking immediate medical help were associated with late arrival. In multivariate analysis, males (OR 2.27, 95%CI, 1.06-4.90) did not seek immediate medical help (OR 9.44, 95%CI 4.0-22.0) and transferred patients (OR 3.61, 95%CI, 1.64-7.92) were associated with arrival after 4.5h. **Conclusions:** Despite concerted efforts to raise public awareness, substantial delays in seeking care after a stroke persist within this population. Future initiatives should focus on comprehensive educational programs targeting both the general population and healthcare professionals across all levels of care to address and mitigate these delays.

Keywords: Stroke; Education; Emergency medical services; Risk factors; Symptoms

Introduction

Stroke, a non-communicable disease, stands as a leading cause of severe neurological disability and the second-highest cause of mortality worldwide [1-4]. In Brazil, stroke accounted for 109.560 deaths in 2023 [5,6], with a staggering 62% increase in the total number of strokes among young adults over the past decade [7,8]. Post-stroke, one-third of patients face challenges in daily living activities [9], which makes cerebrovascular disease a serious public health problem.

Over the past two decades, Brazil has witnessed exponential growth and improvement in Stroke Centers and Emergency Medical Services (EMS) through its stroke line of care [2,10]. The number of stroke centers increased from 35 (with only 5 stroke units in 2008) to 149 (58% with stroke units) in 2018 [2,10]. In April 2012, Brazilian Ministry of Health published Brazilian National Stroke Act, providing financial incentives for thrombolysis, stroke centers, and integrating Public EMS – Serviço de Atendimento Móvel de Urgência (SAMU) – in the stroke line of care [10]. Another important improvement in Brazil is the use of validated smartphone apps and telemedicine. FAST-EDä (a mobile app used by EMS for screening for large vessel occlusion in stroke patients) have accelerated referral patient with probable large vessel occlusion to the most appropriate hospital [11,12]. Additionally, telemedicine through JOIN AppÔ (an app used to attach neuroimage exams and facilitate team discussion) enables smaller hospitals (without neurologists) distant from stroke centers to administer thrombolysis for acute ischemic stroke [13].

However, despite of all structure developed in last years for stroke treatment in Brazil, the number of patients with ischemic stroke undergoing thrombolytic treatment remains low [2]. It is estimated that only 2% [2] receive thrombolytic treatment and the main explanations is delay of patient arrival at the hospital, making the patient ineligible for reperfusion treatment. Timely hospital presentation is fundamental for the successful management of acute however less than 30% of stroke patients arrive at the emergency room within 4.5 hours of symptom onset [2,14], the time window for effective treatment.

Several sociodemographic, clinical and educational factors may contribute to delays in seeking treatment by patient and arriving at the stroke center [14-20]. Previous community-based studies have shown that some factors were associated with delayed arrival, including patients who initially call to a general practitioner, live alone, have a lower score in the Glasgow Coma Scale (GCS), experience ischemic stroke subtype, have a stroke at night, are of older age, experience a stroke at their own home, face greater distances from the hospital, and possess lower educational levels [15,17,18].

A prior community-based study in Brazil, conducted in 2004 and 2005 [3], revealed that 22% of people were unaware of any warning signs of stroke. Moreover, 65% were unfamiliar with

the EMS number, and only 51% would call emergency medical services for a relative exhibiting stroke symptoms. Regarding stroke treatment, only one subject out of 801 answered correctly about the therapeutic window and stroke treatment [3]. These findings underscore the concerning lack of knowledge about stroke among the Brazilian population and may be a contributing factor to delays in reaching hospital emergency services.

Our study investigates the knowledge about stroke by patients affected by this disease in a Brazilian public university hospital and analyzes if its is associated with delay in arrival at the Emergency Department (ED), together with sociodemographic, clinical and educational level variables.

Methods

This is a cross-sectional study with a consecutive sample from a Brazilian public university Comprehensive Stroke Center, from May 2018 to August 2019. Patients with clinical diagnosis of acute stroke (ischemic or hemorrhagic) or Transient Ischemic Attack (TIA) admitted at the ED of Hospital de Clínicas de Porto Alegre (HCPA) were interviewed. They were excluded if: died within first 24 hours, had extra-axial hematomas, had intracerebral hemorrhages secondary to tumors or trauma and patients who were discharged before 48 hours of admission.

The information was collected through interviews that were conducted with patients or caregivers during hospitalization. The selection criterion to know who would be interviewed (patient or caregivers) was based in the score obtained by the Mental Assessment Questionnaire (MAQ) [21]. By convention, if the score was 5 or higher, the patient was considered able to answer the questionnaire with the help of the caregiver. Patients with a score lower than 5 were considered unable to respond to the questionnaire and, in this case, it was answered only by the caregiver.

Data was collected from two questionnaires applied by different blinded researchers. Questionnaire A includes information about demographics and socioeconomic status, medical history, regular medical follow-up (once a year or more) and knowledge about stroke (number of mentioned stroke warning signs, stroke consequences, stroke prevention and knowledge about therapeutic window). Questionnaire B includes hospital admission time, pre-hospital transport, time of symptoms onset or time from last time seen well, distance from the hospital (in relation to the place where the stroke occurred), National Institutes of Health Stroke Scale (NIHSS) scores, type of stroke, worsening of symptoms before reaching the hospital, additional symptoms, like headache, seizure, nausea and vomiting, and level of consciousness (based on first three NIHSS items score). The distance from the hospital was calculated using an itinerary developed in the Google Mapsä app.

By convention, early arrival was defined as within 4.5 hours of stroke symptoms onset or last time seen well. In patients with wake-up stroke or undetermined time of symptoms onset, last time seen well was considered as time of stroke symptoms onset.

The Local Ethics Committee approved the study and the procedures followed were in accordance with institutional guidelines.

Statistical Analysis

All data and statistical analyzes were conducted using SPSS22.0 software (Chicago, IL). Means and standard deviations or medians and interquartile range were used to describe patient's characteristics. The *t-test* for independent samples or the Mann-Whitney test, as appropriate, were used to compare the early and late arrival groups. Categorical variables were compared with Chi-square or Fisher exact test. Multiple logistic regression was performed to identify variables associated with late presentation. All variables that showed an association in the univariate analyses with a $p < 0.1$ were included in the multivariate analysis. A two-tailed $p = 0.05$ was considered statistically significant.

Ethical Aspects

The study was approved by the Ethical Committee of Hospital de Clínicas de Porto Alegre. All patients signed the Consent form to participate in the study.

Results

A total of 154 patients were interviewed; 109 (71%) questionnaires answered by patient and 45 (29%) by caregiver. About type of event, 120 (77.9%) had ischemic stroke, 13 (8.4%) had TIA and 21 (13.6%) had hemorrhagic stroke. Mean age was 64.4 ± 13.5 , 82 (53.2%) were men and 64 (41.5%) patients arrived by transfer (16.9% from outlying hospitals, 9.7% from Primary Health Care Units and 14.9% from Emergency Care Unit or UPA - *Unidade de Pronto Atendimento*, a type of emergency unit that addresses less serious medical conditions in Brazil) (Table1).

Characteristics	
Male gender, n (%)	82 (53,2)
Age, years, mean \pm SD	64.4 \pm 13.5
Transferred patients, n (%)	64 (41.5)
Ischemic stroke or TIA, n (%)	133 (86.3)
NIHSS, median (IQR)	5 (1-9)
Distance from Hospital, kilometers, median (IQR)	13.2 (5.7-21.6)
Arrival by EMS, n (%)	83 (53.8)
Previous stroke, n (%)	61 (39.6)
Knew the EMS number, n (%)	66 (42.9)
Schooling, in years of study, mean \pm SD	7.5 \pm 7.2
Knew three or more stroke signs, n (%)	32 (20)
Perception of first symptom until arrival, in minutes, median (IQR)	203 (110-506)
Last seen well until arrival, in minutes, median (IQR)	328 (167-710)
Arrival before 4,5 hours, n (%)	65 (42.2)
Receive thrombolytic treatment (ischemic stroke), n (%)	30 (25)
SD=Standard Deviation, IQR=Interquartil Range	

Table 1: Patients characteristics.

The median time from symptoms onset to hospital admission was 5.4 (IQR 2.8-11.8) hours and median distance from the Hospital was 13.2 kilometers (IQR 5.7-21.6). Eighty-three (53.8%) patients arrived by Emergency Medical Service (EMS); 26% of strokes occurred over the weekend and 44.8% at night. Ninety-one (59%) sought medical help immediately, 30 (19.4%) sought within six hours and 33 (21.4%) after six hours. Thirty patients (25% of patients with ischemic stroke) received intravenous thrombolytic treatment. Among those who did not seek immediate help, the main reasons were believe that symptoms would relieve (56.9%) and that it wasn't stroke (11%) (Figure1).

Although more than half of the patients (59.7%) reported being aware of what a stroke is, the mean number of mentioned

stroke signs and symptoms was only 1.6 ± 1.2 , knowledge of stroke consequences was 1.9 ± 1.2 and stroke risk factors 3.4 ± 1 . Only 68 (44.2%) would call to SAMU if stroke occurs, 66 (42.9%) knew SAMU number and 91 (59%) knew stroke limited therapeutic time window.

Sixty-five (42.7%) patients arrived before 4.5h (early arrival) and no sociodemographic variable was statistically related with early or late arrival (Table2) however, there was a trend for more male sex in patients that arrived after 4.5 hours ($P=0.06$). Regular annual medical appointments were less common among men compared to women (53.6% versus 72.2%, $P=0.01$), and women were more likely than men to report that they would call SAMU in case of a stroke (52.7% versus 36.5%, $P=0.04$).

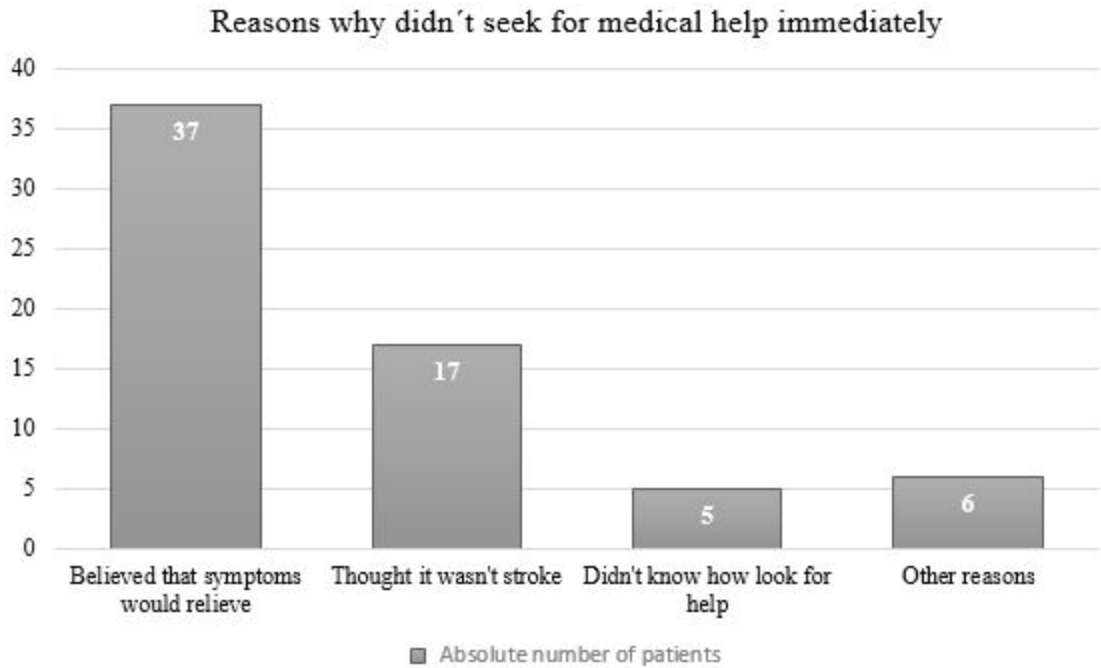


Figure 1: Reasons why didn't seek for medical help immediately.

Among clinical factors, decreased level of consciousness was more frequent in patients with early arrival ($P=0.04$); patients with associated psychiatric disorders arrived later at ED ($P=0.04$) (Table2).

Transferred patients arrived later than those who came directly to the HCPA ($P=0.003$), although the distance from

hospital was not statistically significant (Table3). Patients who sought help immediately arrived earlier than those who, for some reason, were slower to seek medical help ($P<0.001$). In the 8-hour extended window, patients who came through SAMU arrived earlier than those who came by other means, but without statistical difference (60% versus 40%, $P=0.054$).

	<4.5h (65)	>4.5h (89)	P
Sociodemographic variables			
Age, years (mean±SD)	64.7±15	64.1±12.5	0.96
Male,%	44.6	59.5	0.06
Regular medical follow-up (once a year),%	61.5	61.8	0.83
Schooling, in years of study (mean±SD)	7.29±4.5	6.9±4.9	0.56
Internet access and use,%	44.6	46.0	0.75
TV access and use,%	96.9	95.5	0.63
Income/month less than 400 dollars,%	35.3	34.2	0.72
Clinical variables			
Ischemic stroke,%	78.4	75.2	0.59
Decreased level of consciousness,%	44.6	29.2	0.04
NIHSS (median, IQR)	5 (2-11)	4 (1-7,5)	0.43
Previous mRS 0-1,%	69.2	67.4	0.81
Aphasia at presentation,%	30.7	20.2	0.15
Neglect at presentation,%	7.6	10.1	0.57
Symptoms worse,%	36.9	30.3	0.44
Additional symptoms,%	63.0	68.5	0.36
Previous stroke,%	35.3	41.5	0.37
Associated psychiatric disorders,%	13.8	26.9	0.04
SD=Standard Deviation, IQR=Interquartil Range			

Table 2: Early and late arrival according to sociodemographic and clinical variables.

	<4.5h (65)	>4.5h (89)	P
Distance from Hospital, in km (median, IQR)	11.1 (3.7-19.5)	15.1 (6.5-23.5)	0.10
Stroke on weekend,%	23.0	26.9	0.53
Stroke at night,%	44.6	44.9	0.86
Stroke in own house,%	80.0	84.2	0.30
Had stroke alone,%	18.4	17.9	0.99
Transferred patients,%	27.6	52.8	< 0.01
Arrival by EMS,%	55.3	51.7	0.76
Seek medical help immediately,%	83.0	41.5	< 0.01

Table 3: Early and late arrival: contextual of stroke.

The level of stroke knowledge in both groups (early and late arrival) was low. We did not find an association between knowledge of stroke signs and symptoms, stroke consequences or stroke time window for thrombolysis and early arrival (Table 4).

	< 4.5h (65)	> 4.5h (89)	P
Mentioned one or no stroke signal, %	43.0	47.2	0.61
Thought it was stroke, %	40.0	40.4	0.86
Claimed to know what stroke is, %	63.0	56.1	0.48
Knew the therapeutic time window, %	61.5	55.0	0.51
Would call SAMU if stroke occurs, %	44.6	42.6	0.90
Knew SAMU number, %	46.1	40.4	0.55
Mentioned one or no stroke consequences	33.8	37.0	0.67
Number of mentioned stroke risk factors, median (IQR)	4 (3-4.5)	3 (3-4)	0.74

Table 4: Early and late arrival: knowledge about stroke.

Forward logistic regression modeling showed that male sex (odds ratio – OR - 2.27, IC95%, 1.06-4.90), delayed medical help-seeking behavior (OR 9.44, IC95%, 4.0-22.0) and receiving medical care elsewhere before (OR 3.61, IC95%, 1.64-7.92) were significant independent predictors of late arrival.

There was no statistically significant relationship between annual medical appointments at the Primary Health Care Units, watching television and internet use with knowledge about the signs and symptoms of stroke and awareness of the SAMU number.

Discussion

A low number of patients arrived within 4.5h (42.2%), but more than reported in another studies in Brazil (33.7%) and studies in other countries (25-39%) [14,18-20]. This may reflect the excellent work done in Porto Alegre in recent years, with efforts to optimize prehospital care, training with SAMU staff and the use of smartphone applications (FAST-ED and JOIN) have accelerated patients referral to the most appropriate hospital.

In our study, gender was a determining factor in time of arrival at ED. Male patients were more than two times likely to arrive after 4.5 hours compared to females. Previous studies in other populations have not shown this association, but the relationship between health care and stroke knowledge with male sex is known [22,23]. Men are less prone to take care of their own health than women [24-26], and this also seemed to occur in acute stroke. For example, in the same population studied, the number of women undergoing regular medical appointments was statistically higher than men. Other sociodemographic variables such as income, age, education and regular medical appointments did not seem to influence the time of arrival at ED.

A higher NIHSS score did not appear to influence in patient time of arrival. However, those with decreased level of consciousness seemed to arrive earlier. HCPA is a comprehensive

stroke center, so more severe stroke patients, including those with large vessel occlusion, tend to be referred directly via EMS without going to other smaller hospitals. Given the extended time window for thrombectomy (up to 8 hours of symptoms onset during the study period) compared to intravenous thrombolysis, patients with more severe NIHSS scores and symptom onset beyond 4.5 hours were referred to HCPA from locations outside the city. This may determine a difference from previous studies [14,27,28], which showed that higher NIHSS tended to arrive before 4.5h.

However, patients with decreased level of consciousness were more frequent among those who arrived after 4.5h, as noted on previous studies. The frequency of seeking immediate medical help was higher among patients with altered levels of consciousness compared to those without (70.9% versus 52.5%, $P=0.02$). It is reasonable to infer that mental confusion and reduced levels of consciousness prompt the perception that a serious event is occurring, motivating an immediate medical assistance. Immediate medical help-seeking was more frequent among patients with altered levels of consciousness compared to those without (70.9% versus 52.5%, $P=0.02$). It is reasonable to infer that mental confusion and reduced levels of consciousness prompt the perception that a serious event is occurring, motivating an immediate search for medical assistance.

In our study, one fifth of patients reported having some psychiatric illness. It was also observed that these patients were twice as frequent among those who arrived after 4.5h. However, this finding has not been reported in previous studies. Although several studies reported that psychiatric disorders are among the risk factors for stroke [29-31], no studies have shown that they could also influence the time of arrival at ED. The prevalence of psychiatric disorders is higher in southern Brazil [32] and may influence early diagnosis (the challenge of differential diagnosis between stroke and psychiatric disorders) and medical help seek (depressive patients).

HCPA is a referral stroke center for Porto Alegre and the entire state of Rio Grande do Sul. This could explain why severe stroke patients are transferred after initial care at another institution (41.5%). These patients arrived later than patients who came directly to HCPA, although the distance from the stroke site to the HCPA has no statistically significant relationship with the time of arrival. This finding is interesting because it highlights that patients who have acute stroke, regardless of the distance from a Stroke Center, seek help at another institution (Primary Health Care Unit, UPA and smaller hospitals) arrived later at the Stroke Center. Unfortunately, Primary Care Units, UPAs, and most smaller hospitals do not perform intravenous thrombolysis and these patients eventually lose their treatment window and no longer have benefit from thrombolytic therapy. Thus, it is clear that it is still necessary to improve the correct referral of stroke patients, educating the population to either call for an ambulance or proceed directly to a stroke center.

The awareness regarding stroke signs was notably low in our sample. Nearly half of the patients could recall only one or no signs and symptoms of stroke. It is noteworthy that all patients questioned about the signs and symptoms of stroke had recently experienced a stroke, and 40% had a previous stroke, implying that they should be able to at least recall their own symptoms. Out of all patients, 59% were aware of the therapeutic window for thrombolysis, marking a significant improvement compared to a previous study performed in 2005 in Brazil [3] where only 1 out of 801 individuals interviewed was knowledgeable about this time frame. One explanation for not having a statistically significant difference between stroke knowledge and time of arrival is the low level of knowledge in both groups (early and late arrival).

Another important finding was that patients who referred seeking medical help immediately after perception of symptoms arrived much earlier in HCPA. Those who did not seek help immediately were 9.4 times more likely to arrive after 4.5 hours. Although there is no difference regarding the knowledge about stroke with a questionnaire during hospitalization, the reasons for the delay mentioned by these patients reveal that the delay was due to lack of knowledge about stroke recognition, urgency, severity and treatment window for stroke. These data reveal an alarming reality regarding the knowledge about stroke by the population and make clear the urgent need to keep improving this situation, either through health promotion in the Primary Health Care Units, television, internet and stroke campaigns.

However, compared with previous community-based study conducted in Brazil in 2005 [3] and in other countries [22,23,33-37], our study shows an improvement in the last decade in relation to the knowledge about stroke by the population, especially about stroke treatment and knowledge of stroke risk factors. In our study, more than a half of subjects (59%) answered correctly about a therapeutic time window for stroke. About stroke risk factors, in the previous Brazilian study [3] 19% of subjects didn't know any stroke risk factors, while in our study just one of 154 subjects didn't mention any risk factors. Probably this reflect a huge effort

in the last 10 years to improve stroke awareness in Brazil, with annual national campaigns for the population [2,10].

This study has limitations. First, only one Porto Alegre stroke center was included in this study; thus, our sample may not represent the entire patient population of Brazil. Secondly, interviews were conducted after patients had stroke; this could influence the assessment of knowledge about stroke, since the patient's own signs and symptoms and the treatment modality to which they were submitted may suggest the answers to the questionnaires performed. Third, the existence of many transferred patients may influence the assessment of other factors that could be related to time of arrival. For example, there may be some patients who knew the signs and symptoms of stroke and the treatment window, sought immediate medical help, but went to smaller hospitals. However, the recorded time of arrival was when the patient arrived at HCPA. Fourth, in our hospital, we have only ten beds in the Stroke Unit; therefore, many patients remain in the emergency room or adult ICU where data collection becomes more difficult. Fifth, some patients were unable to answer the questionnaires (those with low scores on the Mental Assessment Questionnaire). In this case, the caregivers were interviewed and thus preventing an equal assessment for all patients and the loss of subjects whose family members are not always present.

Nevertheless, compared with data from the HCPA cohort of patients, the sample from this study was very well representative of the reality of our hospital.

Conclusions

This study addresses factors influencing the time of arrival at the emergency department (ED), including gender, psychiatric illness, transferred patients, the level of awareness at presentation, and the immediacy of seeking medical help. It also sheds light on the noteworthy finding of lower knowledge about stroke among patients. Surprisingly, a substantial number of patients managed to arrive within the 4.5-hour window, distinguishing from that observed in previous studies.

It is true that much has improved in stroke care in Brazil, especially after the implementation of the Pilot Project for a National Stroke Plan in 2008 with subsequent approval of thrombolytic treatment and Stroke Unit in the Unified Health System (a Public Health System), both in 2012 [10]. Also, from a joint effort of Brazilian Academy of Neurology, Brazilian Society of Cerebrovascular Diseases and Brazilian Stroke Network, several campaigns against stroke have been conducted in our country since 2005 with the purpose of improving the understanding of this disease by the population [3,10].

However, there are still many patients with low knowledge about stroke, its consequences, signs and symptoms and treatment window. Greater dissemination about stroke, whether on television, on the internet or in primary care is needed. In addition, improving the organization of prehospital service, training of smaller hospitals and the use of telemedicine to avoid the need to transfer patients

to a Stroke Center, which may increase the number of patients treated.

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