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Risk of bleeding and predictors of hemorrhagic transformation in patients with stroke after thrombolysis

Risco de sangramento e preditores de transformação hemorrágica em pacientes com acidente vascular encefálico pós-trombólise

Riesgo de sangrado y predictores de transformación hemorrágica en pacientes con accidente cerebrovascular después de trombólisis

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ABSTRACT

Objective: To analyze the prediction of hemorrhagic transformation in patients with ischemic stroke undergoing thrombolytic therapy and its association with the nursing diagnosis "Risk of bleeding".

Method: Retrospective cohort study in patients with post-thrombolysis ischemic stroke from a hospital in Rio Grande do Sul from January 2019 to December 2021. The patient data were extracted from electronic medical records. After processing, univariable and multivariable analysis was conducted using Poisson regression with robust variance.

Results: 249 patients were analyzed, 43 (17.4%) had hemorrhagic transformation, hospitalization time was 8 (5-12.5) days and 25 (10%) died. The predictors of hemorrhagic transformation were: increased age, pre-thrombolysis National Institute of Health Stroke Scale score and use of oxygen therapy via nasal goggles and Hudson mask. The nursing diagnosis "Risk of bleeding" was not associated with hemorrhagic transformation.

Conclusion: The predictors found can improve the nursing diagnosis "Risk of bleeding", but there was no correlation observed between this and the occurrence of hemorrhagic transformation.

Descriptors: Nursing Diagnosis. Ischemic Stroke. Thrombolytic Therapy. Hemorrhage. Risk Factors. Nursing.

RESUMO

Objetivo: analisar a predição de transformação hemorrágica em pacientes com acidente vascular encefálico isquêmico submetidos à terapia trombolítica e sua associação com o diagnóstico de enfermagem "Risco de sangramento".

Método: estudo de coorte retrospectivo entre pacientes com acidente vascular encefálico isquêmico pós-trombólise de um hospital do Rio Grande do Sul de janeiro de 2019 a dezembro de 2021. Os dados dos pacientes foram extraídos via prontuário eletrônico. Após o processamento, foi realizada análise univariável e multivariável, através da regressão de Poisson com variância robusta.

Resultados: dos 249 pacientes analisados, 43 (17,4%) tiveram transformação hemorrágica, tempo de internação de 8 (5-12,5) dias e 25 (10%) foram a óbito. Os fatores preditores de transformação hemorrágica foram: aumento da idade e do valor da *National Institute of Health Stroke Scale* pré-trombólise e o uso de oxigenoterapia por óculos nasal e máscara de Hudson. O diagnóstico de enfermagem "Risco de sangramento" não mostrou associação com a ocorrência de transformação hemorrágica.

Conclusão: os preditores encontrados podem aprimorar o diagnóstico de enfermagem "Risco de sangramento", porém não houve associação deste com a ocorrência de transformação hemorrágica.

Descritores: Diagnóstico de Enfermagem. AVC Isquêmico. Terapia Trombolítica. Hemorragia. Fatores de Risco. Enfermagem.

RESUMEN

Objetivo: Analizar la predicción de la transformación hemorrágica en pacientes con accidente cerebrovascular isquémico sometidos a terapia trombolítica y su asociación con el diagnóstico de enfermería Riesgo de sangrado.

Método: Estudio de cohorte retrospectivo en pacientes con accidente cerebrovascular isquémico post-trombolisis de un hospital de Rio Grande do Sul de enero de 2019 a diciembre de 2021. Los datos de los pacientes se extrajeron a través de los registros médicos electrónicos. Después del procesamiento, se realizó un análisis univariado y multivariado mediante Regresión de Poisson con varianza robusta.

Resultados: De 249 pacientes analizados, 43 (17,4%) desarrollaron transformación hemorrágica. La duración media de la hospitalización fue de 8 días, con una tasa de mortalidad del 10%. Los factores predictivos de transformación hemorrágica incluyeron edad avanzada, puntaje elevado en la National Institute of Health Stroke Scale previo a la trombólisis y el uso de oxigenoterapia con gafas nasales y máscara de Hudson. No se observó asociación entre el diagnóstico de enfermería Riesgo de Sangrado y la transformación hemorrágica.

Conclusión: Los predictores encontrados pueden mejorar el diagnóstico de enfermería Riesgo de sangrado, pero no hubo asociación entre éste y la aparición de transformación hemorrágica.

Descriptores: Diagnóstico de Enfermería. Accidente Cerebrovascular Isquémico. Terapia Trombolítica. Hemorragia; Factores de Riesgo. Enfermería.

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INTRODUCTION

Ischemic stroke (IS) accounts for approximately 88% of stroke cases. In 2021 alone, the disease was the third leading cause of death in men and the second in women in Brazil[1,2]. The main objective of stroke treatment is revascularization of the affected region, which can be done through thrombolytic therapy with alteplase[3]. This treatment can break up blood clots that obstruct blood flow and is currently the primary treatment for ischemic stroke, as long as patients meet the eligibility criteria for therapy[4].

However, this treatment can lead to complications, with hemorrhagic transformation (HT) being the main complication reported, as is the case with intracranial hemorrhages, which are associated with higher morbidity and mortality[4,5]. HT is caused by thrombolysis and occurs within a period of 24 to 36 hours after the infusion of alteplase[6], with an incidence of approximately 1.1% to 11.4%(7), generating an impact on the prognosis and significant clinical repercussions, from mild symptoms to lethality[8].

Some studies demonstrate risk factors for HT after thrombolytic therapy, such as age, smoking, NIHSS score, atrial fibrillation, and systemic arterial hypertension[9,10]. However, there is a lack of reference studies on preventing these events, as they only identify the predictive factors for HT, without associating them or relating them to the role of nurses. It is known that the perspective and clinical experience of these professionals are crucial for monitoring the patients. To achieve this objective, it is essential to use the nursing process and identify accurate nursing diagnoses, to optimize the quality and effectiveness of the care implemented[11].

The nursing diagnosis (ND) "Risk for bleeding", based on NANDA International Inc (NANDA-I) taxonomy[11], presents only one risk factor (RF) – deficient knowledge of bleeding precautions – and is classified with the lowest level of evidence, 2.1. Therefore, it is important to develop the risk factors for this ND based on scientific evidence. One of the associated conditions of the ND is the treatment regimen[11], which may include thrombolytic therapy, and nurses must be aware of its possible complications, such as HT. Therefore, early and accurate identification of risk factors is essential, as it allows the implementation of preventive measures that can reduce the occurrence of this complication, improving the quality of care, reducing morbidity and mortality, and optimizing health resources[12,13].

Therefore, this study aimed to analyze the prediction of hemorrhagic transformation in patients with ischemic stroke undergoing thrombolytic therapy and its association with the nursing diagnosis "Risk for bleeding".

METHOD

This is a retrospective cohort study. The methodological description of this research was conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[14].

The study was carried out in the emergency department (ED) of a public hospital that serves the Unified Health System (SUS), in the city of Porto Alegre, state of Rio Grande do Sul (RS), in southern Brazil, which is a reference center in the care of stroke patients. The hospital uses the Manchester Triage System (MTS) as a risk classification tool. According to MTS, the patients may be classified into five different levels of priority: emergency; very urgent; urgent; little urgency; and not urgent. For each priority level, there is a recommended period within which initial medical care should be provided according to the classification. In the case of a stroke, the risk classification should be emergency or very urgent, and medical care must be provided within 10 minutes[15].

After risk classification and identification of suspected stroke, the patient is transferred to the stroke unit (ASU) for care. If symptoms started seven hours or less ago, the neurovascular team is called and a CT scan of the skull is requested; in the absence of bleeding, age over 18 years, and the possibility of starting alteplase infusion within 4.5 hours of the onset of symptoms, thrombolysis is performed in the unit mentioned above, according to institutional protocol. The emergency department's VU is intended for critically ill patients in the acute phase of the disease. Therefore, patients who require longer periods of continuous monitoring are transferred to the intensive care unit (ICU).

The institution where this study was carried out has a computerized system to carry out the nursing process. Thus, since 2000, NDs have been based on NANDA-I taxonomy, and all hospitalized patients are diagnosed, and care is prescribed daily by nurses. The research was carried out at the aforementioned institution because it is a reference center in the care of stroke patients.

The following inclusion criteria were adopted for the sample of this study: a) patients of both sexes aged 18 years or older; b) patients treated and admitted to the ED with a diagnosis of ischemic stroke; c) and who underwent intravenous thrombolysis. A total of 263 patients who met the inclusion criteria were evaluated. Of these, 14 were excluded for: a) having medical records with incomplete data regarding thrombolytic treatment.

Monitoring was carried out through the analysis of the electronic medical records of the study participants, from 2019 to 2021, a period stipulated to obtain the necessary sample considering the hemorrhagic transformations (HT). Data were collected from medical records from admission to the ED until 48 hours after administration of the thrombolytic drug. The date of discharge and/or transfer or death of the patient was also considered.

The sample size to determine hemorrhagic transformation in patients who received thrombolytic therapy as a treatment for stroke was calculated, considering a maximum margin of error of 5%, and using the online tool Power and Sample Size for Health Researchers. The confidence level was 95%, and Fisher's exact test was used to estimate the confidence interval, with an expected proportion of hemorrhagic transformation of 2%, the average prevalence of hemorrhagic transformation in post-thrombolysis patients, according to a reference study on the subject[16]. Based on this, the sample size was 249 patients with ischemic stroke undergoing thrombolysis, with an additional 20% for possible patient losses.

The variables were classified into groups for subsequent analysis: a) sociodemographic, such as age, sex, ethnicity, education, marital status, profession, and origin; b) relating to risk classification: main complaint, discriminator used, clinical priority of classification and time to provide medical care – following the Manchester Protocol; c) clinical, such as previous comorbidities, ventilation mode on arrival at the ER, National Institute of Health Stroke Scale (NIHSS), pre-thrombolysis blood pressure (alteplase), pre-and post-thrombolysis laboratory tests, Hemorrhage After Thrombolysis (HAT) scale value, time window for thrombolysis, door-to-needle time, occurrence and types of hemorrhagic transformation (intracranial or systemic); d) ND, such as opening of ND "Risk of bleeding" and its risk factors; and e) outcomes of care, such as length of hospital stay in days, ICU admission and death.

The main outcome analyzed was the occurrence of hemorrhagic transformation in patients with ischemic stroke who underwent thrombolytic therapy. Post-thrombolysis hemorrhagic transformation was considered to include intracranial hemorrhages[6] and others, such as epistaxis, hematuria, bleeding at the venipuncture site and hemorrhages in the gastrointestinal tract[6,17], identified through medical and nursing records in the medical records of the patients.

The research team – composed of a nursing student, a scientific initiation scholarship holder, and two nursing professors working at the hospital – was trained by the main researcher for a week, before data collection, on the procedures to be followed, until there were no doubts when filling out the collection instrument.

An instrument was created to standardize data collection and fill in database variables, minimizing collection biases. A pilot study was conducted with ten patients and two researchers to test the instrument. Patients from the pilot study collection were included in the sample. Data was collected from April to July 202 using a digital Google Spreadsheet and analyzed to check for possible typing errors.

Using the hospital's computerized healthcare database, or query - a database with information provided for the research in spreadsheet format - data on sociodemographic variables, risk classification, length of hospital stay, and the need for ICU admission was collected. The other quantitative and qualitative variables were collected through electronic medical records, including the medical and nursing professionals' documentation of patient progress, laboratory test results, and vital signs records. The variables related to comorbidities and ED were obtained through the anamnesis form and the nurse's documentation of patient progress; death record, and the causes were obtained through the discharge report.

Data on waiting time for medical care from arrival to the ED were also obtained from the hospital's computerized database, based on the calculation of the time of arrival and the start of the medical consultation. According to the protocol, patient care should occur within 10 minutes. The time window for performing thrombolysis was calculated based on the time of onset of symptoms and the time of start of medication infusion, data found in prescription records, and/or medical documentation of the patient's progress based on the time described as the start of infusion. Door-to-needle time was calculated based on the time of patient arrival at the ED and initiation of thrombolytic therapy.

The HAT scale is not routinely performed in these emergency care settings, but was retrospectively assessed through registration in medical records, patient imaging exams, and NIHSS in the doctor/neurologist's documentation by the main researcher. This scale is based on the NIHSS score, extent of hypodensity on cranial tomography, serum glucose, and history of diabetes, and is scored from one to five points. In the study that originated this scale, the rate of intracranial hemorrhage was 2% for a score of zero; 5% for a score of one; 10% for a score of two; 15% for a score of three; and 44% for a score greater than three points[18].

Statistical tests were defined after performing the Shapiro-Wilk test to verify the normality of numerical data. Continuous variables were expressed using mean and standard deviation (normal distribution) or median and interquartile range (25^{th} and 75^{th} percentile) (asymmetric distribution), while categorical variables were presented as frequencies and proportions. Statistical analysis included Chi-square tests for qualitative variables and Student's T-Test and Mann-Whitney test for continuous variables, depending on the normality of the variable. Statistical analysis was analytical, using a 95% confidence interval. Univariate and multivariate analysis was performed using the Poisson regression method with robust variance to estimate the effect of predictive factors concerning the occurrence of the outcome investigated.

The final model was constructed using the backward variable selection method, in which all variables with $p < 0.10$ in the univariate analysis were included in the multivariate model and subsequently eliminated until all remaining variables had $p \leq 0.05$.

The relative risk (RR) was calculated for the associations, with analyses with $p \leq 0.05$ being considered statistically significant. Missing data were treated by pairwise deletion analysis, in which each individual contributed to the model only with the information that was present at the time collected. The analyses were performed using the Statistical Package for the Social Sciences® version 18.0.

This study was linked to the project "Clinical outcomes and management of nursing care for critically ill adult patients: multicenter study", which was approved in its ethical and methodological aspects by the Research Ethics Committee of the study's host institution, under Certificate of Presentation for Ethical Assessment (CAAE) No 32560920.0.1001.5327; and protocol numbers 4.100.693 and 2020-0286. The rigor and confidentiality of information under the General Data Protection Regulation were observed. We now move on to the results of this investigation.

RESULTS

Of the 249 patients included in this study, 43 (17.3%) had hemorrhagic transformation. None of the sociodemographic variables were associated with the outcome of hemorrhagic transformation ($p>0.05$). Information on these variables is described in Table 1.

As for the patients' comorbidities, none were associated with the outcome hemorrhagic transformation ($p>0.05$). The information and the value of association with the outcome can be seen in Table 2.

Table 1 – Sociodemographic characteristics of patients admitted to the emergency department of a public university hospital with a diagnosis of ischemic stroke* who underwent intravenous thrombolysis. Porto Alegre, Rio Grande do Sul, Brazil, 2023

Sociodemographic variables	Total n†(%) 249(100)	Hemorrhagic transformation		p‡
		Yes 43(17.3)	No 206(82.7)	
Age				
Median (IQR§)	69(58.5-77.5)	72(62-80)	68 (56-77)	0.053**
Min-Max††	19-99	43-96	19-99	
Gender (n†= 249)				0.224‡‡
Female	131(52.6)	19(44.2)	112(54.4)	
Ethnicity (n†= 248)				
White	208(83.9)	40(93)	168(82)	0.183‡‡
Black	36(14.5)	3(7)	33(16)	
Brown	4(1.6)	0(0)	4(2)	
Education (n†=218)				
Up to 9 years of schooling	132(60.5)	16(48.5)	116(62.7)	0.327‡‡
10 to 12 years of schooling	56(25.7)	12(36.4)	44(23.8)	
Illiterate	17(7.8)	2(6)	15(8.1)	
From 13 years of age	13(6)	3(9.1)	10(5.4)	
Profession (n†=149)				
Active	102(68.5)	20(76.9)	82(66.7)	0.309‡‡
Inactive	47(31.5)	6(23.1)	41(33.3)	
Marital status (n†=239)				
With a companion	123(51.5)	24(57.1)	99(50.2)	0.417‡‡
Without a companion	116(48.5)	18(42.9)	98(49.8)	

Table 1 – Cont.

Sociodemographic variables	Total n†(%) 249(100)	Hemorrhagic transformation		p‡
		Yes 43(17.3)	No 206(82.7)	
Origin (n†=249)				
Capital	213(85.5)	39(90.7)	174(84.4)	0.751‡‡
Metropolitan region	26(10.5)	3(7)	23(11.2)	
Inland city	9(3.6)	1(2.3)	8(3.9)	
Coast	1(0.4)	0(0)	1(0.5)	

Source: Authors database, 2023
*AVEi = Ischemic stroke; †n = Number; ‡p = Level of significance; §IQR = Interquartile range; ††Min-Max = Minimum-Maximum; ** Mann-Whitney test; ‡‡ Chi-square test.

Table 2 – Comorbidities of patients admitted to the emergency department of a public university hospital with a diagnosis of ischemic stroke* who underwent intravenous thrombolysis. Porto Alegre, Rio Grande do Sul, Brazil, 2023

Comorbidities	Total n†(%) 249(100)	Hemorrhagic transformation		p‡
		Yes 43(17.3)	No 206(82,7)	
Systemic arterial hypertension	188(75.5)	32(74.4)	156(75.7)	0.856§
Three or more comorbidities	133(53.4)	26(60.5)	107(51.9)	0.308§
Diabetes *Mellitus*	99(39.8)	15(34.9)	84(40.8)	0.473§
Dyslipidemia	82(32.9)	19(44.2)	63(30.6)	0.084§
Former smoking	54(21.7)	8(18.6)	46(22.3)	0.590§
Smoking	43(17.3)	6(14)	37(18)	0.527§
Obesity	30(12)	5(11.6)	25(12.1)	0.926§
Atrial fibrillation	29(11.6)	7(16.3)	22(10.7)	0.298§
Alcoholism	17(6.8)	1(2.3)	16(7.8)	0.198§
History of transient ischemic attack	12(4.8)	2(4.7)	10(4.9)	0.955§
Previous alcohol consumption	10(4)	3(7)	7(3.4)	0.277§
Drug user	5(2)	0(0)	5(2.4)	0.302§

Source: authors database, 2023
*AVEi = Ischemic stroke; †n = Number; ‡p = Level of significance; §Chi-square test.

Regarding risk classification in the ED, 218 (87.6%) patients were seen by the doctor within 10 minutes after arriving at the ED (p=0.858); and 166 (66.7%) were not classified during screening. Regarding the 83 (33.3%) patients with risk classification, the "discomfort in adult" flowchart was the most prevalent, in 70 (84.3%) patients, and of these, 11 (15.7%) had a hemorrhagic transformation. Other flowcharts used were "behavioral change" in 3 (3.6%) patients; "headache" in 3 (3.6%); "seizures" in 2 (2.4%); "adult dyspnea" in 2 (2.4%); and "gastrointestinal bleeding" in 2 (2.4%); none of them presented HT. On the other hand, the "fainting" flowchart was used in 2 (2.4%) patients, and 1 (50%) had HT. These variables were not statistically significant in the association with the hemorrhagic transformation outcome (p=0.763).

Among patients with risk classification, the most frequent descriptor was "new neurological deficit less than 24 hours ago" in 64 (77.1%) patients, of which 9 (14.1%) had hemorrhagic transformation; followed by "altered consciousness" in 14 (16.8%), of which 2 (14.2%) had HT; "new abnormal pulse" in 2 (2.4%), of whom 1 (50%) had HT; "poor breathing" in 2 (2.4%) patients; and "very low oxygen saturation" in 1 (1.2%); of these last two, none had HT. "Very urgent" severity was attributed to 81 (97.6%) of the patients with risk classification, of whom 12 (14.8%) had hemorrhagic transformation; "emergency" severity was attributed to 2 (2.4%) patients and none had hemorrhagic transformation. The association between the variables descriptor used and HT (p=0.715); and severity and HT (p=0.610) did not present statistical significance.

In the univariate analyses of the clinical and treatment characteristics of pre-thrombolysis patients, there was an association between the ventilation mode and the NIHSS scale value with the hemorrhagic transformation outcome (p<0.05). Additional information is presented in Table 3.

The pre-thrombolysis cholesterol value was evident in 16 (6.4%) patients in the sample and had an average of 216.25±46.2 mg/dl. There was no significant association with hemorrhagic transformation (p=0.098).

Regarding clinical and post-thrombolysis treatment variables, after univariate analysis, there was an association between prothrombin time and NIHSS scale value with the HT outcome. Further information can be seen in Table 4.

Regarding ICU admission, 45 (18.1%) patients had to leave the ED and be transferred to an ICU after thrombolysis; and of these, 14 (32.6%) had HT (p=0.007). The median length of hospital stay in patients with hemorrhagic transformation was 10 (7-20) days, longer than that of patients who did not have HT: 8 (5-12.5) days of hospital stay (p=0.014).

Regarding hospital mortality, 25 (10%) patients died; of these, 13 (32.2%) had hemorrhagic transformation (p=0.000). According to the chapter of the International Classification of Diseases (ICD), the most prevalent cause of in-hospital mortality in the sample analyzed was related to circulatory system diseases, corresponding to 23 (92%) deaths. Of the 43 hemorrhagic transformations, 18 (41.9%) were symptomatic intracranial hemorrhages; 17 (39.5%) were asymptomatic intracranial hemorrhages; and 8 (18.6%) were minor hemorrhages: bleeding at the puncture site and gingival bleeding.

The ND "Risk of bleeding" was opened in 102 (41%) of the 249 patients who received thrombolytic therapy in the ED; of these, 40 (39.5%) had HT. There was no significant association between this ED and HT (p=0.834). The risk factors listed at the identification of the ED were: adverse effects of therapy for 94 (92.2%) patients, vascular alteration for 5 (4.9%) patients, hematologic disorder, mechanical trauma, and drug therapy with 1 (1%) each, (p=0.171).

Table 5 presents the results of the multivariate analysis regarding the predictive factors related to hemorrhagic transformation.

Once the results have been presented, we move on to the discussion.

Table 3 – Clinical and treatment characteristics of patients admitted to the emergency department of a public university hospital with a diagnosis of ischemic stroke* before undergoing intravenous thrombolysis. Porto Alegre, Rio Grande do Sul, Brazil, 2023

Clinical and treatment variables	Total n†(%) 249(100)	Hemorrhagic transformation		p‡
		Yes 43(17.3)	No 206(82.7)	
Ventilatory mode				
Ambient air ventilation	202(81.1)	27(62.8)	175(85)	0.000§
Goggle-type nasal cannula	27(10.8)	12(27.9)	15(7.3)	
Mechanical ventilation	15(6)	1(2.3)	14(6.8)	
Ventilation with Hudson mask	5(2)	3(7)	2(1)	
Laboratory tests				
Blood glucose (IQR**) (n†=235)	131(106-184)	130(108-168)	132(106-188)	0.922††
Prothrombin time (IQR**) (n†=199)	13.1(12.6-13.8)	13.2(12.6-14.3)	13.1(12,7-13,7)	0.545††
Activated partial thromboplastin time (IQR**) (n†=178)	31.7(28.7-34.6)	32,7(29.3-36.1)	31.5(28.5-34)	0.316††
Platelets (IQR**) (n†=219)	230(187-267)	217.5(164.8-245.8)	231(189-269)	0.105††
Hemoglobin (SD‡‡) (n†=225)	13.5±1.7	13.8±1.8	13.4±1,68	0.245§§
Hematocrit (IQR**) (n†=225)	39.9(37.5-43.2)	40.7(38-44.4)	39.8(37.3-43)	0.348††
Blood pressure				
Systolic blood pressure (IQR**)	147(132-166)	143(130-166)	148(132-166.25)	0.759††
Diastolic blood pressure (IQR**)	80(70.5-90)	80(66-87)	80(71-90)	0.479††
Times				
Thrombolytic window (hours) (IQR**) (n†=241)	3(2:21-3:54)	2:53(2:08-3:45)	3:03(2:25-3:56)	0.133††
Needle-to-door time (hours) (IQR**)	1:05(0:50-1:27)	1:08(0:55-1:27)	1:05(0:48-1:28)	0.453††
Other variables				
National Institute of Health Stroke Scale (IQR**) (n†=236)	8(4-14)	14(7.5-20)	7(4-12)	0.000††

Source: authors database, 2023

*AVEi = Ischemic stroke; †n = Number; ‡p = Level of significance; § Chi-square test; **IQR = Interquartile range; ††Mann-Whitney test; ‡‡§§SD = Standard deviation; §§Student's t-test.

Table 4 – Clinical and treatment characteristics of patients admitted to the emergency department of a public university hospital with a diagnosis of ischemic stroke* after undergoing intravenous thrombolysis. Porto Alegre, Rio Grande do Sul, Brazil, 2023

Clinical and treatment variables	Total n†(%) 249(100)	Hemorrhagic transformation		p‡
		Yes 43(17.3)	No 206(82.7)	
Laboratory tests				
Blood glucose (IQR§)	120(101.5-160)	121(101-176)	119.5(101.8-157.8)	0.534**
Total cholesterol(SD††) (n†=201)	181.6±44.4	174±44.7	183.25±44.3	0.258‡‡
Prothrombin time (IQR§) (n†=134)	14.7(13.5-16.3)	15.5(14.5-16.8)	14.5(13.3-16.2)	0.008**
Activated partial thromboplastin time (IQR§) (n†=126)	33.1(30-37.2)	34.8(32.2-38.5)	32.4(28.4-37.1)	0.023**
Platelets (IQR§) (n†=100)	205(160.3-256)	183(147.8-254.3)	206.5(170-260.5)	0.461**
Hemoglobin (SD**) (n†=138)	13±1.96	13.19±2.3	12.9±1.84	0.245‡‡
Hematocrit (IQR§) (n†=84)	39.3(35.4-42.2)	40.3(35.5-42.3)	39.2(35.6-41.8)	0.960**
Blood pressure				
Systolic blood pressure (IQR§) (n†=246)	137(124-152)	142(121-156)	136(124-152)	0.640**
Diastolic blood pressure (IQR§) (n†=246)	73(65-82)	73(67-82)	74(65-82)	0.948**
Other variables				
National Institute of Health Stroke Scale (IQR§) (n†=228)	6(2-10.7)	11(6-17)	5(2-10)	0.000**
Hemorrhage After Thrombolysis (IQR§) (n†=231)	1(1-2)	2(1-2.5)	2(1-2)	0.024**

Source: authors database, 2023
*AVEi = Ischemic stroke; †n = Number; ‡p = Level of significance; §IQR = Interquartile range; **e Mann-Whitney test; ††SD = Standard deviation; ‡‡Student's t-test.

DISCUSSION

The predictors of hemorrhagic transformation identified in this study were the increase in age and pre-thrombolysis NIHSS score and the use of ventilation with oxygen therapy by goggle-type nasal cannula and pre-thrombolysis Hudson mask. The ND "Risk of bleeding" was not associated with the HT outcome.

The number of cases of post-thrombolysis HT in patients with ischemic stroke varies from 1 to 27%[7,19,20]. However, recent studies conducted in China showed incidence rates of 17.4%[21] and 19.3% [22], data equivalent to those of the present study. This may be related to the significant increase in the incidence of stroke in China due to low socioeconomic status and poor control of risk factors for the disease[23,24]. Although there is also

Table 5 – Predictive factors related to hemorrhagic transformation in patients admitted to the emergency department of a public university hospital with a diagnosis of ischemic stroke* who underwent intravenous thrombolysis. Porto Alegre, RS, Brazil, 2022

Multivariable			
Variable	**RR†**	**CI‡ 95%**	**p§**
Age	1.02	1.00-1.04	0.037**
NIHSS†† pre-thrombolysis	1.07	1.03-1.11	0.000**
Ventilatory mode			
Goggle-type nasal cannula	3.03	1.74-5.26	0.000**
Hudson mask	3.49	1.35-8.99	0.010**

Source: authors databases, 2023
*AVEi = Ischemic stroke; †RR = relative risk; ‡CI = confidence interval; §p = Level of significance; **Poisson regression with robust variance; ††NIHSS = *National Institute of Health Stroke Scale;*

a significant number of cases of the disease in Brazil, there are few studies related to post-thrombolysis HT.

Regarding the risk factors for HT in patients with ischemic stroke undergoing thrombolytic therapy, age was considered a predictor. The older the patient, the greater the risk of developing hemorrhagic transformation. This data is confirmed by recent studies with a methodological design similar to that of this investigation, which sought to identify the prevalence of HT and associate it with predictive factors, as well as with patient outcomes[25,26]. As in this study, the median age of patients who had post-thrombolysis HT was also higher than that of patients who did not have this condition.

Another predictor of HT was the increase in the pre-thrombolysis NIHSS scale score[19,26,27]. A cross-sectional study that aimed to evaluate the outcomes of post-thrombolysis patients in Malaysia found that for each increase of one point on the pre-thrombolysis NIHSS scale, the chance of HT also increased[19]. In the present study, for each one-point increase on the NIHSS scale, the risk of developing HT increased by 7%.

Thrombolytic therapy improves patients' neurological deficits, favoring a reduction in cases of HT[27]. This corroborates the result of this study, since the NIHSS score had a median reduction of 2 points post-thrombolysis. Here, we can see the importance of monitoring and evaluating this scale in the follow-up of patients with thrombolysis, as it is an indicator of the risk of hemorrhage and neurological improvement.

The need for supplemental oxygen via a goggle-type nasal cannula and pre-thrombolysis Hudson mask was also associated with a higher risk of HT. Patients who had some bleeding used more ventilation than those who did not have bleeding, 37.2% vs 15.1%, respectively, although a small number of patients required invasive mechanical ventilation (MV) in both groups. No other studies were found relating the need for oxygen therapy with HT.

However, a study conducted by an English researcher reviewed the harmful effects of hyperoxia. The aforementioned research demonstrated that excess oxygen is related to increased intracranial hemorrhages and mortality and that supplemental oxygen should be used with caution and monitoring of oxygen saturation and pressure (PaO2)[28]. Therefore, it is important to monitor the patient's oxygen saturation and to use supplemental oxygen consciously from the moment the patient is admitted to the health service. The importance of a nurse's clinical assessment at the bedside is highlighted, which guides the necessary interventions and, at the same time, minimizes risks to the patient when applied correctly.

Monitoring these patients and the critical eye of the nurse are necessary interventions to prevent post-thrombolysis hemorrhages. The ND "Risk of bleeding" is accurate, since the main complication of alteplase administration is hemorrhagic transformation. Although there was no significant association between ND "Risk for bleeding" and hemorrhagic transformation in the present study, this diagnosis was opened in almost half of the sample, highlighting the need to refine its risk factor in the NANDA-I taxonomy.

The opening of this ND requires care to prevent hemorrhages, as it early identifies patients at increased risk of developing HT. Post-thrombolysis nursing care was highlighted numerous times in a study that listed the main post-thrombolysis care measures. However, the use of ND "Risk of bleeding" was not addressed[29].

Another study – aiming to review and present current evidence of nursing care in stroke patients treated with thrombolysis and mechanical thrombectomy – reiterated the importance of nursing in this area with updated care based on scientific evidence, including monitoring of vital signs, mainly blood pressure, temperature and oxygen saturation, monitoring of the NIHSS scale and monitoring of the patient's condition, to prevent bleeding, in addition to the response and supervision of the individual after treatment[12].

Therefore, the role of nurses in monitoring patients is visible. This is considered a nursing intervention, as it includes activities that reflect the process of clinical judgment, that is, it defines what to look for and what to do when the anticipated event occurs[30]. This statement corroborates a study that reiterated the importance of nursing in pre-, trans, and post-thrombolysis care, as nursing professionals anticipate patient care, recognize possible complications of the procedure, and maintain patient safety[12]. This nurse's responsibility associated with the ND "Risk of bleeding" can benefit the patient and the quality of nursing care.

In a study carried out in southern Brazil, the authors demonstrated that the ND "Risk of bleeding" is an important indicator of care quality by monitoring the results of laboratory tests related to blood coagulation[13]. This allows nurses to qualify care, monitor patients, and produce evidence to reduce aggravating factors, such as hemorrhagic transformation.

The nurse's clinical perspective makes him/her someone special in his/her work environment, as this professional makes quick decisions in situations that require resolution and foreseeing problems that may occur with patients at risk[12]. Therefore, due to his/her clinical experience, a nurse who knows that a patient receiving thrombolysis has a high risk of developing HT proposes care to prevent bleeding.

One limitation of this study was its methodological design: a retrospective study, which may lead to information bias. Data were collected from electronic medical records, and much information was incomplete and inconsistently recorded by different health professionals. Another limitation is that the HAT scale is not validated in Brazil and, therefore, is not used to assess the risk of intracranial hemorrhage.

The results of this study have internal and external validity since the institution where it was conducted is a reference center for stroke patients. Furthermore, the data allow an analysis of HT cases and associated factors and enable rethinking nursing care for patients undergoing thrombolysis therapy. It is worth mentioning that multicenter and prospective studies are needed to improve HT control strategies in this group of patients.

CONCLUSION

The present study showed that increased age and pre-thrombolysis NIHSS score and the use of ventilation with oxygen therapy by goggle-type nasal cannula and pre-thrombolysis Hudson mask are predictors of HT in patients with ischemic stroke undergoing thrombolytic therapy. The ND "Risk of bleeding" did not show a significant association with the occurrence of this complication.

Therefore, further studies are needed to demonstrate the risk factors for this ND, so that care can be taken to prevent bleeding in patients with ischemic stroke undergoing thrombolysis.

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