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EDITORIAL

Cerebral hemorrhage in Latin America: where are we?

Hemorragia cerebral en América Latina: ¿dónde estamos?

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This number of RMN has allowed us to review some aspects of cerebral hemorrhage in our region. In the first paper, Serrano et al. report a series of patients with intracerebral hemorrhage (ICH), analyzing prognostic factors[1]. The reviewer found the series exciting and wants to comment on clinical data. The first comment is the frequency of ICH among the global series of patients, representing 10.3%, corresponding to similar numbers to those from the series from Europe and North America[2,3]. This number contrasts with numbers reported in Mexico in the RENAMEVASC study, where 28% of acute stroke corresponded to ICH[4]. The authors considered deriving these patients to other hospital services (such as a neurosurgery ward) could explain this finding. This kind of registry must include consecutive patients from all areas of the hospital to avoid bias.

It is interesting to note the low frequency of possible or probable cerebral amyloid angiopathy (just 3.8%). One potential explanation could be the low mean age (62 years). As is well known, the frequency of amyloid angiopathy increases with age[5]. There is a real underdiagnosis of this condition in our region. The Boston criteria[6] is not well known for non-vascular neurologists, including general radiologists and inclusive neuroradiologists. Another potential explanation could be less accessibility to magnetic resonance imaging needed to analyze Boston criteria[6]. It is essential to mention the existence of computed tomography scan criteria such as Edinburg criteria[7].

Another weak point of this series is that it included several cases with arteriovenous malformations as well non-aneurysmal subarachnoid hemorrhage, which can be explained by several potential causes such a reversible vasoconstriction syndrome, peri mesencephalic subarachnoid hemorrhage, and cortical subarachnoid hemorrhage[8]. It is interesting to consider only primary cases of ICH, essentially those due to hypertension, amyloid cerebral angiopathy, secondary to antithrombotic drugs, and cryptogenic.

There are several factors related to prognosis; among them, size of ICH, location, rupture to ventricular system, volume, and age are among the most predictive. One crucial point is the frequency of expanding hematoma related to control or not of arterial pressure. This point was not analyzed in the series. The focus for the treatment of patients after an ICH is the prevention of secondary brain damage, such as clot expansion, secondary brain edema, and intraventricular hemorrhage[9]. The only data analyzed was ventricular irruption, which was reported in 17.6% of cases and was a poor prognosis point.

The mortality rate in this series is relatively low compared with the RENAMEVASC study, which was 30%. The number of patients surgically treated were relatively low and do not explained the low mortality rate.

The present registry represents an important advance in regional organization about stroke care. However, we need to standardize diagnostic criteria as well therapeutical measures.

The series reported by Serrano et al.[1] is an excellent example of real-life conditions in which there is no

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particular protocol treatment for ICH or place of admission of these patients. In this number of RMN, Ouyang and Anderson[10] gave us information about the recent trial INTERACT 3, in which three therapeutic targets were proposed for treating acute ICH[11] and call to action for effective implementation. Interestingly, the study was done in just nine low-income and middle-income countries. The care bundle protocol included the early intensive lowering of systolic bleed pressure (target < 140 mm Hg), strict glucose control (target 6.1-7.8 mmol/L in those without diabetes and 7.8-10 mmol/L in those with diabetes), anti-pyrexia treatment (target body temperature < 37.5°C), and rapid reversal of warfarin-related anticoagulation (target INR < 1.5). The primary outcome was functional recovery, measured with the modified Rankin scale. The results showed that the likelihood of a poor functional outcome was lower in the care bundle group (standard odds ratio 0.86, 95% CI: 0.76-0-97; p = 0.015)[11].

A care bundle is a small but crucial set of treatments that, when implemented together, can improve outcomes[12]. The role of any particular intervention in cluster trials is difficult to attribute, but the strong positive effect was to control blood pressure. An editorial from Ziai et al.[12], Discussed other explanations in this study, such as a promoted multidisciplinary approach with more frequent and efficient neurologic monitoring and not only the adherence with the bundle. Implementing this kind of program in our acute stroke protocols will benefit patients with cerebral hemorrhage.

Finally, another helpful article by López-Alvis et al. analyzes stroke knowledge in two highly educated populations in Mexico City[13]. The authors surveyed 499 participants in a medium-income condominium complex and another group of pharmaceutical company employees with products related to stroke treatment. The authors asked about the definition of stroke subtypes, such as subarachnoid hemorrhage, cerebral venous thrombosis, cerebral infarction, and cerebral hemorrhage. About 68% of surveyed people know correctly the term cerebral hemorrhage. How should we name a stroke in colloquial language? I think it is not helpful for practical reasons to divide the terms of stroke. In Spain, the term ictus is recognized. According to the Royal Academy of Spanish Language, ictus is a cerebral disease of vascular origin present with sudden onset. This concept is the most crucial aspect that people should know to attend immediately to a hospital.

Regarding stroke symptoms in Lopez-Alvis series, 71% recognized at least one, and 53% at least 2. In two similar studies from México City[14] and Querétaro[15], similar conclusions were reached (Table 1). In Querétaro´s series, there was less recognized risk factors and symptoms percentage. This series involves open population in public places. There is poor knowledge about risk factors for stroke; the most commonly recognized risk factor is hypertension, as well as poor understanding of warning symptoms. Family history of stroke was the most common “educational” experience in all three studies. There is an opportunity area to improve. Private and governmental authorities should consider public campaigns for education about stroke with well-defined messages to recognize and treat it immediately.

Table 1. Knowledge about stroke risk factor and symptoms in three Mexican populations

Finding	López-Alvis et al.[13]	Góngora et al.[14]	Uribe et al.[15]
Number	499	330	1297
Mean age	58 years	40 years	44 years
Recognized 1 Risk factor 3 Risk factor	 60% Not informed	 30% 12%	 35% 6%
Recognized 1 Symptom 3 Symptoms	 71% 13%	 36% 2%	 38% 5%

Answering the question in the heading of this editorial, “Where are we?” we are moving forward with creating registries that standardize the diagnosis and treatment of ICH, which was made decades ago with cerebral infarction. A popular word should be recognized in Latin American countries, and Ictus could be an option. We finally have a care bundle incorporating early intensive blood pressure lowering and management protocols for hyperglycemia, pyrexia, and abnormal anticoagulation in patients with ICH presenting within 6 h of symptom onset with positive results. The previous strategies in Latin America (standardized diagnosis employing registries as protocol treatment) should be implemented to improve the outcome of this devastating disease.

Finally, massive educational campaigns should appear for people to recognize the stroke symptoms and attend to the nearest hospital, reducing the different window times in any “Ictus”.

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ORIGINAL ARTICLE

Correlation between dual-phase CTA-SI ASPECTS and automated CT perfusion imaging in patients with acute ischemic stroke beyond the 6-hour window

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Abstract

Background/Objective: *There is controversy regarding the need to use advanced imaging to select candidates for thrombectomy in late window acute ischemic stroke (AIS). Hypoattenuation on CT angiography source images (CTA-SI) in arterial phase has been shown to be more sensitive than Alberta Stroke Program Early CT Score (ASPECTS) of brain parenchyma to determine tissue at risk of ischemia. Our hypothesis is that the addition of a second acquisition at 35-50 seconds could complement the assessment of hypoperfused tissue that fails to receive flow through pial vessels.* **Methods:** *Patients with large vessel occlusion and 6-24 hours from symptom onset, admitted between August 2019 and July 2023, were evaluated with dual-phase CT angiography (CTA) and CT-Perfusion. A vascular neurologist estimated CTA-SI ASPECTS in both phases at the time of data entry into the RECCA registry. In contrast, the post-processing of CT-Perfusion images was performed in an automated way through RAPID© software. The association between automated CT-perfusion values and dual-phase CTA-SI ASPECTS was assessed through a correlation coefficient.* **Results:** *Pearson's coefficient demonstrated a high correlation between ischemic core volume and delayed phase CTA (CTA-DP) ASPECTS with an inverse association of –0.93 and between Tmax ≥ 6 sec volume and arterial phase CTA (CTA-AP) ASPECTS with a value of –0.88.* **Conclusions:** *CTA-derived source images (CTA-SI) in two phases may be useful in the selection of patients with AIS presenting beyond the 6-hour window.*

Keywords: *Dual-phase computed tomography angiography. CT-Perfusion. Late window acute ischemic stroke.*

Correlación entre CTA-SI ASPECTS de doble fase y perfusión por TC con procesamiento automatizado en pacientes con ictus isquémico agudo más allá de la ventana de 6 horas

Resumen

Introducción/Objetivo: *La recomendación actual es realizar el tamizaje de pacientes con ataque cerebrovascular ACV y oclusión de grades vasos LVO (por sus siglas en ingles) potencialmente candidatos a trombectomía mecánica en ventana extendida a través de un estudio de TC perfusión con post procesamiento automatizado. El acceso a TC perfusión no está ampliamente disponible en el mundo, por lo que existe controversia en relación a que sea una herramienta imprescindible.*

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Métodos: *Este es un estudio prospectivo de un registro retrospectivo unicéntrico con pacientes con ACV de circulación anterior, LVO y un tiempo entre 6-24 horas desde el inicio de los síntomas hasta la realización del estudio imagenológico. A todos los pacientes se les realizó un AngioTC en 2 fases, con evaluación de sus imágenes fuentes CTA-SI (por sus siglas en ingles) y un estudio de perfusión con post procesamiento por software RAPID.* **Resultados:** *El coeficiente de Pearson's mostró una alta correlación entre el volumen de núcleo isquémico medido por FSC < 30% y el valor CTA-SI ASPECTS en fase tardía, con una asociación inversa de –0.93.* **Conclusión:** *La interpretación de CTA-SI ASPECTS en 2 fases entrega información congruentes con los resultados automatizados de los mapas de TC perfusión.*

Palabras claves: *Trombectomía. ASPECTS. Endovascular.*

Introduction

Acute Ischemic Stroke (AIS) is the leading cause of death and disability worldwide[1], and reperfusion therapies are very effective in reducing the number of patients who suffer a deterioration in their functional status due to AIS[2,3]. There is relative consensus on the tendency to simplify imaging tests to select patients diagnosed with large vessel occlusion (LVO) in the early window and to dispense with multimodal neuroimaging[4]. However, the potential benefit of mechanical thrombectomy (MT) in patients with ≥ 6 hours of evolution depends on proper selection of slow progressors, which is directly related to a good leptomeningeal collaterality[5]. Perfusion studies have proven to be useful in predicting the volume of ischemic core and critical hypoperfusion[6], although they have the disadvantage of increasing exposure to higher doses of contrast and radiation, in addition to requiring post-processing, which, even with automated software, prolongs the time required to decide on the therapeutic approach[7].

Perfusion studies are not widely available in primary stroke centers, which is a major limitation when it comes to being able to increase the time criteria for selection of patients susceptible to endovascular therapy that could be taken to comprehensive stroke centers. For this reason, selection methods based only on computed tomography (CT) in late-window patients are being explored[8].

The usual neuroimaging protocol for the study of AIS includes CT angiography (CTA) from the aortic arch to the vertex, which is usually performed in the arterial phase[9].

Hypoattenuation in CT angiography source images (CTA-SI) in early arterial phase has been shown to be more sensitive than Alberta Stroke Program Early CT Score (ASPECTS) of brain parenchyma to determine tissue at risk of ischemia, so it could be a good tool to determine viable salvageable tissue in an extended window[10,11]

Our hypothesis is that the addition of a second acquisition at 35-50 seconds could complement the assessment of hypoperfused tissue that fails to receive flow through pial vessels.

Methodology

Our study is a retrospective analysis of a prospective cohort named Registro de Enfermedades Cerebrovasculares de Clínica Alemana de Santiago (RECCA), which registered consecutive adults patients under informed consent approved by the Institutional Ethics Committee. The initial registry included all adult patients with AIS admitted to Clínica Alemana de Santiago from August 2019 to July 2023.

Study inclusion criteria were: 1) patient with AIS between 6-24 hours from symptom onset, 2) NIHSS ≥ 6, 3) LVO of anterior circulation, 4) admission CT-Perfusion and CTA in arterial/delayed phase. Exclusion criteria: 1) incomplete data.

Image and interpretation protocol

The post-processing of CT-Perfusion images was performed in an automated way through RAPID© software, which considers a candidate for extended window endovascular therapy those patients whose ischemic core determined by CBF < 30% was not greater than 50 ml and the mismatch between Tmax > 6 sec/CBF < 30% volume ≥ 1.8.

CTA from supra-aortic trunks to vertex was performed in arterial and delayed phase at 35-50 seconds.

A vascular neurologist performed the estimation of CTA-SI ASPECTS in both phases at the time of data entry into the RECCA registry, which was done blind to the results of the perfusion study. A parallel evaluation of the CTA-SI was done by a neuroradiologist who was blind to both the clinical history and the results of the multimodal neuroimaging with automated processing. In case of a discrepancy, consensus could be reached by considering a third evaluation carried out by an external neuroradiologist.

Mismatch was considered when the difference between arterial arterial phase CTA (CTA-AP) ASPECTS and delayed phase CTA (CTA-DP) ASPECTS was ≥ |2| points (Figures 1 and 2).

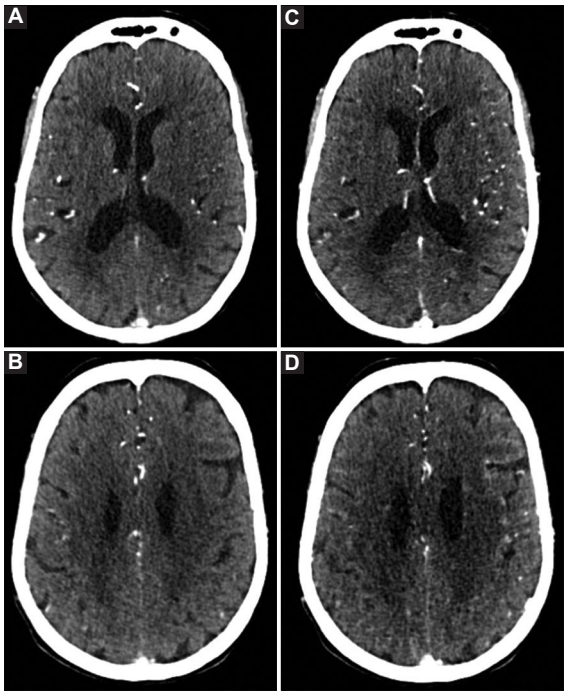

Figure 1. Occlusion in M1 segment of the left middle cerebral artery. **A** and **B** correspond to the arterial phase. **C** and **D** correspond to the delayed phase with filling by leptomeningeal vessels in the M1-M2-M4 and M5 region of ASPECTS. Considering a significant mismatch, the patient underwent mechanical thrombectomy.

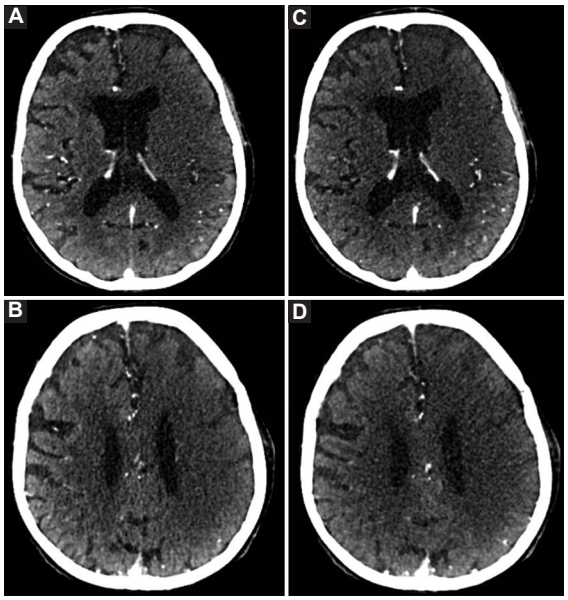

Figure 2. Occlusion in M1 segment of the left middle cerebral artery. **A** and **B** in arterial phase with low CTA-SI ASPECTS. **C** and **D** in delayed phase without significant changes.

Statistical analysis

The normality of quantitative variables was evaluated through the Shapiro-Wilk test, using descriptive statistics to calculate the mean, standard deviation, median and interquartile range. Strength of association between continuous variables of the automated perfusion study and the CTA evaluation was assessed through Pearson's correlation coefficient. In addition, the association between categorical variables of the automated study and visual assessment was assessed using Fisher's exact test. To predict the outcome of a categorical variable of the perfusion study by logistic regression, all clinical and demographic characteristics at admission were used as independent variables, as well as the results of the CTA study. The data were processed with STATA version 17.0.

Results

During the study period, 22 patients met the inclusion criteria. The mean age was 77.8 years (range 48-94 years), the median NIHSS score was 15 (IQR 10-21) and the median time from symptom onset to CT was 11 hours (Tables 1 and 2). CTA-AP ASPECTS—CTA-DP ASPECTS mismatch was present in 14 of the 22 patients, with no discrepancy between vascular neurologist and neuroradiologist.

Pearson's coefficient demonstrated a high correlation between ischemic core volume and CTA-DP ASPECTS with an inverse association of -0.93 p 0.0001 (Figure 3), and between Tmax ≥ 6 sec volume and CTA-AP ASPECTS with a value of -0.88 p 0.0001 (Figure 4).

There was a significant association between patient selection under DEFUSE 3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3) criteria and the assessment of CTA-AP ASPECTS—CTA-DP ASPECTS mismatch with a p-value of 0.002. In addition, there was a direct relationship between the probability of being a candidate for MT by RAPID automated CT-Perfusion criteria and a higher CTA-SI ASPECTS value in delayed phase, with a perfect association for CTA-SI ASPECTS values ≥ 8.

Discussion

Hypoattenuation on CTA-SI has been evaluated qualitatively with CBF and CBV maps, demonstrating a higher correlation with CBF drop, suggesting a significant approximation to critically hypoperfused tissue[12]. Although, to date the association has only been made from CTA-SI in arterial phase and there is no data when it is compared

Table 1. Patients with CTA-AP ASPECTS—CTA-DP ASPECTS-mismatch. Baseline clinical and imaging characteristics (n = 14)

Variable	Mean	Median	Interquartile range
Age	78	78.5	(70-86)
NIHSS admission	15	14	(6-22)
Time onset-CT	12	11	(6,5-19)
Core volume (CBF < 30%)	25	17	(7-31)
Critical Hypoperfusion (Tmax > 6 sec)	125	112	(51-174)
CTA-AP ASPECTS	6	6	(5-7)
CTA-DP ASPECTS	8	9	(7-10)

NIHSS: National Institutes of Health Stroke Scale; ASPECTS: Alberta Stroke Program Early CT Score; CBF: cerebral blood flow; Tmax: time-to-maximum.

Table 2. Patients without CTA-AP ASPECTS—CTA-DP ASPECTS- mismatch. Baseline clinical and imaging characteristics (n = 8)

Variable	Mean	Median	Interquartile range
Age	78	82	(71-89)
NIHSS admission	17	19	(10-24)
Time onset-CT	11	11	(7-16)
Core volume (CBF < 30%)	118	117	(47-187)
Critical Hypoperfusion (Tmax > 6 sec)	160	203	(51-225)
CTA-AP ASPECTS	5	5	(3-7)
CTA-DP ASPECTS	6	6	(4-8)

NIHSS: National Institutes of Health Stroke Scale; ASPECTS: Alberta Stroke Program Early CT Score; CBF: cerebral blood flow; Tmax: time-to-maximum.

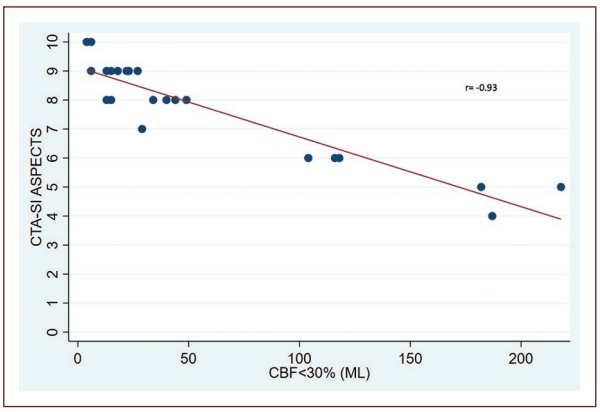

Figure 3. Scatter plot of Pearson's correlation coefficient. A significant negative correlation between ischemic core volume (x-axis) and CTA-DP ASPECTS (y-axis).

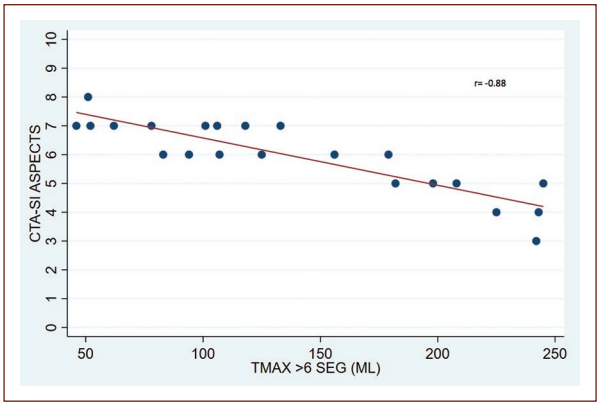

Figure 4. Scatter plot of Pearson's correlation coefficient. A significant negative correlation between Tmax ≥ 6sec (x-axis) volume and arterial CTA-AP ASPECTS (y-axis).

with the volumetric values offered by the automated software. Adequate assessment of the volume of hypoperfused and infarcted tissue is essential for the selection of slow progressors[13,14], who are potential beneficiaries of late-window endovascular therapy[15]. However, according to our results, the assessment of dual-phase CTA seems to be a semiquantitative tool comparable to the multimodal study with validated metrics.

CTA-DP ASPECTS showed a high approximation to what we consider nonviable tissue, with a 25th percentile on ASPECTS 7 appearing to be a possible lower limit for ischemic core on that quantitative score. Moreover, the CTA-SI in the arterial phase presented a high correlation with what we determined by imaging consensus as critical hypoperfusion, which includes viable tissue.

Therefore, these results provide information in the direction of the feasibility of choosing patients in extended window with imaging protocols with greater availability, shorter acquisition time and lower irradiation. In addition, it is possible that dispensing with CT-Perfusion could increase the number of patients who can benefit from TM, since there is growing evidence that advanced imaging studies lead to overselection[16].

A clinical trial called MR CLEAN LATE was recently published, which aimed to evaluate the efficacy of extending the selection of patients for endovascular therapy beyond 6 hours based on the presence of collateral flow in the CTA. Although this trial demonstrated that endovascular treatment between 6 and 24 hours after symptom onset is safe and effective in patients with ischemic stroke

due to occlusion of large vessels of the anterior circulation and any collateral arteries visible on CTA baseline, this study showed more benefits for patients with fewer collaterals and more clots, so stratification into degrees of collateral flow does not seem to be a useful strategy.

It seems essential to us to highlight that in the MR CLEAN LATE[17], the median of NCCT ASPECTS of the endovascular group was 9 (interquartile range [IQR] = 7-10), which coincides with the median of CTA-DP ASPECTS of the group with arterial-delayed mismatch in our study.

Limitations

This study has some limitations. First, because of its retrospective nature, we cannot exclude a certain selection bias. Second, the small sample size decreses the power of the study and increases the margin of error.

Conclusions

In conclusion, dual-phase CTA could be used similar to CT-Perfusion and derive information on salvageable and non-salvageable tissue. It could also be used to select patients eligible for thrombectomy in the late time window, however, because of study limitations, these findings should be interpreted as preliminary and require replication.

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Conflicts of interest

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Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

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

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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ORIGINAL ARTICLE

Stroke knowledge in two highly educated populations in Mexico City

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Abstract

Background/Objective: *Stroke knowledge is variable within and between countries. It is determined by school grade, geographical location, and language barriers. This study aims to evaluate the knowledge of stroke symptoms, risk factors, and treatment in a specific population in Mexico.* **Methods:** *We surveyed volunteer participants among the inhabitants of a medium-income condominium complex and employees of a pharmaceutical company located in Mexico City between 2016 and 2018. We collected information regarding knowledge of stroke definitions, symptoms, risk factor identification, and treatment.* **Results:** *We surveyed 499 participants at both sites, with a median age of 44 years (interquartile range 31-70) and mean years of education of 16.09 years (SD 3.67). The recognition of different definitions regarding stroke was highly heterogeneous, with "brain hemorrhage" and "stroke" being the most known. Among participants, 70% knew at least one stroke symptom. Out of four risk factors, a mean of 3 are identified when prompted, with dyslipidemia being the least acknowledged. While 70% of participants recognize stroke as treatable, only 12-25% know about intravenous thrombolysis. There was no significant difference in overall stroke knowledge between surveyed sites.* **Conclusions:** *Knowledge about stroke remains highly heterogeneous in our population. While the knowledge of the general presentation of stroke is higher than in other studies, probably due to the higher mean school education, the awareness of treatment options is low. New public education programs should consider including this information, because it may improve the proportion of cases treated promptly.*

Keywords: *Stroke. Knowledge. Health education. Risk factors. Signs.*

Conocimiento de la enfermedad vascular cerebral en la Ciudad de México

Resumen

Introducción/Objetivo: *El conocimiento de la enfermedad vascular cerebral (EVC) varía entre países y dentro de los mismos. Está determinado por la escolaridad, localización geográfica, barreras de lenguaje y más. Este estudio proporciona información reciente sobre este tema, a través de la medición del conocimiento sobre los síntomas de la EVC, factores de riesgo y tratamientos, en una población de la Ciudad de México.* **Métodos:** *Realizamos una entrevista a participantes voluntarios en un condominio de ingreso medio y a empleados de una empresa farmacéutica en Ciudad de México, entre 2016 y 2018. Recolectamos información acerca del conocimiento de definiciones de EVC, síntomas, factores de riesgo y tratamientos.* **Resultados:** *Realizamos 499 entrevistas entre ambos sitios, con mediana de edad de 44 años (interquartile range 31-70) y*

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media de escolaridad de 16.09 años (SD 3.67). El reconocimiento de diferentes definiciones relacionadas a la EVC fue altamente heterogéneo, siendo "hemorragia cerebral" y "EVC" los más reconocidos. Adicionalmente, 70% reconoció al menos 1 síntoma de EVC. De 4 factores de riesgo, se identificaron una media de 3, siendo dislipidemia el menos reconocido. Aunque el 70% reconoce la EVC como tratable, sólo un 12-25% conoce la trombolisis intravenosa. No hubo diferencia significativa entre ambos sitios. **Conclusiones:** *El conocimiento de la EVC permanece altamente heterogéneo en nuestra población. Mientras el conocimiento sobre la presentación de la EVC fue mayor a otros estudios, probablemente por una mayor escolaridad, el conocimiento del tratamiento es bajo. Los programas de educación deben considerar incluir esta información, ya que puede mejorar la proporción de casos tratados en tiempo oportuno.*

Palabras clave: *Enfermedad vascular cerebral. Conocimiento. Educación en salud. Factores de riesgo. Signos.*

Introduction

Accounting for 85% of all stroke-related deaths worldwide, acute stroke is a significant public health problem, especially for countries undergoing epidemiological transition[1], In Mexico, stroke is the seventh leading cause of death, with over 19,000 deaths in 2021[2]. Stroke is also a leading cause of disability in adults and the second most common cause of dementia. Given its impact on the economically active population and quality of life, improving stroke prevention and treatment must be of high priority for public health-care systems worldwide.

Acute stroke can present with multiple signs and symptoms, usually affecting one side of the body and potentially associated with decreased alertness[3]. Sometimes, its initial presentation is subtle and may not be recognized by bystanders. There has been substantial effort to strengthen the recognition of stroke among health-care personnel and the general population[4]; however, specific studies regarding its impact in Mexico have yet to be conducted[5].

Stroke prevention is more cost-efficient than treatment. This is done through modifiable risk factors control, such as a healthy diet, physical activity, and pharmacological treatment[6]. Acute reperfusion treatments (intravenous thrombolysis or mechanical thrombectomy) have improved functional outcomes; however, these therapies can only be applied in certain scenarios and within a specific timeframe. In Mexico, 66% of stroke patients arrive at a hospital after 6 h of symptom onset, reducing the chances of successful reperfusion therapy[1]. In a recent Mexican study, 17.4% of patients arrived < 4.5 h, and only 7.6% received intravenous thrombolysis[7].

Stroke knowledge varies worldwide and even within countries[8], with up to 70% recognition of at least one symptom and one risk factor. Among the Mexican population, information regarding public knowledge of acute stroke treatments is lacking[9]. Increased stroke knowledge could lead to earlier recognition of stroke and potentially increase the proportion of patients arriving in time for reperfusion therapy. Our study provides updated information about stroke knowledge in the general population.

Materials and methods

For this study, we designed a questionnaire addressing stroke knowledge, including its definition and associated concepts, risk factors, symptoms, and treatments. This questionnaire was divided into six different sections: (1) knowledge of different terms used by non-healthcare professionals to name "stroke;" (2) definition of common terms associated with stroke; (3) recognition of the main clinical manifestations of stroke; (4) recognition of risk factors for stroke; (5) knowledge of acute treatment of stroke; and (6) perceived stroke mortality.

The first section consisted of applicants answering all the terms they knew in Spanish that were equivalent to stroke, which is very variable among native Spanish speakers. In the second, we asked the participants to define in their own words different terms related to "stroke" ("brain infarction," "brain hemorrhage," "subarachnoid hemorrhage," "cerebral venous thrombosis," "transient ischemic attack," and "aneurysm"). In the third, we asked the participants to answer all the symptoms they knew of stroke openly, and we compared the answers to a pre-established list; if they did not name any of these pre-established symptoms, we prompted the responses, and we requested them to answer "yes" or "no." In the fourth part, we provided a list of risk factors for stroke, including four correct risk factors (hypertension, diabetes, dyslipidemia, and obesity) and six wrong answers (sexually transmitted disease [STD], pregnancy, hepatitis, asthma, cataract, gastritis), to which participants answered "yes" or "no" if they considered it to be associated with increased stroke risk. Finally, we investigated whether they recognized stroke as a treatable disease, the correct treatments they knew about, and whether they were aware of intravenous

thrombolysis and mechanical thrombectomy. In the condominium-complex group, the questionnaire included the following questions: "Do you know how much time we have to administer the thrombolytic therapy after the first symptom?" and "Out of 100 patients suffering from stroke, how many do you think will die?" These questions were not asked in the pharmaceutical company survey to reduce bias because these data are included in sales strategies. The complete survey is provided as supplementary material.

We trained 4th-year medical students in the systemized application of the survey, who then applied the survey to willing participants aged 18 years and older, under supervision from the authors. The survey was applied in two locations in Mexico City: A middle-class condominium complex (Villa Olímpica – a condominium complex in the south of Mexico City and close to the National Autonomous University of Mexico – inhabited by several researchers from this University), and the headquarters of a pharmaceutical company (producers of Alteplase).

The permit was submitted to the authorities of each site to survey inhabitants and workers. We had permission accepted in 2016 by the condominium and in 2018 by the pharmaceutical company. Each site was surveyed over 2 days, the first (condominium complex) in December 2016 and the second (pharmaceutical company) in August 2018. We do not consider that the conduction of the survey in two different years poses a risk for different degrees of knowledge, given that no promotion or educational program for stroke existed or was promoted in those years in Mexico City. The questionnaire was applied to all volunteer inhabitants at the condominium in a door-to-door search, and in the pharmaceutical company, we only applied it to non-medical administrative personnel, which included employees of the sales, accounting, and marketing departments.

The permit was submitted to the authorities of each site to survey inhabitants and workers. We had permission accepted in 2016 by the condominium and in 2018 by the pharmaceutical company. Each site was surveyed over 2 days, the first (condominium complex) in December 2016 and the second (pharmaceutical company) in August 2018. We devised a composite score, ranging from 0 to 12 points, to summarize and compare results between groups. Surveys with missing data were excluded from the study.

Statistical analysis

Categorical variables are presented as frequencies with proportions; normality testing for continuous variables was performed using the Kolmogorov–Smirnov test; these variables are reported as median with interquartile range (IQR) or as mean with standard deviation as appropriate; differences between non-normally distributed variables were tested using the Mann–Whitney U-test for independent samples, to compare the composite score results between surveyed groups and Spearman's rho for exploring the correlation between age and education level with composite score results. Analyses were performed using IBM SPSS Statistics version 20 (IBM Corp., Armonk, NY, USA).

Results

In total, we surveyed 535 people, excluding 36 surveys due to being incomplete. Table 1 summarizes results from 499 participants, with 277 in the condominium complex group (median age 58 years [IQR 43-70]; 55% female; mean years of education 16.7 [SD 4.40]) and 222 in the company's building (median age 33 [IQR 27-42] years; 54.9% male; mean years of education 15.3 [SD 2.28]). Age was higher in the condominium complex group, and the educational level was significantly lower among the company group.

Regarding stroke concepts, half of the participants correctly defined stroke and cerebral infarction. Brain hemorrhage was the most correctly defined concept in 68.7%, but subarachnoid hemorrhage and transient ischemic attack were the lowest (8% and 9.6%, respectively). Brain aneurysm, a concept commonly associated with stroke in Spanish laypeople language, was correctly defined only in 18.4%.

The recognition of initial stroke symptoms was good overall, with 71% recognizing at least one sign and 53.7% recognizing two or more. Perhaps, the downside point is that a third part of the participants could not identify any symptoms. The complete Cincinnati triad was only mentioned by 13.2%, possibly due to our country's need for a specific stroke education program. True risk factors were extensively recognized in all participants, and false risk factors were rarely recognized, besides pregnancy and STD which were referred to as risk factors by approximately a fifth of participants.

Stroke treatment knowledge was higher in the company than in the condos, which is expected since they produce Alteplase. Despite this, 75.8% of participants could not mention a single treatment for stroke. When applying the composite score, there was no statistically significant difference between the groups' overall stroke knowledge.

Table 1. Result summary

Variable	Group 1: condominium (n = 277) (%)	Group 2: company (n = 222) (%)	Total (n = 499) (%)
Age in years	56 (43-70)	33 (27-42)	44 (31-60)
Male sex	107 (45.1)	130 (54.9)	237 (47.5)
Years of education	16.71 (4.40)	15.31 (2.28)	16.09 (3.67)
Familiarized with stroke, (%)	156 (56.3)	101 (45.5)	257 (51.5)
Defined brain infarction	141 (50.9)	79 (35.6)	220 (44.1)
Defined brain hemorrhage	196 (70.8)	147 (66.2)	343 (68.7)
Defined SAH	26 (9.4)	14 (6.3)	40 (8.0)
Defined CVT	87 (31.4)	62 (27.9)	149 (29.9)
Defined TIA	34 (12.3)	14 (6.3)	48 (9.6)
Defined brain aneurysm	77 (27.8)	15 (6.8)	92 (18.4)
Stroke symptom knowledge			
0	102 (36.8)	40 (18.0)	142 (28.5)
1	42 (15.2)	47 (21.2)	89 (17.8)
2 or more	133 (48.0)	135 (60.8)	268 (53.7)
Mentioned cincinnati triad	42 (15.2)	24 (10.8)	66 (13.2)
Identified true risk factors	3.07 (1.18)	2.92 (1.10)	3.00 (1.15)
Identified false risk factors	0.96 (1.31)	0.81 (1.09)	0.89 (1.21)
Recognized stroke as treatable	195 (70.4)	156 (70.3)	351 (70.3)
Identified stroke treatments			
0	217 (78.3)	161 (72.5)	378 (75.85)
1	48 (17.3)	55 (24.85)	103 (20.6)
2 or more	12 (4.3)	6 (2.7)	18 (3.6)
Defines IVT	35 (12.6)	56 (25.2)	91 (18.2)
Composite score	6 (4-8)	6 (4-8)	6 (4-8)
	p = 0.861		

*Age and composite score described in median and IQR; education level, true risk factors recognized, and false risk factors recognized are described in mean and standard deviation.: Independent samples Mann–Whitney U-test. Composite score: Defines brain infarction (1 point), defines brain hemorrhage (1 point), recognizes Cincinnati triad (1 point), number of stroke symptoms recognized (none = 0 points, 1 = 1 point, 2 or more = 2 points), true risk factors identified (1 point per each), number of stroke treatments known (none = 0 points, 1 = 1 point, 2 or more = 2 points), defines IVT (1 point).
SAH: subarachnoid hemorrhage; CVT: cerebral venous thrombosis; TIA: transient ischemic attack; IV: intravenous thrombolysis.

Figure 1 describes the recognized proportion of surveyed risk factors. Hypertension was the most recognized risk factor, with 95%, while dyslipidemia was the least known risk factor with 60%. Although no false risk factor was recognized more than any true ones, unrelated diseases such as cataracts can be identified as such when suggested.

In the extended version of the questionnaire for the condominium group (n = 277), we obtained the following responses. Regarding the window time to administer thrombolytics, we obtained 48 responses (17.3%), of which 36 (75%) considered a window to apply thrombolytics < 3 h, 1 (2.08%) between 3 and 4.5 h, and 11 (22.9%) > 4.5 h. Furthermore, in this group, the average perceived mortality from stroke was 39.7% (0-100) with 122 participants (44%) reporting < 30% mortality, 93 (33.5%) between 30 and 60%, and the remaining 62 (22.3) > 60%.

We found no correlation between age and composite score (p = 0.92), with a weak correlation (0.230) between education level and composite score (p < 0.001).

Discussion

This study found that stroke knowledge in these selected Mexican populations remains heterogeneous, ranging from a greater understanding of risk factor recognition to a deficient knowledge of stroke definitions and treatments. It is worthwhile to compare the overall results with those obtained by Góngora-Rivera et al. in 2003, also obtained in a median-income population in Mexico City[9]. Knowledge of at least one stroke symptom was higher in our study

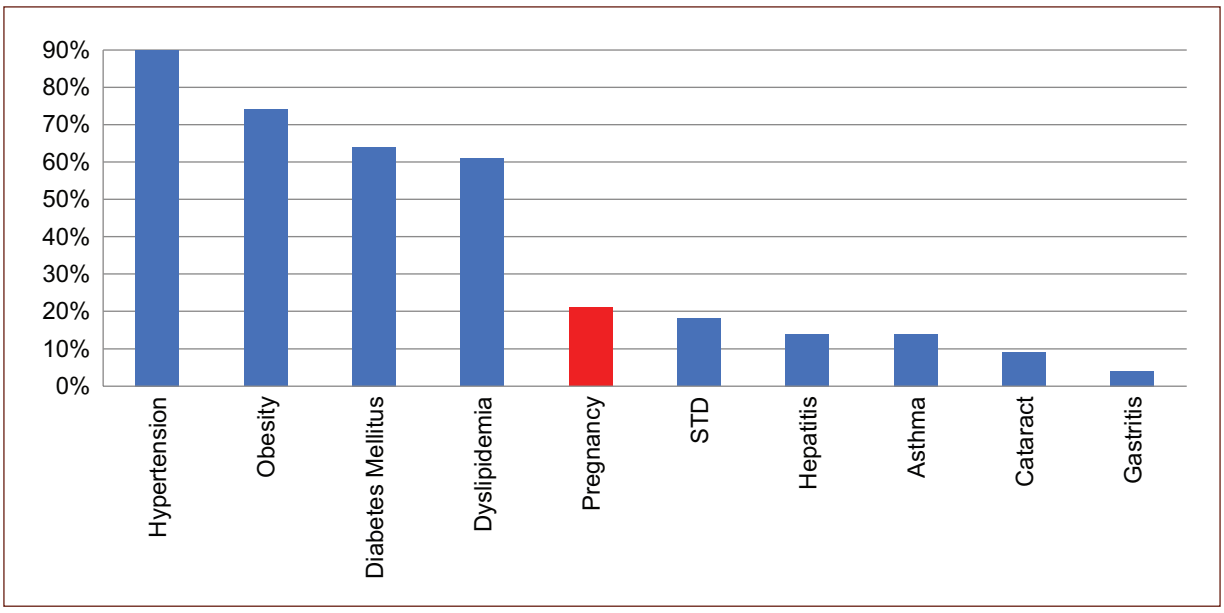

Figure 1. True (blue) and false (red) risk factors recognized by participants in %.

(33% vs. 60%). The proportion of risk factor recognition was also higher in our study; however, the differences in methodology could explain this finding (prompted answers vs. open questions). The use of distractors (false risk factors) was only used in our study, demonstrating a low recognition of these compared to the actual risk factors, and indicating a low level of misinformation in this area.

The lack of universal terminology in Spanish for stroke makes it difficult to establish public information programs to recognize acute stroke signs and symptoms accurately. This factor may contribute to the poor knowledge among our population[10]. Most of our population uses different terms to name a stroke. However, as demonstrated in our questionnaire, they lack a deeper understanding of these diverse concepts. This language barrier problem represents a challenge for developing stroke education programs in Spanish-speaking countries[11]. This may not be exclusive to the Spanish-speaking population, as this remains understudied. As an example, some of the interviewed population refer to hemorrhage as "*derrame*" ("blood spillover"). They may also consider it a synonym of "aneurysm," and both terms are at least as commonly used by the general population. It is essential to recognize this lingual disparity when comparing the knowledge of stroke between diverse language-speaking people, and critical for creating and promoting adequate education programs, which cannot be the same for all.

The recognition of presenting stroke symptoms was far greater than in earlier studies in our city[9]. For example, the percentage of people able to recognize one alarm symptom was almost double. The proportion of recognition of initial symptoms was also high compared to similar studies in other Latin American countries. In Colombia, an open-ended questionnaire demonstrated that 65% could not name an initial stroke symptom, and 54% could not name a risk factor[12]. In Brazil, 22% could not mention any presenting symptom, closer to the proportion found in our study[13] Given differences in methodology, these comparisons must be interpreted with caution; however, they could be explained by greater years of education in our selected population. Paralysis on one side of the body and mouth deviation is the most recognized symptoms; moreover, other important presenting symptoms such as coma or acute visual disturbances were less in this study.

One crucial point in our study, which has not been previously searched for in our country and is only seldom investigated in other survey-based studies, is the knowledge of thrombolytic and interventional therapies for stroke and the existence of a window time. It has been previously demonstrated that knowledge of these points is low among the general population[14]. Another important fact is that understanding risk factors and stroke presentation may not be associated with a higher proportion of patients arriving in window time, as found in an interview study in Brazil[15]. This has also been observed even among the more exposed to stroke population of health-care professionals. This could mean that there is not enough divulgation of these problems among the general population, but it

could also represent the more complex nature of these terms. Directing efforts toward increasing knowledge in these areas may be helpful[16]. In a study done in patients hospitalized for acute stroke, the factors associated with arrival within the window time for IVT were recognition of the first symptom as part of the stroke, the use of an ambulance, and the knowledge of the existence of a thrombolytic therapy[17,18].

The variation in survey years could introduce bias, as the prominence of mechanical thrombectomy may have increased during that period. Despite the absence of any promoted educational programs for stroke treatment in Mexico City during those years, we cannot guarantee that company personnel remained uninformed on this matter, and we recognize this as a limitation in this study.

Conclusion

Knowledge of stroke, in general, is determined by years of education and the language-specific terms for stroke at the general population level. Despite the greater general knowledge with increasing years of schooling, the knowledge of thrombolytic therapies and time windows for reperfusion therapies was low even among our educated population. We hope that our data could be helpful in the development of public education programs, aiming at creating information directed in lay language (but unified) terms, and about the importance of very early hospital arrival in functional outcomes and prognosis.

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The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

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

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Supplementary data

Supplementary data are available at DOI: 10.24875/RMN.23000045. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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ORIGINAL ARTICLE

Intracranial hemorrhage outcomes in the Latin American Stroke Registry

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Latin American Stroke Registry, Mexico City, Mexico

Abstract

Background: *Intracranial hemorrhage (ICH) carries a significant morbidity and mortality burden; however, there is scarce information in Latin American.* **Objective:** *To analyze the functional prognosis and mortality rates among participants in the Latin American Stroke Registry (LASE).* **Methods:** *Eighteen centers across Latin American compiled data on demographics, vascular risk factors, clinical stroke description, ancillary tests, and functional outcomes in hospital stay of patients included from January 2012 to January 2017. All these variables were analyzed based on functional outcome at hospital discharge.* **Results:** *We included 495 patients with ICH, representing 10.3% of all collected stroke subtypes in LASE. The median in-hospital stay was 9 days (interquartile range, 1-30); 285 (57.6%) were male (median age, 62 years) and 210 female (median age, 65 years). A poor functional outcome (modified Rankin scale, 3-6) was observed in 214 (43.2%) patients, with 62.5% of women (p < 0.009). Mortality was documented in 12.5% of ICH patients. The Kaplan-Meier survival curves presented difference in mortality, with higher frequency in patients > 80 years (HR 1.89, 95%CI 1.07-3.35, p = 0.028), with GCS < 8 (HR 0.19, 95%CI 0.11-0.33, p = < 0.001), ventricular irruption (HR 1.88, 95%CI 1.09-3.24, p = 0.0282), and hematoma volume > 30 cc (HR 2.36, 95%CI 1.17 - 4.77, p = 0.016).* **Conclusions:** *Our study demonstrates a poor functional prognosis in 43.2% of ICH patients, with the risk factors for higher mortality being age over 80 years, higher GCS values, and ventricular irruption in the LASE. Our collaborative study contributes substantial insight into the factors influencing ICH occurrence, prognosis, and outcomes in Latin America.*

Keywords: *Intracranial hemorrhage. Latin America. Stroke registry. Stroke outcome.*

Resultados de la hemorragia intracraneal en el Registro Latinoamericano de Enfermedad Vascular Cerebral

Resumen

Introducción: *La Hemorragia Intracraneal (ICH) conlleva una importante carga de morbilidad y mortalidad; sin embargo, existe escasa información en Latinoamérica.* **Objetivo:** *Analizar el pronóstico funcional y las tasas de mortalidad entre los*

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participantes del Registro Latinoamericano de Enfermedad Vascular Cerebral (LASE). **Métodos:** *Dieciocho centros de toda Latinoamérica recopilaron datos demográficos, factores de riesgo vascular, descripción clínica, pruebas auxiliares y resultados funcionales en la estancia hospitalaria de los pacientes incluidos entre enero de 2012 y enero de 2017. Todas estas variables se analizaron en función del resultado funcional al alta hospitalaria.* **Resultados:** *Se incluyeron 495 pacientes con ICH, que representan el 10.3% de todos los subtipos de enfermedad vascular cerebral en LASE. La mediana de estancia hospitalaria fue de 9 dias (rango intercuartil, 1-30); 285 (57.6%) fueron hombres (mediana de edad, 62 años) and 210 mujeres (mediana de edad, 65 años). Un mal resultado funcional (Escala modificada de Rankin, 3-6) fue observado en 214 (43.2%) pacientes, con un 62.5% de mujeres (p < 0.009). Se documento mortalidad en 12.5% de los pacientes con ICH. Las curvas de supervivencia de Kaplan-Meier presentaron diferencias en la mortalidad, con mayor frecuencia en pacientes > 80 años (HR 1.89, 95% IC 1.07-3.35, p = 0.028), con GCS < 8 (HR 0.19, 95% IC 0.11-0.33, p = < 0.001), irrupción ventricular (HR 1.88, 95% IC 1.09-3.24, p = 0.0282), y volumen del hematoma > 30 cc (HR 2.36, 95% IC 1.17-4.77, p = 0.016).* **Conclusiones:** *Nuestro estudio demuestra un mal pronóstico funcional en 43.2% de los pacientes con ICH, siendo los factores de riesgo de mayor mortalidad la edad mayor de 80 años, los valores más bajos de GCS y la irrupción ventricular en el LASE. Nuestro estudio colaborativo aporta información sustancial sobre los factores que influyen en la aparición, el pronóstico y los resultados de la ICH en Latinoamérica.*

Palabras clave: *Hemorragia Intracraneal. Latinoamérica. Registro de Enfermedad Vascular Cerebral. Resultado de la enfermedad vascular cerebral.*

Introduction

Stroke is one of the leading causes of death and disability worldwide. In 2019, the global burden of stroke had 6.5 million deaths and 143 million disability-adjusted life-years (DALY)[1,2]. Intracerebral hemorrhage (ICH) represents approximately 20% of strokes and is its most severe and least treatable form.

The incidence of ICH is 3.41 million[2,3] but can vary significantly based on geographic location, population demographics, among other epidemiologic characteristics. ICH accounts for 5 to 20% of cerebrovascular disease in high-income countries (HICs); however, in low-and middle-income countries (LMICs), the disease burden is higher for ICH. Although the reasons for the higher burden of disease derived from ICH compared to ischemic stroke are not entirely established in LMICs, several factors have been identified, such as high prevalence of poorly controlled hypertension and high sodium intake in local diets[4]. Hospital-based studies from Ecuador, Mexico, Chile and Argentina report a proportion of ICH between 23 and 40%[5,6]. There is also a high incidence of ICH in Asia[5] and in black compared to white populations from HICs[7].

Additionally, ICH produces the highest mortality (50%)[8] and accounts for 42% of all the disability-adjusted years lost due to stroke[6] Despite all the above data, there are few ICH data published from LMICs of the Latin American region, and the scarce data available has been mainly derived from single-center hospital registries, which present the inherent selection bias of this type of study[9].

The LASE (Latin American Stroke Registry) initiative was instituted using robust data compilation and structured methodology to explore multiple stroke outcomes in a population-based sample from tertiary hospitals in Latin America. The present study analyzes the functional outcome, recurrence and death among LASE participants with ICH.

Material and methods

The LASE is a multicenter stroke registry from tertiary referral hospitals with ongoing stroke registries from Central and Andean Latin America, designed to improve knowledge of stroke In the region. Participating sites recruited patients from January 2012 to January 2017. The corresponding Institutional Ethics Committee approved all stroke datasets by international and local research regulations and waived the need for signed informed consent. Still, the patient or a family member verbally agreed to the record of anonymized data in the registry. LASE data comes from 18 centers located in seven Latin American countries. Ten centers from Mexico [Mexico City (5), Durango, Morelia, Madero and Guadalajara (2)], two from Colombia (Bogotá and Cali), two from Perú (both in Lima), and one center from Argentina (Buenos Aires), Costa Rica (San José), Paraguay (Asunción), and Ecuador (Quito). The complete methods of the LASE registry have been published elsewhere[10].

Study's definitions and criteria

Spontaneous ICH was defined as a blood collection within the brain parenchyma secondary to vascular

rupture- that was neither traumatic nor aneurysmal in origin. The inclusion criterion for the present analysis was patients with ICH confirmed by imaging studies. We included cases without a demonstrated aneurysmal or traumatic cause[11]. The cause of ICH was attributed to hypertension in patients with a history of hypertension with regular o irregular treatment and ICH located in sites traditionally associated with hypertension[11]. Cerebral amyloid angiopathy is a cerebral deposition of amyloid-β, this etiology was attributed to cases with features such as lobar hemorrhage, lobar microhemorrhages and superficial siderosis[12]. Only patients aged 18 years and older were included. Cases diagnosed with subarachnoid hemorrhage and those with incomplete information were excluded. Information was collected from the original datasets of each center and compiled into a single database by two authors (FS and MAB). The data includes demographic characteristics such as age, sex, and place of residence. Registered vascular risk factors were hypertension, atrial fibrillation, ischemic cardiopathy, diabetes mellitus, and smoking (current or former). Clinical characteristics, such as the NIHSS and Glasgow Como Scale at admission, were also documented. All patients underwent at least one brain imaging study (CT or MRI) to confirm ICH diagnosis. Clinical outcome was systematically recorded at discharge, as measured by the modified Rankin scale (mRs). Follow-up was not included since most centers only register in-hospital data. A poor clinical outcome was defined as a mRs ranging from 3 to 6, while a good clinical outcome was characterized by a score of 0 to 2. Mortality in this period was analyzed regardless of whether death was considered or not related to ICH.

Statistical analysis

Continuous data is summarized by the mean and standard deviation (SD) or the median and interquartile range according to the results of normality tests (Kolmogorov-Smirnoff test). Categorical data is presented as counts and percentages.

Association analysis of continuous data (age, in-hospital length stay) was done with the Mann–Whitney U or Student t-test according to normality. The chi-squared test or Fisher's exact test adjustment was employed for dichotomous data (including vascular risk factors, demographics, type of ICH, functional outcome, recurrence, and death).

Kaplan–Meier survival curves and the Log-Rank test were utilized to evaluate the absolute risk of death in ICH events during the acute in-hospital period. Significance was defined at $p < 0.05$. Hazard ratios (HRs) and 95% CIs were calculated.

All statistical analyses were calculated using the SPSS 29.0.1.0 software package (SPSS Statistics for Windows, IBM Corp., Armonk, NY).

Results

Demographics

We recruited data from 5336 patients, 508 of these patents were excluded because of the absence of complete information (medical records and neuroimaging). Only 4828 patients with a confirmed imaging diagnosis and complete inpatient clinical information were included in the analysis. Among these patients, 495 corresponded to intracranial hemorrhage, representing 10.3% of all collected stroke subtypes in LASE.

Of the 18 participating centers, three centers did not contribute patients to the database because their neurosurgery departments were responsible for the evaluation, treatment, and follow-up of ICH patients, and the corresponding clinical neurology departments had no access to the data. The median age of all patients was 64 years (interquartile range, 18-94). Among the patients, there were 285 (57.6%) males (median age, 62 years, interquartile range, 18-94) and 210 (42.4%) females (median age, 65 years, interquartile range, 18-93).

Vascular risk factors

The most common vascular risk factor was hypertension, identified in 339 patients (68.5%), followed by smoking (12.9 %) and diabetes (17.8 %). The predominant etiology was hypertensive in 75 % of cases, 5.9% had arteriovenous malformatios, 4% had no aneurysmal subarachnoid hemorrhage, 3.8% had cerebral amyloid angiopathy, 2.8% were related to drugs (anticoagulants/antiplatelet) and 7.7% were undetermined due to incomplete studies. Table 1 presents the general characteristics and risk factors based on functional prognosis upon hospital discharge.

In-hospital outcome

Intracerebral hemorrhage presented an in-hospital bad functional outcome, with mRs of 3-6 observed in

Table 1. General characteristics, vascular risk factors, etiology and treatment according to functional prognosis at hospital discharge

Variable	Good clinical outcome mRs 0 - 2 (n = 281 [%])	Poor clinical outcome mRs 3 - 6 (n = 214 [%])	Total (n = 495)	p value
Age, y[a]	73 (24-89)	67 (37-90)	68 (24-90)	< 0.001*
Male	176 (62.6%)	109 (50.9%)	285 (57.6%)	0.009
Hospital stay, d	8 (1-34)	10.5 (SD 8.3)	9 (1-30)	0.280*
Risk factors				
Hypertension	174 (61.9%)	165 (77.1%)	339 (68.5%)	< 0.001
Diabetes mellitus	35 (12.5%)	53 (24.8 %)	88 (17.8%)	< 0.001
Current smoking	41 (18.3%)	23 (11.2%)	64 (14.9%)	0.121
Coronary disease	8 (2.8%)	11 (5.1%)	19 (3.8%)	0.188
Hypercholesterolemia	34 (12.1%)	31 (14.5%)	65 (13.1%)	0.330
Atrial fibrillation	9 (3.2%)	13 (6.1%)	22 (4.4%)	0.125
Clinical and image				
NIHSS at admission	10 (0-23)	15 (6-32)	12.5 pt (0-32)	< 0.001*
Ventricular irruption	34 (12.1%)	53 (24.8%)	87 (17.6%)	< 0.001
Hematoma volume > 30 cc	5 (1.8%)	26 (12.2%)	31 (6.3%)	< 0.001+
Etiology				
Hypertensive	189 (67.3%)	185 (86.4%)	374 (75 %)	< 0.001
Amyloid angiopathy	7 (2.5 %)	12 (5.6%)	19 (3.8%)	0.074
Arteriovenous malformatios	13 (4.6%)	16 (7.5%)	29 (5.9%)	0.181
Drugs	4 (1.4%)	10 (4.7%)	14 (2.8%)	0.052+
No aneurysmal SAH	11 (3.9%)	10 (4.7%)	21 (4.2 %)	0.678
Not determined incomplete studies	16 (5.7 %)	22 (10.3%)	38 (7.7%)	0.058
Treatment				
Conservative	273 (97.2%)	200 (93.5%)	473 (95.6%)	0.048
Medical Intensive	8 (2.8%)	14 (6.5%)	22 (4.4%)	0.048
Surgical	13 (4.6%)	17 (7.9%)	30 (6.1%)	0.125

[a]Median (Interquartile Range).
*_P_ value U-Mann-Whitney Wilcoxon.
+Fisher's Exact Test.

214 patients (43.2%): 62.6% in women versus 50.9% in men (p = 0.009). The stroke recurrence during hospitalization was 5.9% (29 patients).

The mortality rate was 12.5% (62 patients). The risk of death was found non-significantly higher in men (6.9%) compared to women (5.7%) (p = 0.64). The optimal age cutoff for mortality was 80 years, with an area under curve (AUC) of 0.602. The Kaplan Meier survival curves, categorized by age, hematoma volume, ventricular irruption and Glasgow Coma Scale, are presented in Figure 1. However, there is a difference in mortality, with higher frequency, in patients aged over 80 years (HR 1.89, 95%CI 1.07-3.35, p = 0.028), with GCS below 8 (HR 0.19, 95%CI 0.11-0.33, p = < 0.001), ventricular irruption (HR 1.88, 95%CI 1.09-3.24, p = 0.0282), and hematoma volume exceeding 30 cc (HR 2.36, 95%CI 1.17-4.77, p = 0.016).

Discussion

This analysis showed that ICH represents 10% of our registry. This finding is of great importance since it indicates an underreporting of ICH in the region. In some LASE sites, ICH represented less than 5% of stroke cases, which is lower than other reported ICH series. This could be associated with the fact that in some centers, patients with ICH are managed by the neurosurgery service. The management of acute stroke, especially ICH, in Latin America differs from other regions, and several countries do not have a national plan for stroke[13]. However, many of the ICH cases occur in low and middle-income countries, such as those included in LASE, mainly explained by lower levels of consciousness and poor control of

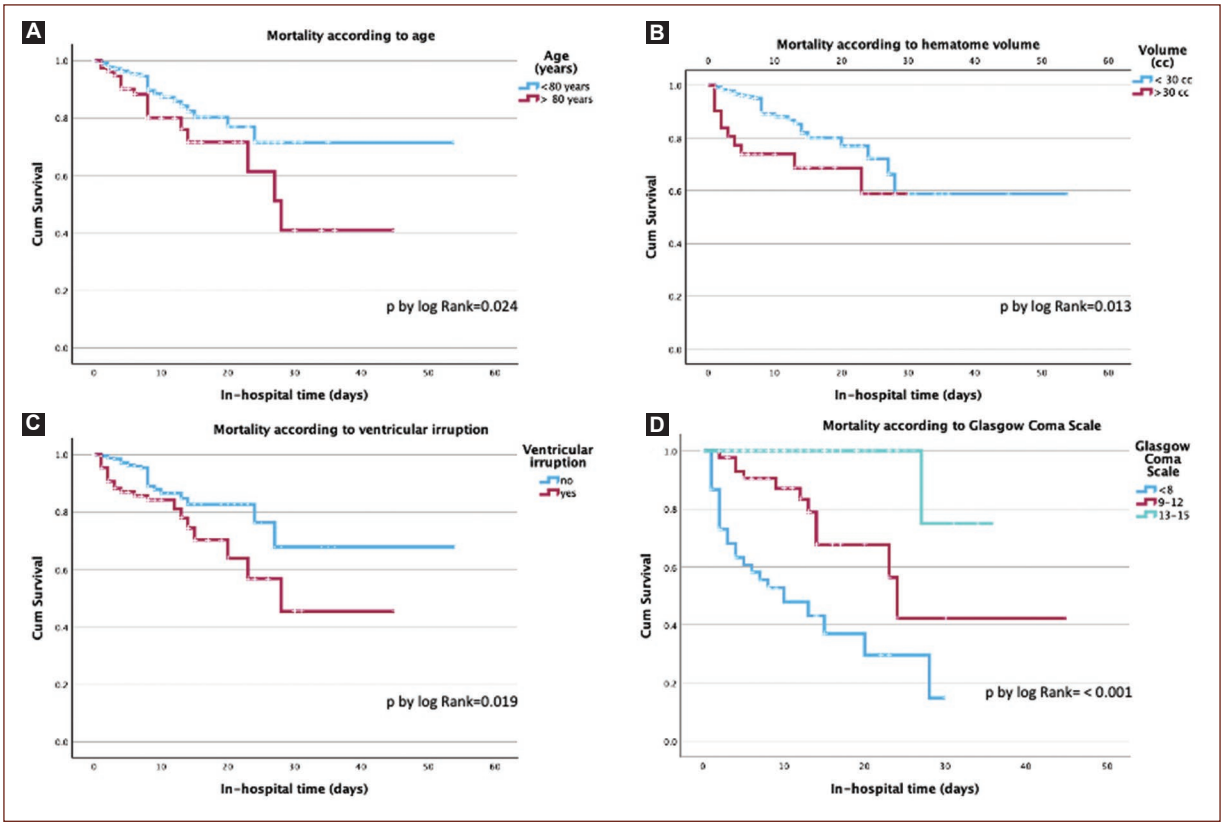

Figure 1. Kaplan-Meier curves: **A:** mortality according to age, **B:** mortality according to hematoma volume, **C:** mortality according to the occurrence of ventricular irruption and **D:** mortality according to Glasgow Coma Scale.

hypertension. In this registry, nearly 60% of the ICH were hypertensive. Management of this critical risk factor could reduce the functional and socioeconomic impact of ICH.

Exploring the factors contributing to ICH within Hispanic populations, the National Institute of Neurology and Neurosurgery-Stroke Registry in Mexico[14] highlighted the prevalence of hypertension (85.1%) among ICH patients Our study also identified a high prevalence of hypertension (68.5%) in ICH patients within LASE. Other risk factors revealed in our study included diabetes mellitus in 17.8% of the cases, which is higher compared to other reports where it is 9%[15,16].

Our findings also mirrored previous reports, indicating a worse functional outcome among ICH patients. 43% of our cases had poor functional prognosis, with a mortality rate of 12.5%, mainly attributed to advanced age (> 80 years), greater bleeding severity (ventricular irruption and hematoma volume exceeding 30 cc) and GCS below 8. Midline shift, lobar and supratentorial bleeds as well as high presenting SBP and nonconsumption of leafy green vegetables, have also been described as predictors of mortality[16].

In the RENAMEVASC (a Mexican stroke registry), a 30-day mortality rate of 30% was reported, with a bad functional outcome present in 31% of the participants[17]. Romano et al. observed comparable stroke severity between Mexican and Miami Hispanic populations (11.6 + 7.6 in Mexico, 11.3 + 8.4 in Miami, p = 0.84)[18], notably, Hispanics in the United States exhibit a heightened risk of ICH compared to non-Hispanic whites (OR 2.6, CI 1.4-6.1)[18].

Our study represents a significant collaborative effort in Latin America, encompassing over 4000 patients from 18 diverse hospitals across seven countries. However, it has multiple limitations. First, the study has the inherent bias of retrospective observational studies. Second, there is a sub-representation of ICH cases, which does not accurately represent this stroke subtype's reality in the entire country. Additionally, the unevenness of the data regarding the distinct aspects of ICH management across the participant countries should be emphasized. Finally, it was impossible to

register follow-up data from the participants, which does not add to our understanding of the mid and long-term outcomes of ICH. Despite these limitations, the LASE initiative is and will continue to be a valuable tool to improve stroke knowledge, providing accurate and systematically recorded data from Latin American patients with stroke. Additionally, our findings highlight the urgent need for more reliable data on ICH in Latin America and serve as a call to action to identify and control arterial hypertension early.

Conclusion

Our study demonstrates a poor functional prognosis in 43.2% of ICH patients, with the risk factors for higher mortality being age over 80 years, higher GCS values, and ventricular irruption. Our collaborative study contributes substantial insight into the factors influencing ICH occurrence, prognosis, and outcomes in Latin America. While sharing similarities with global stroke registries, it provides valuable region-specific information that could guide targeted interventions and healthcare strategies. Additionally, the complexities of ethnic and genetic influences on ICH risk are highlighted, as well as the importance of continuous monitoring and improvement of healthcare practices to enhance outcomes in this population.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

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

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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REVIEW ARTICLE

Bundled care to optimize outcome after intracerebral hemorrhage: action for effective implementation

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Abstract

Patients who experience acute intracerebral hemorrhage (ICH) are not managed with urgency or level of coordinated care as those with acute ischemic stroke. This is largely due to the lack of any proven treatment for ICH, which has led to therapeutic nihilism and a low threshold for the withdrawal of active care in these patients. The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3) is a landmark study which used a novel, quality improvement, implementation design across 122 hospitals in 10 countries, to show that the early intervention of bundled care with time- and target-based metrics, can substantially improve outcomes for patients who suffer ICH. We advocate the widespread adoption of an early bundle of care focused on urgent time-based metrics for the control of elevated blood pressure and other abnormal physiological parameters, and the emergency reversal of anticoagulation, for patients with ICH. Such coordinated interdisciplinary stroke care will optimise the chances of patients all over the world surviving free of major disability after suffering an ICH.

Keywords: *Intracerebral hemorrhage. Protocols. Health outcomes. Implementation. Stroke services.*

Atención agrupada para optimizar los resultados tras una hemorragia intracerebral: medidas para una aplicación eficaz

Resumen

Los pacientes que sufren una hemorragia intracerebral aguda (HIC) no se tratan con la urgencia ni el nivel de atención coordinada que los que sufren un ictus isquémico agudo. Esto se debe en gran medida a la falta de un tratamiento probado para la HIC, lo que ha llevado a un nihilismo terapéutico y a un umbral bajo para la retirada de los cuidados activos en estos pacientes. El tercer Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3) es un estudio de referencia que utilizó un novedoso diseño de implementación para la mejora de la calidad en 122 hospitales de 10 países, con el fin de demostrar que la intervención temprana de la atención agrupada con métricas basadas en el tiempo y los objetivos puede mejorar sustancialmente los resultados de los pacientes que sufren HIC. Abogamos por la adopción generalizada de un paquete de atención temprana centrado en parámetros urgentes basados en el tiempo para el control de la presión arterial elevada y otros parámetros fisiológicos anormales, y la reversión urgente de la anticoagulación, para pacientes con HIC. Esta atención interdisciplinaria coordinada optimizará las posibilidades de que los pacientes de todo el mundo sobrevivan sin discapacidades graves tras sufrir una HIC.

Palabras claves: *Hemorragia intracerebral. Protocolos. Resultados sanitarios. Implementación. Servicios de ictus.*

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Introduction

Acute intracerebral hemorrhage (ICH) is the most serious and least treatable form of stroke, which accounts for approximately 20% of nearly 20 million new cases of stroke that occur in the world each year[1]. Compared to modern reperfusion therapy with thrombolytics and endovascular clot retrieval which has transformed systems of care for patients with acute ischemic stroke, there has not been any clearly proven medical or surgical treatment for ICH. This has led to disorganized and widely variable patterns of care for patients with ICH, a sense of nihilism among clinicians, and frustration in the research community. Fortunately, this situation has now changed with the positive results announced for several completed randomized and controlled trials (RCTs) in ICH in early 2023, led by the third intensive care bundle with blood pressure (BP) reduction in acute cerebral hemorrhage trial (INTERACT3)[2].

INTERACT3 was undertaken to resolve the controversy over the effects of early intensive BP lowering treatment in acute ICH. Although elevated BP is common after the onset of ICH and strongly associated with poor outcomes, RCTs that have evaluated early intensive BP control have produced inconsistent results that have been limited to patients with mild-moderate ICH who do not require neurosurgical intervention[3]. This level of evidence has restricted the uptake of a relatively simple and low-cost management strategy in clinical practice, and where guidelines have generally produced an intermediate strength to the recommendations given toward treatment[4].

What we now know?

INTERACT3 was a landmark study in producing a positive result through conduct on an international scale and overcoming the adversity of the COVID-19 pandemic. It used a novel, quality improvement, and stepped-wedge cluster randomized "implementation" design across 121 hospitals in 10 countries, including Mexico, between December 2017 and December 2021, to show that the early intervention of bundled care with time- and target-based metrics can substantially improve outcomes for patients who suffer ICH. The care bundle protocol included the early lowering of systolic BP (target < 140 mmHg), strict glucose control (target 6.1-7.8 mmol/L in those without diabetes and 7.8-10.0 mmol/L in those with diabetes), antipyrexia treatment (target body temperature ≤ 37.5°C), and rapid reversal of warfarin-related anticoagulation (target international normalized ratio < 1.5) within 1 h of treatment, in patients where these variables were abnormal. The likelihood of a poor functional outcome, measured on the distribution of full range of scores on the modified Rankin Scale (mRS), was less in the care bundle group (common odds ratio 0.86, 95% confidence interval 0.76-0.97; p = 0.02). The favorable shift in scores on the mRS in the care bundle group was generally consistent across a range of sensitivity analyses. Patients in the care bundle group had significantly improved survival, better health-related quality of life, shorter time in hospital, and fewer serious adverse events, than those in the usual care group. Treatment with the care bundle in every 35 patients was estimated to prevent one patient from death or major disability.

What are the implications on INTERACT3?

The INTERACT3 results provide strong support for the rapid control of BP and other physiological variables to be incorporated into clinical practice as a part of active management plan for this serious disease. Given requirements to standardize best practice and use quality performance indicators to reduce unwarranted clinical variation in healthcare, the care bundle protocol is a welcome addition to the list of evidence-based management strategies to compliment reperfusion and other protocols that are now in place for patients with acute ischemic stroke. The combination allows an implementation strategy to enhance stroke services in both low- and middle-income countries (LMIC) as well as in many parts of high-income countries. The global stroke community and accreditation organizations should be engaged to standardize recommendations over the incorporation of the care bundle protocol in guidelines and as advocates for relevant education activities and updates of policies.

As a hybrid effectiveness-implementation trial, INTERACT3 simultaneously tested the effect of a simple and widely applicable intervention while measuring the implementation processes and addressing contextual factors that may have impacted on the uptake of the intervention in routine clinical practice. Some implementation difficulties were noted through a process evaluation embedded in INTERACT3. Of note were concerns that health professionals had that the protocol-defined targets for systolic BP and glycemic control might harm patients, and there being contextual factors in relation to staffing processes and medication supply in low-resource areas[5]. Thus, before implementation can proceed, efforts need to be made to reduce such safety concerns in clinicians and nurses over the care bundle

and in finding solutions to ensure equipment (i.e., infusion pumps and electronic BP monitors) and intravenous antihypertensive agents are readily available.

What next?

Several INTERACT3 investigators are collaborating with the World Stroke Organization (WSO) to incorporate the care bundle as a recommendation in the organization's Living Clinical Guidelines to improve clinical practice for ICH management. Efforts are also being made to seek donations and sponsorship to support the availability of resources (e.g., electronic BP monitors, infusion pumps for insulin, and intravenous antihypertensive medications) in LMIC. Ongoing communication, engagement, and partnerships with a variety of stakeholders, and the broader stroke community network, will facilitate the translation of the care bundle into clinical practice.

A broad multifaceted implementation program will help to promote the uptake of the care bundle globally and identify implementation strategies that are appropriate at regional/national levels. Training and education could be incorporated under such a program to improve knowledge and assist behavioral change for local adaption of the care bundle. In the minimal setting of Sub-Saharan Africa (SSA), for example, stroke services are often configured within general medical services, and there are few established stroke units/essential services. Through WSO, an implementation program incorporating the INTERACT3 care bundle together with thrombolysis management and other evidence-based care strategies, training, policies, and investment could help advance the quality of care and minimize the burden of stroke in SSA. Such a program could be a welcome additional to enhancing stroke services in Mexico where current systems are not optimal for the recovery and survival of patients who suffer from ICH.

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Conflicts of interest

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Ethical disclosures

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REVIEW ARTICLE

Semiology of the neurocritical patient: understanding the language of neurological signs

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Abstract

A fundamental aspect of caring for neurocritical patients is interpreting and understanding their neurological signs and symptoms. This will be a helpful key to determining the brain injury or dysfunction's location, extent, and severity. The semiotics of the neurocritical patient encompasses various domains, including motor, sensory, cognitive, and autonomic functions. A comprehensive understanding of the semiotics of the neurocritical patient empowers clinicians to make timely and accurate diagnoses, predict outcomes, and implement targeted therapeutic interventions. It also enables effective communication among the interdisciplinary team members involved in the patient's care. This article review shows the importance of accurately recognizing and deciphering these signs to guide clinical decision-making.

Keywords: *Semiology. Neurocritical care. Neurological signs. Diagnostic tools. Neurological examination.*

Semiología del paciente neurocrítico: comprensión del lenguaje de signos neurológicos

Resumen

Un aspecto fundamental en el cuidado del paciente neurocrítico es la interpretación y comprensión de sus signos y síntomas neurológicos. Esta será una clave útil para determinar la ubicación, el alcance y la gravedad de la lesión o disfunción cerebral. La semiótica del paciente neurocrítico abarca varios dominios, incluyendo funciones motoras, sensoriales, cognitivas y autonómicas. Una comprensión integral de la semiótica del paciente neurocrítico permite a los médicos realizar diagnósticos oportunos y precisos, predecir resultados e implementar intervenciones terapéuticas específicas. También permite una comunicación efectiva entre los miembros del equipo interdisciplinario involucrado en el cuidado del paciente. La revisión de este artículo muestra la importancia de reconocer y descifrar con precisión estos signos para orientar la toma de decisiones clínicas.

Palabras claves: *Semiología. Cuidados neurocríticos. Signos neurológicos. Herramientas diagnósticas. Exploración neurológica.*

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Introduction

The neurological patient usually confuses the examiner because of the complexity of the nervous system (central and peripheral). They are typically patients who are suffering from severe and sometimes fatal diseases. The intensive care unit (ICU) is no exception for this type of situation since this is where the most complex patients of the entire hospital are, in most cases, fighting daily against death, either because of the neurological disease itself or because of the multiple systemic complications.

This article review aims at medical students, generalist physicians, residents, and specialists in neurological sciences. It aims at the initial approach of all patients with neurological pathology so that, over and over, the neurological examination is more orderly, systematic, and logical to provide the patient with a proper approach, prompt diagnosis, and rapid establishment of medical and sometimes surgical treatment[1].

In the following pages, you will find in a very summarized and concise way the evaluation of the main aspects to take into account for the assessment of the neurological patient. In addition, we propose a decision-making algorithm based on current evidence so the reader can have a guide when assessing a neurocritical patient, reducing the risk of error in diagnosis and treatment (Fig. 1).

Neurocritical anamnesis: unveiling unknown territory

The performance of an adequate anamnesis is paramount to ensure precise diagnosis and effective treatment. This is a formidable task in critical illness and especially taxing when patients are confused, aphasic, or, worse, sedated, and intubated. Gathering all relevant information about the patient's medical background, including past illnesses, surgeries, medications, and allergies, is essential (ideally, given by close family members), but these often must travel separately, arriving significantly after the patient. This information enables health-care providers to make informed decisions and provide the best possible care to their patients since it allows for a subjective vision of the nosological entity that affects the person and objectively with directed questions can be routed and understanding the natural history of the most frequent diseases of daily medical practice. It is crucial to consider fundamental factors such as sex, age, and gender. Since they make the person more or less at risk of presenting a specific pathology or make one diagnosis more probable than another. We can expect to miss important points; they accumulate quickly in the heat of the moment[2,3].

In the intensive care setting, most of the time, the clinical condition of the patient makes it impossible to obtain as detailed anamnesis as desired, which is why family members are a fundamental part of this first step of the clinical history since they are the ones who will provide the most data on the onset of symptoms, whether these were sudden or gradual, associated with particular clinical situations (weight loss, behavioral or behavioral changes, fever, seizures, sensory or motor disturbances, and among others)[4]. When obtaining medical history, gathering comprehensive details regarding any prior medical conditions, the treatments received, and the approach taken to manage them is crucial. This information can provide valuable insights into a patient's health status and guide healthcare professionals in making informed decisions regarding their care (Arterial hypertension, diabetes mellitus, hormonal disorders, etc.) With this knowledge, any clinical changes or emerging symptoms can be explained and addressed more effectively[5].

Ensuring patient safety is an essential aspect of healthcare, and one of the critical measures to take is to check for any allergies the patient may have. This step is high-priority as it helps any adverse reactions or negative outcomes that may arise from exposure. It is crucial to confirm or rule out the consumption of substances of abuse, such as drugs or alcohol, since it is not uncommon for these to affect the mechanism of action of drugs frequently used in the ICU or, more regularly, for patients with drug dependence to require higher doses than usual or shorter intervals between doses. Another essential aspect of being considered is exposure to pollutants or substances with carcinogenic potential (wood smoke, tobacco, heavy metals, pesticides, etc.) since they can be fundamental in understanding lesions that are identified as imaging studies are evaluated[5].

At the end of the anamnesis, a review by systems should be done to evaluate aspects that currently afflict the patient since, in some situations, the reason for the current consultation is not the same as at the beginning of the symptomatology or has been accompanied by other alterations that are important to highlight in the history. Aspects such as pain, weight loss, associated symptoms such as fever or cough, gastrointestinal problems, or changes in skin color can help the evaluating physician to identify aspects that give greater weight to define the diagnosis of a patient or that, on the contrary, suggest non-neurological clinical entities that may have repercussions in the nervous system[6].

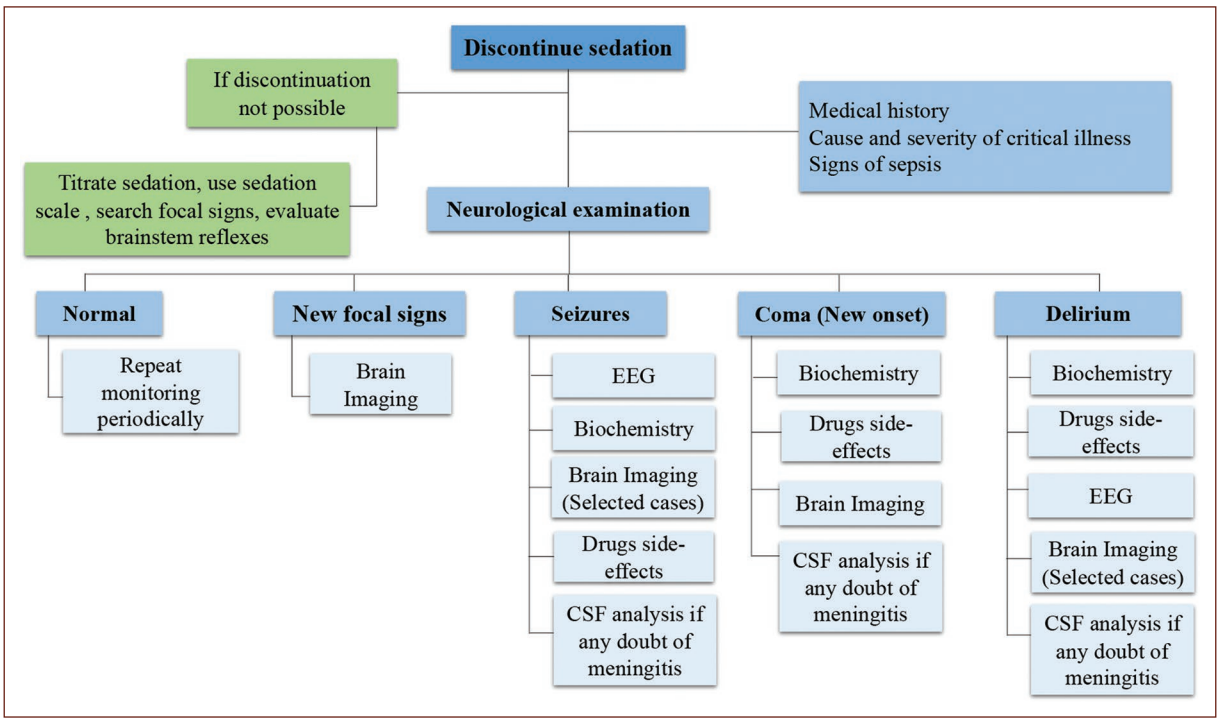


Figure 1. Algorithm diagnostic approach to acute brain dysfunction in intensive care unit.

Neurocritical exploration: unmask neurological signs through physical examination

An adequate evaluation of the physical examination of the neurological and neurocritical patient is the cornerstone to understanding the current pathology on many occasions or why the association with other findings in different systems or organs. In the neurocritical patient, it is the tool that takes on greater weight for the physician since due to the patient's acute and severe condition of the patients, it is not possible to make a structured and complete interview of the patient. It is for this reason that the reader (student, general practitioner, or resident) should gradually become familiar with the clinical manifestations of different nosological entities and create an algorithm of approach according to the objective findings that are obtained, thus in case of being front of a similar patient will be more familiar and therefore, the fear or distrust in their knowledge will be less and therefore be able to provide better care to their patients. It is not surprising that neurocritical patient is not to the liking of all health personnel since, in many cases, they are patients with behavioral and behavioral alterations that make them difficult to treat, either because they are aggressive or because they do not want to respond to questioning or collaborate in the physical evaluation, which makes the student initially avoid this type of patient[7,8].

The physical examination has several parts that should ideally be evaluated, organized, and systematically. Still, it should be noted that it is not always possible to do it in the same order or the same number of maneuvers, which is why the examiner must create increasingly dynamic strategies in the evaluation and interpretation of clinical signs that help to guide the most likely diagnosis, which in many cases will be confirmed by both imaging and paraclinical studies (Fig. 2).

It is vital to identify findings that may suggest intra lesions on physical examination, such as retroauricular ecchymosis (Battle's sign) or palpebral ecchymosis (raccoon eyes) that may occur in patients with skull base fractures. It is possible to identify tongue lesions in individuals who experience epileptic seizures[1].

To ensure a more objective neurological evaluation, it is important to recognize the initial stabilization of the patient. This begins with assessing the airway as the first step; it is essential to identify which patient requires securing the airway with invasive devices to avoid cerebral hypoxia, aspiration of secretions, and thus secondary pulmonary infectious processes[6]. Among the different aspects to evaluate which patient requires

intubation are the Glasgow coma scale (GCS) (Table 1)[9] and assess which patient's state of consciousness is better to secure the airway and thus avoid more sequelae; as a general rule, all patients with GCS < 9 should have a secured airway. However, it is essential to rule out intoxications that can reduce the state of consciousness and thus decrease the GCS score to avoid intubation in patients who sometimes do not require it (especially in alcoholic intoxication and hypoglycemia). It is also vital to evaluate ventilatory aspects that inform the physician which patient may require assisted ventilation, such as the use of accessory muscles for breathing, foreign objects in the oral or nasal cavity that interfere with the adequate passage of air to the lungs, poor management of secretions or abundant bleeding that may cause bronchoaspiration and thus aspiration pneumonia. Fundamental for an objective assessment of the neurological examination is to maintain a mean arterial pressure between 65 mmHg and 70 mmHg to ensure adequate cerebral and spinal perfusion pressure. In some cases, revitalization with intravenous fluids or vasopressor drugs is necessary to provide these goals[1,6,9].

Once the patient is stable or as stable as possible, a directed neurological examination consistent with the patient's clinical status should be performed since completing every aspect of the neurological evaluation is impossible. Ideally, a rapid evaluation of the patient's mental component should be done from the moment the physician approaches the patient; they may notice changes in their behavior or behaviors that already provide information about possible pathologies or even affected encephalic areas. Initially, the patient's consciousness should be evaluated, starting with alertness[10]. It is advisable to categorize the patient into one of the following categories:

– Alert: The patient has and keeps his eyes open, can pay attention, and follows orders
– Drowsy: The patient opens his eyes to auditory stimulus and keeps them open for over 10 s. However, if there is no stimulus, the patient closes them again. The patient is able to obey simple commands
– Stuporous: The person opens the eyes to tactile or painful stimulus and cannot keep them open for more than 10 s despite external stimuli. Usually does not obey simple commands
– Comatose: The patient does not open his eyes despite vigorous painful stimuli. It is necessary to secure the airway to avoid the risk of bronchial aspiration or cerebral hypoxia.

The physician needs to detect changes in the state of alertness since several situations can simulate neurological deterioration and not necessarily be caused by central pathologies, such as hypoglycemia, alcoholic and non-alcoholic intoxication, hydroelectrolyte disorders (especially dysnatremia), exogenous or endogenous intoxications, alterations in renal function, and among others. For this reason, the physical examination will direct the subsequent medical conduct. However, it is not the objective of this review[10,11].

The degree of consciousness of a neurocritical patient can also be assessed objectively with the FOUR scale (Fig. 3)[12], which allows a more precise staging of the degree of response according to four essential parameters (ocular response, motor response, brain stem reflexes, and respiration). It is essential to evaluate the degree of sedation since most neurocritical patients are under the effects of drugs that cause the neurological examination may be modified or may not be able to develop all the

Table 1. Glasgow coma scale: the Glasgow coma scale provides a practical method for assessing impairment and estimating coma severity based on eye, verbal, and motor criteria

Response	Scale	Score
Eye opening response	Eyes open spontaneously	4 points
	Eyes open to verbal command, speech, or shout	3 points
	Eyes open to pain (not applied to face)	2 points
	No eye opening	1 point
Verbal response	Oriented	5 points
	Confused conversation, but able to answer questions	4 points
	Inappropriate responses, words discernible	3 points
	Incomprehensible sounds or speech	2 points
	No verbal response	1 point
Motor response	Obeys commands for movement	6 points
	Purposeful movement to painful stimulus	5 points
	Withdraws from pain	4 points
	Abnormal (spastic) flexion, decorticate posture	3 points
	Extensor (rigid) response, decerebrate posture	2 points
	No motor response	1 point

Minor brain injury: 13–15 points; Moderate brain Injury: 9–12 points; Severe brain injury: 3–8 points.

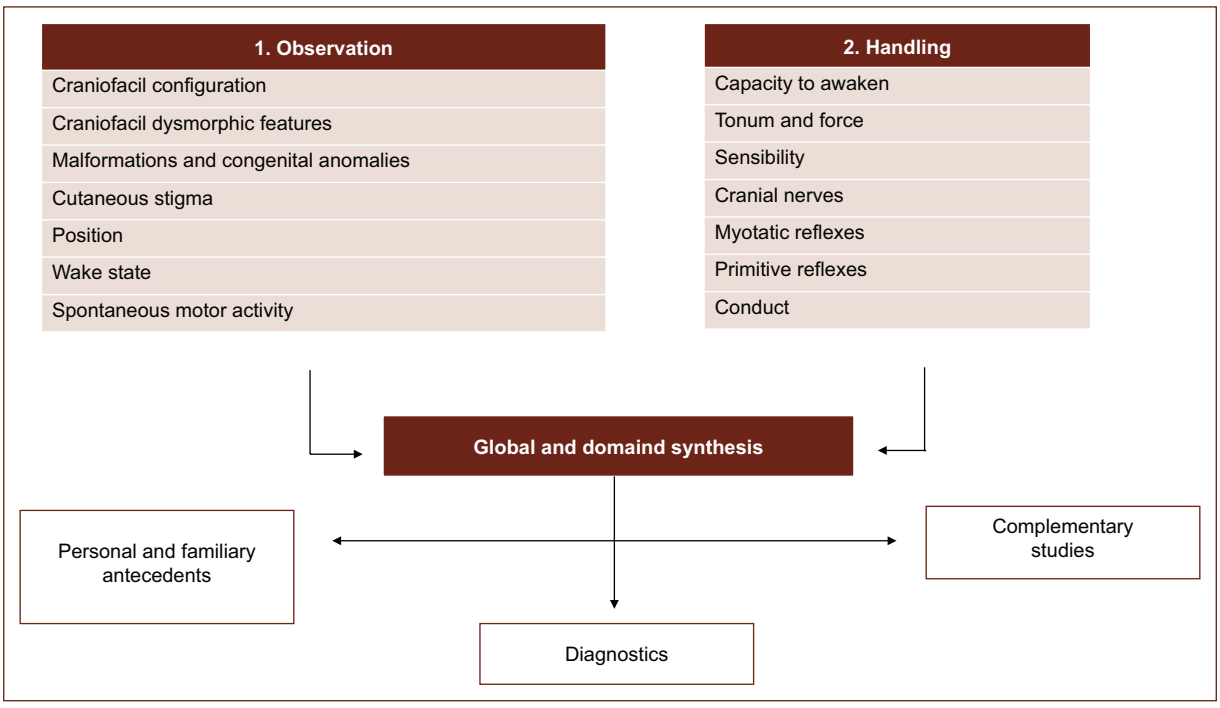


Figure 2. Example dynamic physical examination. Adaptaded from Sharshar et al., 2014.

activities of an adequate neurological examination; the Richmond agitation and sedation scale (Table 2)[11]. The degree of consciousness of a neurocritical patient can also be assessed objectively with the FOUR scales, which allows a more precise staging of the degree of response according to the four essential parameters[12].

Frequently, there is some degree of disorientation in patients hospitalized in ICUs since, on many occasions, the lights are kept on day and night, and the circadian cycle is not adequately identified. There are also many internal and external monitoring systems with alarms and light bulbs that turn on and off 24 h a day, and some patients remain alone in the rooms, which increases the risk of disorientation and delirium[7,8].

Language assessment is quite complex, and for the neurocritical patient, it is often necessary to be very specific to identify aphasia or dysphasia of a motor, sensorineural, or mixed type (Fig. 4). From the first moment, the physician introduces himself and greets the patient; he is performing the language evaluation since if the patient understands what is being discussed, obeys orders, and emits sounds, it is logical to think there are no significant alterations at this level. It is also important to evaluate the fluency of spoken language and speech coherence as they may be altered in patients with delirium, bipolar disorders (manic phase), and disorganized thinking. The speed of speech and the number of ideas that are expressed evaluate not only the language but also the speed of thought so that tachylalia and flight of opinions can give a picture of the degree of mental compromise in the patient[1,2,4].

Finally, it is essential to clarify that more areas are evaluated in the mental part but that, due to the clinical context of the patient, are not usually evaluated but that should be kept in mind in specific cases, and that may require more elaborate strategies carried out by psychologists or psychiatrists. A fundamental aspect that the reader should not forget is that before thinking or making diagnoses of mental illnesses, all possible organic causes that may lead to cognitive alterations should be ruled out since, many times, the reason is processes that can be medically corrected and thus resolve the clinical change. It is also important to rule out structural lesions before thinking about mental illnesses; that is why neuroimaging should be done to evaluate possible collections, masses, and cerebral edema before the psychiatrist's evaluation[13].

Neurocritical assessment of motor system: enhancing physical examination

An essential part of the physical examination of the neurocritical patient is the evaluation of strength in the four extremities, which requires the active collaboration

Table 2. The Richmond agitation–sedation scale. The Richmond agitation sedation scale is an instrument designed to assess the level of alertness and agitated behavior in critically ill patients

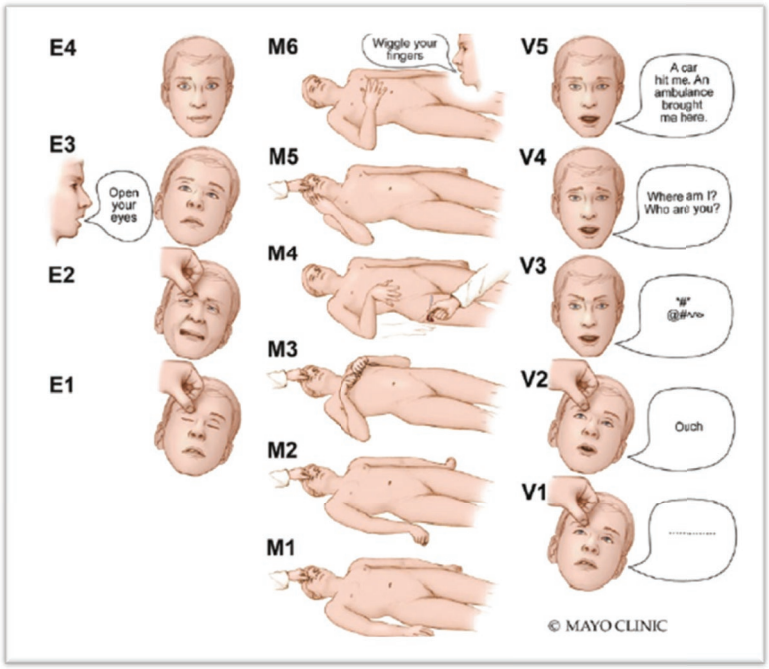
Score	Term	Description
+4	Combative	Overtly combative or violent, immediate danger to staff
+3	Very agitated	Pulls on or removes tubes or catheters, aggressive behavior toward staff
+2	Agitated	Frequent non-purposeful movement or patient ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
–1	Drowsy	Not fully alert, sustained (> 10 s) awakening, eye contact to voice
–2	Light Sedation	Briefly (< 10 s) awakens with eye contact to voice
–3	Moderate sedation	Any movement (but no eye contact) to voice
–4	Deep sedation	No response to voice, any movement to physical stimulation
–5	Unarousable	No response to voice or physical stimulation
Procedure		
1.	Observe patient. Is patient alert and calm (Score 0)?	
2.	Does patient have behavior that is consistent with restlessness or agitation?	
	Assign score+1 to+4 using the criteria listed above.	
3.	If patient is not alert, in a loud speaking voice state patient's name and direct patient to open eyes and look at speaker. Repeat once if necessary. Can prompt patient to continue looking at speaker.	
	Patient has eye opening and eye contact, which is sustained for more than 10 s (Score-1).	
	Patient has eye opening and eye contact, but this is not sustained for 10 s (Score-2).	
	Patient has any movement in response to voice, excluding eye contact (Score-3).	
4.	If patient does not respond to voice, physically stimulate patient by shaking shoulder and then rubbing sternum if the is no response.	
	Patient has any movement to physical stimulation (Score-4).	
	Patient has no response to voice or physical stimulation (Score-5).	

Adapted from Sessler et al. 2002[11].

of the patient to be more objective. Usually, the patient does not undergo a gait test in the critical care unit; however, at the time of admission and as long as the clinical condition allows it, special attention should be paid to the gait pattern since it may indicate to the physician alterations of both upper and lower motor neurons. It is vital to identify hemiparetic, tabetic, or ataxic gait, which in many cases may be secondary to contralateral cortical, posterior medullary, or cerebellar alterations, respectively[14].

An easy scale to implement in the ICU is the Daniels scale, which allows us to give a more specific degree of paresis and thus be able to see the evolution of the same and thus define whether there is a neurological deterioration or, on the contrary, improvement at the motor level. For its proper completion, the patient's collaboration is required, which is why it is not possible to evaluate critically ill patients in many cases. For patients with spinal cord trauma, it is essential to correctly complete the ASIA scale (Table 3)[15] by evaluating all ten muscle groups it assesses. Remember that the higher the lesion, the greater the patient's motor, sensory, or sphincter involvement[14].

The evaluation of reflexes should become a daily activity of the physical examination and not only at the musculotendinous level but also myocutaneous, cremasterine, and bulbocavernosus reflexes, especially in patients in the context of spinal cord trauma since they will differentiate patients with complete spinal cord injury from incomplete and thus change the prognosis



Eye response (E)	Brainstem reflexes (B)
4 = eyelids open, tracking, or blinking to command	4 = pupil and corneal reflexes present
3 = eyelids open but no tracking	3 = one pupil wide and fixed
2 = eyelids closed but open to loud voice	2 = pupil or corneal reflexes absent
1 = eyelids closed but open to pain	1 = pupil and corneal reflexes absent
0 = eyelids remain closed with pain	0 = absent pupil, corneal, and cough reflex
Motor response (M)	**Respiration (R)**
4 = thumbs-up	4 = not intubated, regular breathing pattern
3 = localizing to pain	3 = not intubated, Cheyne -stokes breathing pattern
2 = flexion response to pain	2 = not intubated, irregular breathing
1 = extension response to pain	1 = breathes above ventilator rate
0 = no response to pain or myoclonus status	0 = breathes at ventilator rate or apnea

Figure 3. The FOUR scale. Adapted from Wijdicks et al., 2005[12].

of improvement. It should be remembered that the evaluation of reflexes also guides the examiner about alterations of upper or lower motor neurons. When evaluating the plantar response, it should be described whether it is neutral, in flexion or extension (Babinski reflex), which is another vital sign that may indicate upper motor neuron pathologies[16].

In patients with neuroinfection or subarachnoid hemorrhage, a certain degree of nuchal rigidity on cervical flexion is frequent, or pain may also be experienced starting in the nuchal region and extending to the head and interscapular region. In patients with suspected meningitis, it is critical to evaluate whether there is a pain in cervical flexion accompanied by flexion of the hips and knees (Brudzinski's sign) or pain in flexion of the knees when performing hip flexion (Kernig's sign)[6,17].

Comatose patient

Most patients in the ICU are in an altered state of consciousness and, in many cases, under invasive mechanical ventilation, so they cannot cooperate with the examiner,

Table 3. Impairment scale ASIA. Spinal cord injuries are classified in general terms of being neurologically "complete" or "incomplete" based on sacral sparing. Sacral sparing refers to the presence of sensory or motor function in the most caudal sacral segments

ASIA impairment scale	Description
A	Complete. No sensory or motor function is preserved in the sacral segments S4–S5.
B	Incomplete. Sensory but no motor function is preserved below the neurological level and includes the sacral segments.
C	Incomplete. Motor Function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade< 3 (grades 0–2).
D	Incomplete. Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade≥ 3.
E	Normal. Sensory and motor functions are normal.

ASIA: American spine injury association.

and many of the maneuvers or strategies described above cannot be carried out. However, this does not mean that a neurological examination adapted to the patient's clinical conditions should not be performed[18]. As mentioned at the beginning of the chapter, the verification of the state of consciousness is the first step before continuing with the clinical evaluation and can be carried out through the GCS, which was created for the context of cranioencephalic trauma but has been used worldwide and is used in many contexts other than trauma. The patient may be with airway protective measures or due to ventilatory failure and not necessarily neurological. It is for this reason that the motor response is the most important since it allows the evaluator to identify if the patient can understand the order given, process the message, and generate the motor response that is indicated; when it is not possible, it is necessary to perform painful stimuli both centrally (supraorbital, trapezius, and sternum) and peripherally (nail matrix or subungual of the third finger of the hands) to identify what kind of movements the patient generates. It is essential to clarify that the minimum score is 3[5,6].

Taking into account the weaknesses of the GCS, the FOUR scale was created, which allows a more objective evaluation of patients with a poor verbal response, either because of their underlying pathology or because they are under mechanical ventilation; it consists of four sections and as an essential differential point evaluates the respiratory pattern visualized in the ventilation equipment. It also examines eye-opening, extraocular movements, and following simple verbal commands. It has a minimum score of zero and a maximum score of 16[16,18].

When examining a patient with altered consciousness, it is essential to carefully study the pupil size and reactivity associated with vital signs and respiratory pattern because although it is not common (<20% of cases), they present Cushing's triad given by hypertension, bradycardia, and altered respiratory pattern indicating increased intrapressure that requires immediate medical or even surgical management of the same[5,18].

Once a cervical spine lesion has been ruled out, oculocephalic reflexes should be evaluated by performing rapid head movements and observing the movement of the eyes, which will typically move toward the side where the head is turned. Still, a few seconds later, however, if the gaze goes simultaneously with the head (wrist eyes), it is considered that they are abolished and should be interpreted as a lesion at the pontic level where the nuclei of the VIII PC are located[8,19]. The oculovestibular reflex is evaluated with the instillation of water in the external auditory canal, initially at a temperature of 4°C and later with water at 27°C. The objective is to verify the nystagmus caused by the instillation of water and its rapid phase depending on whether it is hot or cold[6]. However, it is a cumbersome maneuver that is often omitted because it is not entirely standardized and familiar to ICU health personnel.

Conclusion

The semiology of the neurocritical patient is as broad as the patient who is outside the ICU; despite not having in all cases collaboration by the patient for the different maneuvers, it is possible to perform simple tests at the bedside that along with the rest of the physical examination, anamnesis and imaging and paraclinical studies help the physician to perform an initial approach and subsequently management directed to the type of pathology or injury that the patient presents. The medical student, generalist physicians, resident, and specialist must perform a daily neurological examination of their patients to identify small changes in the evolution and thus verify progress or deterioration that may require changes in the various medical behaviors[18].

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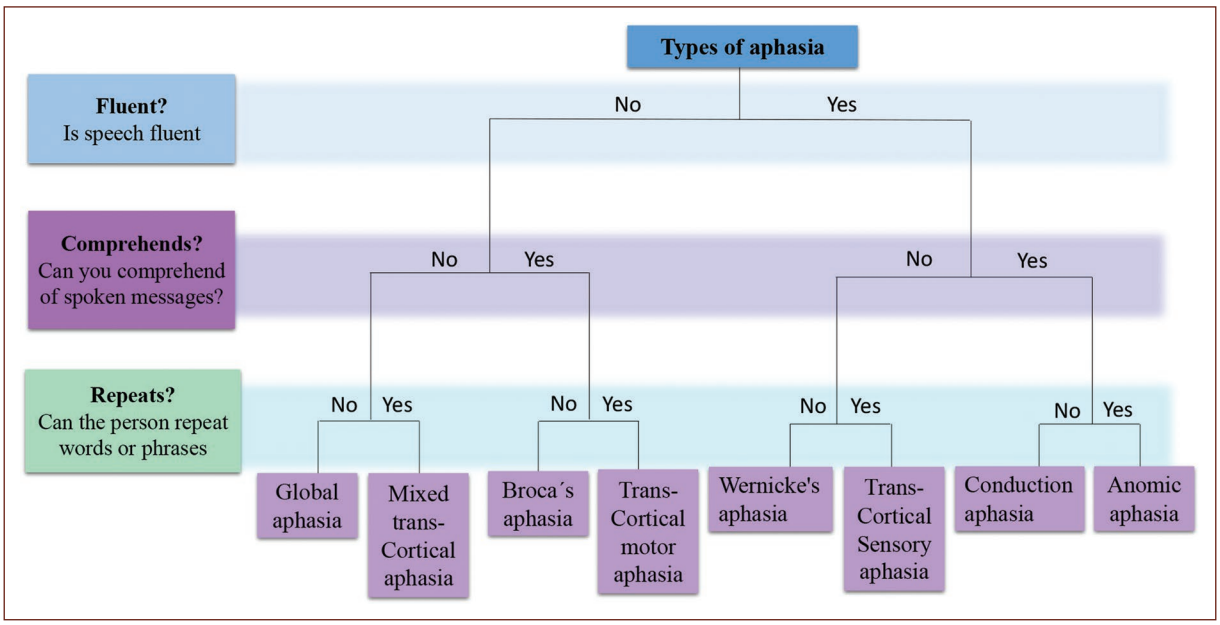

Figure 4. Assessment types of aphasia. Adapted from Wijdicks, 2022[3].

Conflicts of interest

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

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

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