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Etiological characterization of ischemic stroke in a neurovascular care unit in Mexico

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Abstract

Objective: *This study aimed to elucidate the diagnostic experience of our neurovascular care unit (NCU) in managing consecutive cases of cerebral infarction, detailing the prevalence of etiologies using the Trial of Org 10172 in acute stroke registry (TOAST) classification and comparing it with prior Mexican studies.* **Methods:** *A descriptive study of consecutive cases was conducted on patients diagnosed with ischemic stroke hospitalized in our NCU from September 2019 to July 2022. Patients underwent standardized diagnostic assessments by internists and neurologists, including neuroimaging (computed tomography [CT] and/or magnetic resonance imaging of the brain) and complementary studies (carotid Doppler ultrasound, 24-h Holter monitoring, echocardiogram). All patients had TOAST etiological classification, National Institute of Health Stroke Scale, and modified Rankin Scale evaluations.* **Results:** *A total of 738 subjects (57% male and mean age of 61 years) were included. Hypertension (61%), diabetes (49%), and dyslipidemia (11%) were common risk factors. Neuroimaging was performed on 95.7% of patients, with CT being the most prevalent (72.8%). The TOAST classification revealed 31.3% atherothrombotic, 24.7% lacunar, 15.4% cardioembolic, and 25.5% cryptogenic cases.* **Conclusions:** *The establishment of NCUs enhances ischemic stroke management, improving patient outcomes and reducing recurrence. Until stroke units become widespread, a structured evaluation by trained specialist physicians remains essential.*

Keywords: Stroke. Etiology. Neurovascular care unit.

Caracterización etiológica del ictus isquémico en una unidad de cuidados neurovasculares en México

Resumen

Objetivo: *Este estudio tuvo como objetivo detallar la experiencia diagnóstica de nuestra Unidad de Cuidados Neurovasculares (UCN) en el manejo de casos consecutivos de ictus isquémico, detallando la prevalencia de etiologías utilizando la clasificación TOAST y comparándola con estudios previos en México.* **Métodos:** *Se realizó un estudio descriptivo de casos consecutivos en pacientes diagnosticados con ictus isquémico-hospitalizados en nuestra Unidad de Cuidados Neurovasculares desde septiembre de 2019 hasta julio de 2022. Los pacientes fueron sometidos a evaluaciones diagnósticas*

estandarizadas por internistas y neurólogos, que incluyeron neuroimagen (TC y/o RMN cerebral) y estudios complementarios (ultrasonido Doppler carotídeo, monitoreo Holter de 24 horas, ecocardiograma). Todos los pacientes tuvieron clasificación etiológica TOAST, evaluaciones NIHSS y escala modificada de Rankin. **Resultados:** Se incluyeron un total de 738 sujetos (57% hombres, edad media 61 años). La hipertensión arterial (61%), la diabetes (49%) y la dislipidemia (11%) fueron factores de riesgo comunes. Se realizó neuroimagen en el 95.7% de los pacientes, siendo la TC la más prevalente (72.8%). La clasificación TOAST reveló casos aterotrombóticos (31.3%), lacunares (24.7%), cardioembólicos (15.4%) y criptogénicos (25.5%). **Conclusiones:** Un enfoque sistemático en la evaluación del ictus isquémico puede mejorar los resultados del paciente y reducir los riesgos de recurrencia, subrayando el papel fundamental de los médicos especialistas en el manejo del ictus isquémico dentro del sector de la salud pública.

Palabras clave: Ictus isquémico. Etiología. Unidad de Cuidados Neurovasculares.

Introduction

Ischemic stroke is one of the leading causes of death and disability worldwide[1], as well as a major cause of hospitalization in neurology services. In 2019, the incidence of ischemic stroke in Mexico was 58.6/100,000 inhabitants, occurring in men in 56.5% of cases[2]. Ischemic stroke represents a significant public health issue globally, resulting in substantial clinical impairment in patients, associated residual disability, decreased work capacity, and socioeconomic burden on families[3].

The etiological classification of ischemic stroke is a contentious issue in Mexico due to limited availability for patient evaluation, including laboratory and imaging studies. It is common for adjunct studies such as Doppler ultrasound of neck vessels, echocardiography, and imaging of intracranial arteries with magnetic resonance angiography or computed tomography (CT) angiography to be deferred to subsequent visits, leading to a higher percentage of cases with undetermined etiology.

Current guidelines for the management of acute cerebral infarction consider complementary studies essential for achieving accurate etiological definition and, consequently, better patient care. This becomes feasible with the presence of neurovascular care units (NCUs) or stroke units[4] and the standardization of quality indicators, including complementary studies and therapeutic response times, thus improving patients' functional status at discharge, preventing intrahospital complications, and stroke recurrence[5-7].

The primary objective of this study was to detail the experience of our NCU in the standardized diagnostic approach of consecutive cerebral infarction patients, describing the prevalence of etiologies according to the Trial of Org 10172 in Acute Stroke Registry (TOAST) classification[8] and comparing it with previous publications in Mexico.

Materials and methods

A descriptive study of consecutive cases was conducted, including patients diagnosed with ischemic stroke registered in the i-Registro-Neurovascular database of the Neurology Service at the "Dr. José Eleuterio González" University Hospital and hospitalized in our NCU between September 2019 and July 2022.

All included patients underwent standardized diagnostic evaluation by internists and neurologists, which consisted of an initial neuroimaging study (CT and/or magnetic resonance imaging [MRI] of the brain), as well as complementary studies for the etiological determination of cerebral infarction, including carotid Doppler ultrasound, 24-h Holter monitoring, and transthoracic echocardiogram (TTE) or transesophageal echocardiogram (TEE). All included patients underwent ischemic stroke classification according to the TOAST criteria[8,9]. Stroke etiology was determined as positive when classified as either probable–indicating strong clinical, imaging, and ancillary test support for a specific cause with most alternative etiologies excluded–or possible, where the available evidence suggested a particular cause, though further investigations might be required for definitive confirmation. If neither classification could be assigned with confidence, the stroke was designated as cryptogenic. This approach adhered to the original TOAST criteria established by Adams et al. In addition, the National Institute of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS) were used for patient evaluation during their hospital stay.

Comorbidity was defined for patients who: (1) were known to have the disease, (2) had a personal history of the disease, or (3) were under treatment with medications. A sedentary lifestyle was defined as not engaging in physical activity beyond daily activities. Young stroke was defined for patients who had ischemic stroke before the age of 55[10].

Categorical variables were reported as frequencies and percentages, whereas numerical variables were reported as measures of central tendency and dispersion. IBM SPSS Statistics version 25 was used for statistical analysis.

Results

A total of 738 subjects were included (57% male), with a mean age of 61 years (SD 14). The most prevalent risk factors within our sample were arterial hypertension (61%), diabetes mellitus (49%), and dyslipidemia (11%). 31% (n = 229) of cerebral infarctions occurred in patients under 55 years old. The average length of hospital stay was 8.66 days (SD 6.34). Upon admission, the mean NIHSS score was 8.07 points (SD 5.94). Regarding complications, 2.8% (n = 21) of patients suffered from cerebral hemorrhage/hemorrhagic transformation, and 1.5% (n = 11) suffered from a recurrent cerebral infarction. A complete description of patient characteristics is found in table 1.

The neuroimaging evaluation was performed on 95.7% of patients during hospital admission for suspected ischemic stroke, with non-contrast CT being the most frequently used, performed in 72.8% of cases. Subsequently, during hospitalization, complementary studies performed were: (1) angiotomography, magnetic resonance angiography, or transcranial Doppler in 95.3% of patients, for evaluation of intracranial vasculature; (2) Holter monitoring for at least 24 h in 64% of patients (although 92% had telemetry in their first 24 h of hospitalization); (3) TTE or TEE in 97.6% of patients; (4) Doppler ultrasound of the extracranial carotid and vertebral arteries in 92.7% of patients. A complete description of the imaging evaluation of patients is found in table 2.

Regarding etiological classification by TOAST within our sample, following interpretation of clinical and paraclinical studies, 31.3% (n = 231) corresponded to atherothrombotic origin, 24.7% (n = 182) lacunar, 15.4% (n = 114) cardioembolic, and 3.1% (n = 23) of other determined etiology. Despite the clinical and paraclinical methodology used for patient evaluation, 25.5% (n = 188) were finally classified as having undetermined or cryptogenic etiology.

Among evaluated patients who experienced a cerebral infarction before the age of 55, 62.4% (n = 143) were male, and 14.4% (n = 33) had a history of previous cerebral infarction. Regarding the etiological origin of ischemic stroke, it was found that 24.5% (n = 56) were of atherothrombotic origin, 32.3% (n = 74) lacunar,

Table 1. Population characteristics

Baseline characteristics	Total population (n = 738)
Sex (males), n (%)	419 (56.8)
Age (mean, SD)	61.17 (14)
Personal history, n (%)	
Diabetes mellitus	363 (49.2)
Hypertension	450 (61)
Dyslipidemia	84 (11.4)
TIA	29 (3.9)
Smoking	311 (42.1)
Alcoholism	338 (45.8)
Substance abuse	42 (5.7)
Sedentary lifestyle	510 (69.1)
Admission assessment	
NIHSS (mean, SD)	8.07 (5.94)
mRankin, n (%)	
0-2	273 (37.0)
3-5	444 (60.2)
TOAST, n (%)	
Atherothrombotic	231 (31.3)
Lacunar	182 (24.7)
Cardioembolic	114 (15.4)
Other determined cause	23 (3.1)
Cryptogenic	188 (25.5)
Complications, n (%)	
Cardiovascular	4 (0.5)
Cerebral hemorrhage/Hemorrhagic transformation	21 (2.8)
Recurrent cerebral infarction	11 (1.5)
Urinary tract infections	7 (0.9)
Kidney failure	4 (0.5)
Pneumonia	14 (1.9)
Discharge evaluation	
NIHSS (mean, SD)	5.68 (5.77)
mRankin, n (%)	
0-2	384 (52.0)
3-5	312 (42.3)
Length of hospital stay (mean, SD)	8.66 (6.34)
In-hospital mortality, n (%)	20 (2.7)

TIA: transient ischemic attack; NIHSS: National Institutes of Health Stroke Scale; TOAST: trial of org 10172 in acute stroke treatment; SD: standard deviation.

10.5% (n = 24) cardioembolic, 3.9% (n = 9) of other determined etiology, and 28.8% (n = 66) cryptogenic. At hospital discharge, 50% (n = 94) of this subgroup of patients had a score of 0-2 on the mRS. Complications included 3.1% (n = 7) suffering from cerebral hemorrhage/hemorrhagic transformation.

Discussion

Ischemic stroke remains one of the leading causes of morbidity and mortality globally. Its multifactorial

Table 2. Diagnostic imaging

Diagnostic imaging studies, n (%)	Total population (n = 738)
Simple computed tomography	537 (72.8)
Simple magnetic resonance imaging	567 (76.8)
Computed tomography or magnetic resonance imaging	706 (95.7)
Computed tomography and magnetic resonance imaging	398 (53.9)
Angiotomography, magnetic resonance angiography, or transcranial Doppler	703 (95.3)
Carotid and vertebral Doppler ultrasound	684 (92.7)
24-h Holter monitor	471 (63.8)
Transthoracic echocardiogram (TTE)	535 (72.4)
Transesophageal echocardiogram (TEE)	25 (3.4)
Echocardiogram (ETT o ETE)	721 (97.6)

nature demands both precise diagnosis and personalized treatment. In this context, specialist physicians and neurologists play a crucial role in the initial evaluation, identification of underlying causes, and final diagnosis of ischemic stroke, as well as in identifying factors contributing to the recurrence of this disease. Standardized evaluation is essential for minimizing resulting brain damage and optimizing patient prognosis[11].

The etiological epidemiology of ischemic stroke in Mexico, as in other countries with economic health limitations, remains a poorly studied topic, with variable results according to available documented information[2,12]. Within the RENAMEVASC study, the cardioembolic subtype (24.7%) was designated as the most frequent etiological cause of ischemic stroke in Mexico, followed by lacunar (19.4%) and atherothrombotic (14.7%) subtypes. However, the classification of "Undetermined" as the ultimate cause of ischemic stroke corresponded to 36.6%, being the most frequent[13]. Similarly, in the subset of the PREMIER database, the most frequent etiological causes of ischemic stroke were cardioembolic (22%), lacunar (19%), and atherothrombotic (8%) subtypes. However, the "Cryptogenic" classification was also assigned a percentage of 42%[14].

It is interesting to evaluate, within this subset, the analyzed data and the proportionality of the etiological causes of ischemic stroke in patients evaluated within public medical centers compared to private centers.

In public medical centers, a proportion of cryptogenic ischemic stroke cases of 45% was reported, whereas in private centers, it was 28%, generating a reduction of 17%. In public centers, the main imaging study performed for the evaluation of patients with ischemic stroke corresponded to CT of the skull, whereas in private centers, it was MRI of the skull, together with transcranial and carotid Doppler ultrasound, angiography, and echocardiogram[14].

On the other hand, Arauz et al. documented in the registry of the National Institute of Neurology and Neurosurgery that atherothrombotic was the most frequent etiological cause (25.1%), followed by cardioembolic and other determined etiology, with 24.5% and 17%, respectively. Truly cryptogenic etiology was documented in 6.4% of cases, and indeterminate cause with incomplete evaluation was documented in 11.2%. It is important to note that within their evaluation, 94.3% of patients underwent CT scans during their initial assessment, of which 71.77% underwent MRI after their initial assessment. Vascular evaluation was performed using cervical US in 50.4%, angio CT in 11.4%, and angio MRI in 18.3%. 34.5% underwent TTE as part of their evaluation. In addition, 12.9% of cases were evaluated using serum prothrombotic proteins[15]. A detailed comparison of etiological causes of acute ischemic stroke across different Mexican cohorts is presented in table 3.

A thorough evaluation of cardiovascular risk factors is imperative to understand the etiology of ischemic stroke. Specialist physicians should conduct meticulous analyses of patients to detect comorbidities that could contribute to the development of this pathology[16]. Internists play a fundamental role in managing these conditions, which may require anticoagulant therapy, antiplatelet medications, or surgical interventions[17]. Furthermore, close collaboration among specialist physicians, such as internists, neurologists, cardiologists, and vascular surgeons, is essential to accurately determine the etiological cause of stroke, facilitating the provision of comprehensive care for ischemic stroke through a more complete evaluation and additional therapeutic plans[18].

In situations where conventional risk factors do not fully explain the etiology of ischemic stroke, especially in patients < 55 years old, it is necessary to conduct a comprehensive investigation focused on possible underlying vasculopathy or coagulopathies, using specialized tests such as vascular imaging and thrombophilia panels, to identify less common but equally relevant

Table 3. Etiological characterization

Stroke etiology by TOAST classification	iReNe 2022 (%)	PREMIER 2018§ (%)	PREMIER 2018	RENAMEVASC 2011 (%)	Arauz, et al. 2018 (%)
Atherothrombotic	31.3	8	17	14.7	25.1
Lacunar	24.7	19	16	19.4	15.1
Cardioembolic	15.4	22	20	24.7	24.5
Other determined etiology	3.1	5	9	4.6	17
Cryptogenic	25.5	42	28	36.6	6.4
Mixed	NR	5	9	NR	NR

Etiological classification by TOAST in various studies.
§Data obtained from the general population. Data was obtained from private hospitals.
NR: not reported.

causes of ischemic stroke[18]. By closely evaluating these risk factors and defining the etiology of ischemic stroke in patients, internists can take preventive measures to reduce the likelihood of occurrence or recurrence of a stroke[19]. In addition, routine health screening with prothrombotic screening coverage in patients under 55 years of age may help improve the determination of the cause of heart attack.

Recognizing and classifying the etiology of ischemic stroke, especially in populations with a high prevalence of cardiovascular risk factors, is essential for effective management of secondary prevention, improving short and long-term functional outcomes, reducing the burden of disability, improving quality of life, and reducing mortality related to this disease.

Conclusion

The establishment of NCUs enhances the initial evaluation, management, monitoring, and secondary prevention of patients with acute ischemic strokes. In the public health-care sector of our country, specialist physicians play a critical role in diagnosis, management, and risk factor identification, ensuring timely and accurate care, particularly in the absence of stroke units outside major urban centers. Until the widespread implementation of dedicated stroke units becomes feasible, adopting a standardized approach to ischemic stroke evaluation could substantially improve functional outcomes and reduce recurrence rates.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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