





Stroke in young adults

Infarto cerebral en adultos jóvenes

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Abstract

Background Stroke is the second leading cause of mortality and disability in the world. It is less prevalent in people under 50 years of age but has an important impact on society and the healthcare system. The Trial of Org in Acute Stroke Treatment (TOAST) etiological classification system includes 5 categories: atherothrombotic, cardioembolic, lacunar, rarely occurring (unusual), and of undetermined origin. The etiological range of ischemic stroke in patients under 50 years of age is more heterogeneous than in older patients.

Objective To establish the most frequent etiology of ischemic stroke in patients under 50 years of age in Mediláser S.A. clinics of Tunja and Neiva in the years 2013 to 2017.

Methodology A descriptive, observational, retrospective, cross-sectional, retrospective study. The clinical history of patients under 50 years of age with a diagnosis of ischemic stroke confirmed by neuroimaging (Computed Tomography – CT or Magnetic Resonance Imaging - MRI) in the aforementioned clinics between 2013 and 2017 was reviewed. The etiology of ischemic stroke was determined according to the TOAST classification.

Results 69 patients were identified. The mean age was 39 years (SD: 2). Male/female ratio of 1.3/0.7. Regarding etiology, 22 % were associated with cardioembolic origin, 7 % atherothrombotic, 4 % small vessel, 6 % unusual, and 30 % undetermined. The mortality rate was 13% overall. In 70 % of the cases, the cerebral area most affected was the middle cerebral artery. Arterial hypertension was the risk factor most frequently associated with stroke, present in 38 % of cases. **Conclusions** The incidence of ischemic stroke increases significantly after the age of 40 years. Arterial hypertension also represents an important risk factor for experiencing a stroke before the age of 50 years.

Resumen

Antecedentes El accidente cerebrovascular (ACV) representa la segunda causa de muerte e incapacidad en el mundo. Es menos prevalente en menores de 50 años, pero genera un importante impacto en la sociedad y el sistema de salud. El sistema de clasificación etiológica del Trial of Org in Acute Stroke Treatment (TOAST) incluye 5 categorías: aterotrombótico, cardioembólico, lacunar, debido a causas poco frecuentes (inhabitual) y de origen indeterminado. El abanico etiológico del ACV isquémico en menores de 50 años es más heterogéneo respecto a pacientes de mayor edad.

Objetivo Establecer la etiología más frecuente del ACV isquémico en menores de 50 años en las clínicas Mediláser S.A de Tunja y Neiva entre 2013 y 2017.

Metodología Estudio descriptivo, observacional, retrospectivo de corte transversal. Se revisó el historial clínico de pacientes menores de 50 años con diagnóstico de ACV isquémico confirmado por neuroimagen (Tomografía Computarizada – TC o Resonancia Nuclear Magnética – RNM) en las clínicas mencionadas entre los años 2013 y 2017. Se determinó la etiología de ACV isquémico según la clasificación del TOAST.

Keywords

Stroke, etiology, young adult, risk factors.

Palabras clave

Accidente cerebrovascular, etiología, adulto joven, factores de riesgo.

Resultados Se encontraron 69 pacientes. La media de edad fue de 39 años (DS: 2). Relación hombre/mujer de 1,3/0,7. Respecto a la etiología, 22 % fueron relacionados con origen cardioembólico, 7 % aterotrombótico, 4 % de pequeño vaso, 6 % inusual y 30 % indeterminado. La tasa de mortalidad general fue del 13 %. En el 70 % de los casos, el área cerebral más afectada fue la arteria cerebral media. La hipertensión arterial fue el factor de riesgo más frecuentemente asociado al ACV, presente en el 38 % de los casos.

Conclusiones La incidencia de accidente cerebrovascular isquémico aumenta considerablemente a partir de los 40 años. La hipertensión arterial también representa un factor de riesgo importante para experimentar un accidente cerebrovascular antes de los 50 años.

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Introduction

Stroke is the second leading cause of death and disability in the world after ischemic heart disease (1). Despite being a prevalent entity, variable information is available about its frequency and distribution in developing countries. However, in general terms, stroke is less prevalent in the population under 50 years of age, regardless of the geographic region studied (2,3). It is reported that approximately 15% of all strokes occur in young adults (4). Stroke causes severe disability in terms of cognitive and social impairment in two-thirds of stroke survivors, which has an impact on the patient's quality of life (5-7). The consequences of stroke in young adults have a high impact on the family, society, and the health system, with a high economic cost, in addition to the loss of useful life for the patient in his or her most productive stage (3,8,9).

Traditionally, the etiological classification system of the Trial of Org in Acute Stroke Treatment (TOAST) involves 5 categories: atherothrombotic, cardioembolic, lacunar, due to unusual causes, and undetermined; the last category includes those patients with cerebral infarction whose etiological association cannot be determined after an exhaustive study, because of incomplete studies, and cases in which more than one possible etiology coexists. A stroke of unusual etiology is defined as a cerebral infarction in which, after a correct diagnostic study, the etiology cannot be attributed to any of the other categories; such cases may correspond to autoimmune disorders, myeloproliferative disorders, or arterial dissection (10).

The etiological range of ischemic stroke in patients under 50 years of age is more heterogeneous than in older patients. Among the etiological mechanisms that stand out in this population group are atherothrombotic and cardioembolic origin, the last of which is linked to patent foramen ovale (PFO). Regarding the pathophysiological mechanisms derived from PFO, paradoxical embolism, in situ thrombosis and increased susceptibility to the development of arrhythmias have been described. However, it is believed that there is an underdiagnosis of hypercoagulable states related to the presence of shunt and ischemic stroke (11). Data on ischemic stroke in young adults at the national level are scarce. In our region, no study on the subject has been recorded, so this article provides data on the impact of this event locally.

Materials and methods

The present study is a descriptive, observational, retrospective, cross-sectional study. The database of the Índigo Histórico system of the Mediláser S.A. clinics in Tunja and Neiva was

reviewed, including patients under 50 years of age with a diagnosis of ischemic stroke who were hospitalized between 2013 and 2017. Patients with a discharge diagnosis of ischemic stroke in patients younger than 50 years were selected. Ischemic stroke was defined as a focal neurological deficit, with a duration longer than 24 hours, and demonstrated by neuroimaging (CT or MRI).

Patients with transient cerebral ischemia (TIA), hemorrhagic stroke, cerebral venous sinus thrombosis, patients younger than 15 years, and patients referred to another institution without completing etiological studies were excluded. The etiological classification was based on the TOAST (Trial of Org in Acute Stroke Treatment) system. The affected vascular territory was classified into the anterior, middle, and posterior cerebral regions. Statistical analysis was performed using IBM SPSS Statistics 19.

Results

It was found that 69 patients met the inclusion criteria. Figure 1 shows a summary of the etiological frequency. The largest number of patients suffered ischemic stroke of undetermined origin (30%), followed by cardioembolic stroke (22%). When analyzing the cases of stroke of undetermined etiology, it was found that 35% of these cases failed to establish a possible etiology despite performing all the necessary studies, 25% of the cases had more than one possible etiology (such as a patient with atrial myxoma associated with unspecified autoimmune microangiopathy), and 40% of the patients showed incomplete studies. Three cases of stroke of unusual etiology were found (one case of Takayasu arteritis and 2 cases of traumatic vertebral artery dissection).

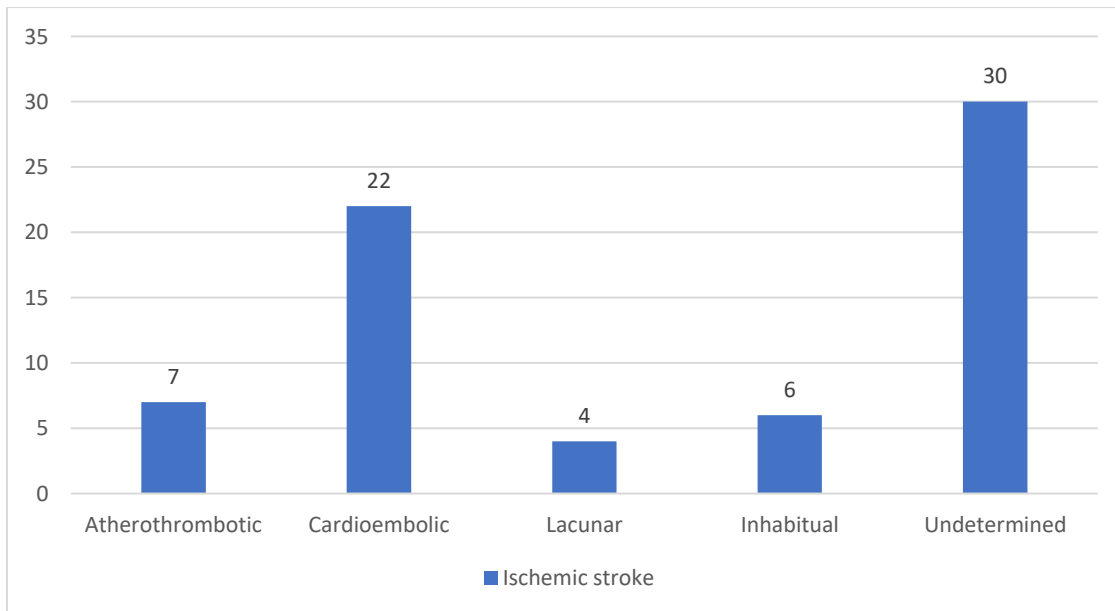


Figure 1. Distribution of ischemic stroke in patients under 50 years of age according to etiology.

Table 1 outlines the main characteristics of the population. The average age was 39 ± 2 years. The male to female ratio was 1:1. The most prominent cardiovascular risk factor was arterial hypertension (38% of cases), emphasizing that 10% of these patients presented with stroke in the context of a hypertensive crisis. Thirty-five percent of individuals had no identifiable risk factors. Cardioembolic stroke was associated with PFO in 26% of cases.

Table 1. General characteristics and risk factors of patients with ischemic stroke under 50 years of age at the Mediláser S.A. clinics in Neiva and Tunja

General characteristics and risk factors		
		% (n=69)
Age		39 (2) *
Sex	Male	57 (40)
Risk Factors	Hypertension	37 (26)
	Dyslipidemia	9 (6)
	Obesity	7 (5)
	FOP ⁺	26 (18)
	Diabetes	10 (7)
	None	34 (24)
Hospital mortality		13 (9)

*Media (DS)

+Foramen oval permeable (FOP)

The distribution of the affected cerebral territory can be seen in Figure 2. The most compromised circulation was the middle cerebral artery territory, regardless of the etiology of the stroke ($P = 0.07$). The frequency of ischemic stroke of the anterior cerebral artery increased considerably after the age of 40 years ($P = 0.01$). The association between arterial hypertension and involvement of the anterior cerebral artery stands out ($P = 0.05$).

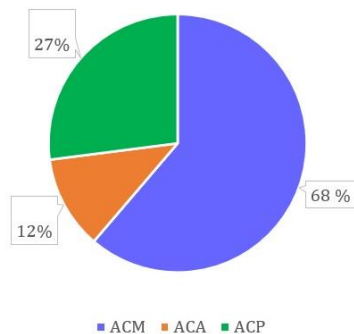


Figure 2. Affected brain territory.

Note: ACM/MCA Middle Cerebral Artery; ACA Anterior Cerebral Artery; ACP/PCA Posterior Cerebral Artery.

Table 2 provides a summary of the main characteristics associated with mortality. The overall mortality associated with ischemic stroke was 13%, with a greater impact in the group of patients with posterior cerebral circulation involvement (44% of those who died). Mortality was higher in men than in women, regardless of the etiology of the stroke. No cases were found of death due to stroke of lacunar or atherothrombotic origin.

Table 2. Characteristics associated with mortality

Characteristics	Mortality		<i>P</i>
	Negative (%)	Positive (%)	
Total	60 (12)	9 (88)	N.A
Age			
≤ 30	13 (86)	2 (14)	
≥ 30	47 (85)	7 (15)	0,500
Sex			
Male	33 (83)	7 (17)	
Female	27 (93)	2 (7)	0,197
Artery			
Middle cerebral artery			
Yes	44 (92)	4 (8)	
No	16 (76)	5 (24)	
Etiology			
Atherothrombotic	7 (100)	0 (0)	
Cardioembolic	20 (91)	2 (9)	
Lacunar	4 (100)	0 (0)	
Inhabitual	5 (83)	1 (17)	
Undetermined	24 (80)	6 (20)	0,509

Discussion

Stroke, like other cardiovascular diseases, is highly prevalent worldwide and tends to affect mainly patients who are male. A prospective cohort study of patients with arterial hypertension with a follow-up of 8.4 years on the sex difference in the incidence of stroke indicated that approximately 25% more cases occur in men than in women (12). A retrospective study conducted in China on the prevalence, incidence, and mortality of stroke describes that there is no statistically significant difference when comparing incidence between men and women under 50 years of age (13). The present study revealed no differences in terms of sex distribution, although mortality was higher in men.

In agreement with international studies, this paper showed a high percentage of ischemic stroke of undetermined origin (14-16). Possible explanations for these findings include the death of patients before the diagnosis was established, referral to other institutions due to the need for other interventions, early discharge, or loss of outpatient follow-up of patients that did not allow completion of studies (such as immunological analysis, for example). During an observational, multicenter study carried out in 15 European cities on ischemic stroke in patients under 50 years of age, in about 40% of the cases the etiology was undetermined (15).

Another cross-sectional study in 2013-2014, multicenter in different countries, reported that 15% were younger than 50 years of age and 24% met criteria for stroke of undetermined etiology (16). However, in patients older than 50 years, there is an inversely proportional relationship between age and undetermined etiology, since atherothrombotic origin is much more common in this type of patient.

Stroke secondary to PFO was evident in a significant number of cases. It is estimated that persistent PFO in adults is a common finding, with a prevalence of 25% in the general population (17). In recent years, multiple studies suggest that PFO can be detected in 40% to 56% of young adults with stroke of unknown origin (11). However, the true factors that could increase the risk of cerebral ischemia in the presence of PFO alone without other comorbidities (prothrombotic diseases) have been much debated, because paradoxical embolism is responsible for stroke in a very limited number of patients, such as when a thrombus located in the interatrial septum is discovered through the defect by a turbulence phenomenon.

Conventional cardiovascular risk factors play an important role in the development of stroke in young patients. This study revealed a significant percentage of patients with arterial hypertension (37%). This data is consistent with other studies in which the presence of conventional risk factors has been documented (7,13,18); it is estimated that there is a directly proportional relationship between the stage of hypertension and the probability of stroke (19). A follow-up study of a previously healthy population over a 5-year period that included more than 9,700 individuals demonstrated the association of arterial hypertension with stroke in 64% of cases (20).

On the other hand, a retrospective observational study, using the database of the Taiwan national health insurance system, identified patients with a first episode of stroke between 2000 and 2013, which showed that 59.6% of cases had hypertension associated with the event and that 71.5% of patients with a previous diagnosis of hypertension had poor adherence to medical treatment (21).

Conclusions

The etiological range of ischemic stroke in patients under 50 years of age is more heterogeneous than in older patients. Similar to other international research studies, an exact etiological diagnosis (indeterminate) could not be established in most cases, since a substantial number of cases had incomplete studies. The most frequent etiology of ischemic stroke in the population under 50 years of age, after undetermined origin, was cardioembolic. Paradoxical embolism represents an important pathophysiological mechanism in the presence of structural congenital heart disease such as a right-to-left shunt; patent foramen ovale was an important finding in this study in the population under 50 years of age with stroke.

It was found a significant percentage with arterial hypertension as the main cardiovascular risk, increasing the probability of suffering a cerebral infarction in the population under 50 years of age. Prevention and adequate management of traditional risk factors play a very important role in reducing the incidence of the disease.

The most affected cerebral territory was the middle cerebral artery. However, higher mortality was observed in the posterior cerebral artery group, since the posterior cerebral fossa has a greater vital susceptibility because it contains the medulla oblongata of the brain stem; control of the respiratory and cardiovascular center of the organism, so it can be concluded that patients under 50 years of age who suffer a cerebral infarction have a high risk of mortality during the event.

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Declarations Authors state no conflict of interest.

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