Ischemic Stroke at Young Age: The Burden of Diabetes

AVC Isquémico em Idade Jovem: O Fardo da Diabetes

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Abstract

Introduction: Stroke is a major cause of morbidity and mortality worldwide and its incidence is increasing in younger populations. Diabetes is a known risk factor for ischemic stroke, but its prevalence in stroke patients varies widely. Few studies have specifically investigated the prevalence of diabetes in young adult patients with ischemic stroke. Our goal was to quantify the frequency of diabetes among young adults admitted due to ischemic stroke and compare clinical outcomes between patients with and without diabetes.
Material and Methods: We conducted a retrospective observational study at a tertiary hospital over a one-year period from November 2019 to October 2020. The study population included all patients less than 65 years old with ischemic stroke who were admitted to the hospital during the study period. Data was collected from medical records, including demographic data, clinical presentation, laboratory results, imaging studies, and clinical outcomes.
Results: A total of 850 patients were admitted with ischemic stroke during the study period, of whom 140 (16.5%) were less than 65 years old. Most patients were male (69%), with an average age of 54.1 years (SD ± 8.9). Of the 140 young adult patients with ischemic stroke, 49 (35%) had diabetes. Two of these patients were newly diagnosed with diabetes.
Patients with diabetes were more likely to have hypertension ($p < 0.001$) and dyslipidemia ($p < 0.001$) than those without diabetes. The length of hospital stay was similar in both groups ($p = 0.131$). Only one patient died during hospitalization, and this patient did not have diabetes.
Conclusion: The prevalence of diabetes in young adult patients with ischemic stroke in our study was high, with almost one-third of the patients having diabetes. Even in young patients, diabetes is comorbid with other risk factors, such as hypertension and dyslipidemia.

Keywords: ischemic stroke; type 2 diabetes; young adults

Resumo

Introdução: O acidente vascular cerebral (AVC) é uma das principais causas de morbilidade e mortalidade em todo o mundo e a sua incidência está a aumentar nas populações mais jovens. A diabetes é um fator de risco conhecido para AVC isquémico, mas a sua prevalência em doentes com AVC varia amplamente. Poucos estudos investigaram, especificamente, a prevalência de diabetes em doentes adultos jovens com AVC isquémico. O nosso objectivo foi quantificar a frequência de diabetes em adultos jovens internados por AVC isquémico e comparar os resultados clínicos entre doentes com e sem diabetes.
Material e Métodos: Efectuámos um estudo observacional retrospectivo num hospital terciário durante um período de um ano, de novembro de 2019 a outubro de 2020. A população do estudo incluiu todos os doentes com menos de 65 anos e diagnóstico de AVC isquémico que foram admitidos no hospital durante o período do estudo. Os dados foram colectados dos registos médcos, incluindo dados demográficos, apresentação clínica, resultados laboratoriais e de exames de imagiologia e resultados clínicos.
Resultados: Durante o período do estudo, um total de 850 doentes foram internados por AVC isquémico, dos quais 140 (16,5%) tinham menos de 65 anos. A maioria dos doentes era do sexo masculino (69%), com uma média de idades de 54,1 anos (DP ± 8,9). Dos 140 doentes adultos jovens com AVC isquémico, 49 (35%) tinham diabetes. Em dois desses doentes a diabetes foi diagnosticada quando do internamento.
Os doentes com diabetes tinham maior probabilidade de apresentarem hipertensão arterial ($p < 0,001$) e dislipidemia ($p < 0,001$) do que aqueles sem diabetes. O tempo de internamento foi semelhante nos dois grupos ($p = 0.131$). Apenas um doente faleceu durante o internamento, sendo que este doente não era diabético.
Conclusão: No nosso estudo, a prevalência de diabetes em doentes adultos jovens com AVC isquémico foi elevada, correspondendo a quase um terço dos doentes. Mesmo em doentes jovens, a diabetes é comórbida com outros fatores de risco, como hipertensão arterial e dislipidemia.

Palavras-chave: acidente vascular cerebral isquémico; diabetes tipo 2; adultos jovens

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> INTRODUCTION

Stroke and diabetes are distinct conditions that exhibit several overlapping characteristics. Both impact blood vessels, and both are linked to vascular risk factors such as hypertension and dyslipidemia, leading to a rise in cardiovascular disease burden. The prevalence of both ailments is increasing, contributing to the current global mortality rates.

Stroke is commonly associated with older age. However, it can also occur in younger individuals, being one of the top 10 causes of death in young adults. In fact, the incidence of stroke in people aged 18-50 years has been increasing in recent years, accounting for 16% of all strokes. [1] Ischemic stroke accounts for most stroke cases, and its risk factors include hypertension, dyslipidemia, smoking, and diabetes. [2] The consequences of stroke in young age are not negligible, as it can result in long-term disability, reduced quality of life, and premature death. Young stroke survivors also face unique challenges, such as loss of income and social isolation. The impact of stroke at a young age is not limited to the individual affected, as it can also have a profound impact on their families, friends, and society, considering the number of productive life years lost.

Diabetes is a well-established risk factor for ischemic stroke, being estimated that up to one-third of all strokes are associated with diabetes. Moreover, diabetes is associated with poorer outcomes after a cerebrovascular event, namely morbidity and mortality. The relationship between diabetes and stroke has been extensively studied in older adults, but its association with stroke at a young age is complex, less well understood, and the available evidence is limited. The incidence of diabetes is increasing worldwide, and this trend is particularly pronounced in young adults, leading to speculation that diabetes may be a contributing factor to the rising incidence of stroke at a young age. Also, cerebrovascular complications make diabetic patients more susceptible to a stroke event and this risk is magnified in younger individuals and in patients with hypertension and complications in other vascular beds. [3]

This study aims to quantify the frequency of diabetes among young adults admitted due to ischemic stroke and compare clinical outcomes between patients with and without diabetes. We hypothesized that diabetes is an important risk factor in young adults admitted with ischemic stroke.

> METHODOLOGY

We conducted an unicenter retrospective observational study at a Portuguese tertiary hospital over a one-year period from November 2019 to October 2020. The study population included all adult patients less than 65 years old with ischemic stroke who were admitted to the hospital during the study period. We considered any ischemic stroke regardless of its etiology, confirmed or suspected by clinical presentation and imaging studies. Patients with hemorrhagic, venous or unspecified/undefined stroke were excluded from the study.

The data was collected from medical records, including demographic data (age and gender), Rankin Scale before the acute event, clinical presentation (National Institutes of Health Stroke Scale score at admission), past history and/or current presence of stroke risk factors (hypertension, diabetes, dyslipidemia, smoking, obesity, cardiac valvular disease, arrhythmias, endocarditis, patent *foramen ovale*, previous stroke or transient ischemic attack, prothrombotic conditions, arterial dissections, vasculitis or vascular diseases, and oral contraceptives), and clinical outcomes (length of hospitalization and mortality).

The primary outcome of interest was the incidence of ischemic stroke at a young age among patients with diabetes, compared to patients without diabetes. Secondary outcomes included the severity of clinical presentation, the presence of other cardiovascular risk factors, the length of stay in the hospital, and mortality rate.

The statistical analysis was performed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA). The data was presented as frequencies, percentages, means, and standard deviations. The Chi-square test was used to compare categorical variables, and the student's t-test was used to compare continuous variables. The level of statistical significance was set at $p < 0.05$.

> RESULTS

A total of 850 patients were admitted with ischemic stroke during the study period, of whom 140 (16.5%) were less than 65 years old (Figure 1). The average age of those 140 patients was 54,2 years (S.D ± 9,0). Sixty nine percent of the patients less than 65 years old were male (n = 97), with an average age of 54,1 years (S.D ± 8,9).

Of the 140 young patients with ischemic stroke, 49 (35.0%) had diabetes, specifically type 2 diabetes. Forty-seven (95.9%) of these patients were 45 to 64 years old and only two (4.1%) were under 45 old. Two of the patients were diagnosed with diabetes at the time of hos-

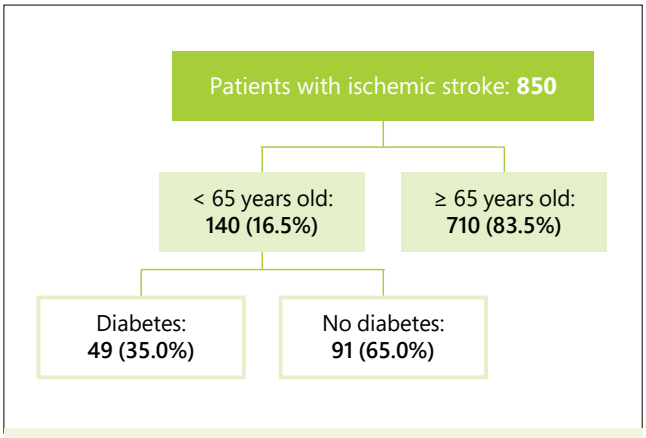

Figure 1 - Flowchart of patients included in the study.

pital admission. Data regarding the severity of strokes could not be collected due to incomplete records. Only one patient, from the non-diabetic group, died during hospitalization, due to non-specified cause.

When comparing the average age of ischemic stroke in patients with and without diabetes, the latter group showed a lower average age (56.9 ± 6.3 *vs.* 52.7 ± 9.8, respectively; p = 0.002). Patients with diabetes present more frequently arterial hypertension (83.7% *vs.* 49.5%; p < 0.001), dyslipidemia (67.3% *vs.* 29.7%; p < 0.001) and obesity (22.4% *vs.* 9.9%; p = 0.043). Arterial dissection was only diagnosed in the non-diabetics group.

Non-diabetic patients were hospitalized during shorter periods, but the results were not statistically significant when compared with the diabetic patients group (Table 1).

The cardiovascular risk factors presented in each group (diabetes group and non-diabetes group) are outlined in Table 1.

Patients aged 45 or older presented a significantly higher frequency of diabetes when compared with the younger population (Table 2).

Table I - Demographic characteristics and cardiovascular risk factors between patients with and without diabetes in each group.

	Diabetes (n = 49; 35%)	No diabetes (n = 91; 65%)	
Age	56.9 ± 6.3	52.7 ± 9.8	**p = 0.002**
Female	15 (30.6%)	28 (30.8%)	P = 0.985
Male	34 (69.4%)	63 (69.2%)	
Length of stay	15.7 ± 25.4	9.4 ± 13.3	p = 0.131
Arterial hypertension	41 (83.7%)	45 (49.5%)	**p < 0.001**
Dyslipidemia	33 (67.3%)	27 (29.7%)	**p < 0.001**
Smoking	22 (45.8%)	44 (48.4%)	p = 0.777
Obesity	11 (22.4%)	9 (9.9%)	**p = 0.043**
Peripheral arterial disease	0	2 (2.2%)	p = 0.542
Arrhythmia	4 (8.2%)	7 (7.7%)	p = 0.999
Endocarditis	0	0	NA
Patent *foramen ovale*	1(2.0%)	7 (7.7%)	p = 0.261
Prothrombotic state	0	2 (2.2%)	p = 0.542
Arterial dissection	0	10 (11.0%)	**p = 0.015**
Valvulopathy	6 (12.2%)	5 (5.6%)	p = 0.195
Oral contraceptives	0	2 (2.2%)	p = 0.545

NA = not available.

> DISCUSSION

In our retrospective study, we found that diabetes was observed in 35% of ischemic stroke patients below the age of 65, with a prevalence of 1,4% among patients under 45. The prevalence we founded is lower than that reported in a previous study, where the frequency of diabetes among ischemic stroke patients aged 18 to 45 was 17%. [4] However, in our study, the prevalence of diabetes among ischemic stroke patients above the age of 45 was significantly higher at 33.6%. These results can be attributed to the fact that, between the ages of 45 and 64, the etiology and risk factors associated with ischemic stroke begin to resemble those observed in the elderly population. [5]

Classically, younger patients present different etiologies for ischemic stroke, such as carotid dissection, hypercoagulable state, genetic disorders, patent *foramen ovale* or inflammatory vasculopathies. [6] Also, some other permanent or transient risk factors such as smoking, use of oral contraceptives, migraine, trauma, use of illicit drugs, and pregnancy or puerperium have a more important role in this age group than in older adults. [7] However, traditional risk factors for stroke such as hypertension, dyslipidemia, and diabetes, which promote atherosclerosis, cannot be neglected in those young patients. [8] Indeed, data from Portugal suggest that early atherosclerosis was responsible for an important percentage of ischemic stroke. [4]

Furthermore, it is important to highlight that among our sample of ischemic stroke patients, 65% were individuals without diabetes, which is a higher proportion compared to diabetic patients. This finding contradicts

Table II - Prevalence of diabetes in the group younger than 45 years old.

	Diabetes		No diabetes		
	Within diabetes group	% of total	Within no diabetes group	% of total	
< 45 years	2 (4.1%)	1.4%	20 (22%)	14.3%	p = 0.006
45 to 64 years	47 (95.9%)	33.6%	71 (78%)	50.7%	

the existing literature, which indicates that among patients under the age of 55 with stroke, those with diabetes face a more than 10-fold increased risk. [9]

When analyzing the age at which stroke occurs in patients with and without diabetes, we made an intriguing discovery. Among patients with diabetes, a significant majority (95.9%) had a stroke between the ages of 45 and 64, which is a higher proportion compared to individuals without diabetes in the same age group. Surprisingly, 22% of non-diabetic individuals experienced a stroke before the age of 45. We initially anticipated that diabetic patients would have an earlier onset of ischemic stroke compared to those without diabetes, considering that diabetes is a well-known cardiovascular risk factor.

Interestingly, the existing literature on this topic indicates a higher incidence of ischemic stroke among patients with diabetes, which led us to anticipate that the diabetic population would be relatively younger when experiencing stroke. However, it is important to note that most studies do not specifically focus on the age group examined in our study, and the findings regarding this aspect are not consistently aligned. This inconsistency in the literature could be attributed to the varying cutoff age points used in different studies. The lower age limits for inclusion range from 15 to 18 years, while the upper age limits range from 45 to 65 years. Additionally, considering the time of diabetes diagnosis could also provide valuable insights. In fact, there is evidence suggesting a correlation between the duration of diabetes and the risk of cerebrovascular disease. [3]

We observed that our diabetic patients had significantly elevated blood pressure and cholesterol levels compared to the nondiabetic patients ($p < 0.001$). These findings are consistent with recent studies that indicate the growing involvement of traditional risk factors, such as hypertension and dyslipidemia, in the pathophysiology of ischemic stroke among younger individuals. [7,10–12] It is noteworthy that the incidence of cardiovascular disease mortality increases in both diabetic and non-diabetic patient cohorts as cholesterol and blood pressure levels rise. [13] However, the strong association between diabetes and ischemic stroke is not solely attributed to the presence of these comorbidities, as diabetes itself is an independent risk factor for ischemic stroke. [14,15]

Our study has limitations. Firstly, it is retrospective in nature, relying on electronic records as the primary source of data, which imposes limitations on the available information. Additionally, the lack of comprehensive data on stroke type and severity in the electronic records restricted our ability to make detailed comparisons between patients with and without diabetes. Lastly, the absence of a control group comprising individuals older than 65 years old limited the scope of our study and constrained the conclusions that can be drawn from it.

> CONCLUSION

Ischemic stroke in young adults is far less common than in older adults, but it is associated with catastrophic consequences. Underlying pathogenesis and risk factors vary, but traditional risk factors such as diabetes seem to be increasing in the younger, resembling those seen in the elderly. This is supported by our study, where we found a high prevalence of diabetes in young patients with ischemic stroke, with almost one-third having diabetes. Even in younger adults, diabetes is highly comorbid with hypertension and dyslipidemia, although causes defined in younger patients are still frequent. Therefore, along with screening of most common risk factors in younger age, young ischemic stroke survivors should have traditional risk factors screened and aggressively managed for long-term risk reduction. <

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The authors declare that they have no conflicts of interests/*Os autores declaram a inexistência de conflitos de interesses.*

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