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*Primary Study*

# INTERSTROKE Angola: A multicenter Prospective Case–Control Study in a Sub-Saharan African Country.

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## Abstract

**Background:** Stroke is a major cause of disability and mortality worldwide. Sub-Saharan Africa has one of the highest prevalence rates; however, the actual magnitude of the disease in this region remains unknown. We aimed to study the modifiable risk factors for stroke in patients admitted to tertiary hospitals in Luanda, Angola, in 2022–2023.

**Methods:** We conducted a prospective case–control study in four tertiary hospitals in Luanda, Angola. The cases were patients with stroke manifestations within 5 days or who presented with such manifestations within the first 72 hours of admission, and the controls were patients with no history of previous stroke or transient ischemic attack. The cases and controls were matched in a 1:1 ratio on the basis of the age of the cases. Data were prospectively obtained using physical surveys structured by the authors on the basis of the INTERSTROKE study. Descriptive statistics were used, and the difference between means was calculated using Student's t-test.

**Results:** The final population comprised 314 participants, with 157 cases and 157 controls. The average age of the cases was 61 years (±13.9), with 59% of the cases < 65 years old. There was a predominance of males among the cases (56.1%). The ischemic form of stroke was the most frequent (73.2%), and 27.4% of patients had a favorable outcome (score of five) according to the Glasgow Outcome Scale. After one month, 35.6% had a score between zero to three on the modified Rankin Scale. All the risk factors assessed had a significant difference between the groups (hypertension: $t = 42.071$, $p < 0.01$; smoking: $t = 30.992$, $p < 0.01$; increased waist-to-hip ratio: $t = 47.967$, $p < 0.01$; sedentary lifestyle: $t = 53.237$, $p < 0.01$; diabetes: $t = 55.964$, $p < 0.01$; alcohol intake: $t = 32.319$, $p < 0.01$; and increased body mass index [≥25 kg/m2]: $t = 15.813$, $p < 0.01$).

**Conclusion:** The findings show that these factors can serve as important targets for stroke prevention.

**Keywords** : stroke, Africa, case–control studies.

## INTRODUCTION

Stroke is the second leading cause of death and the third leading cause of acquired disability in adults worldwide. [1,2] The Global Burden of Disease showed that in 2019, there were 101 million cases, 12.2 million new cases, and 6.55 million deaths worldwide. [1,3]

Stroke mortality varies with the degree of socioeconomic development of the region, with more than half of cases occurring in economically emerging countries. [3,4] Part of this stroke burden comes from the African continent, where the disease shows common patterns despite regional variations, that is, stroke primarily affects younger groups and results in very high mortality. [5–7]

On this continent, the annual incidence rate is approximately 316 cases/100,000 inhabitants, with a prevalence of up to 1,460/100,000 inhabitants; furthermore, there is a 3-year mortality rate of over 80%, with 1 African having a new stroke every 10 seconds. [7,8] Among the regions in the continent, sub-Saharan Africa is considered the most critical, with an estimated prevalence of 981 cases/100,000 inhabitants. [9–11] In Angola, the actual magnitude of cerebrovascular disease is not yet known; however, national studies have shown that stroke is an important cause of medical emergencies. [12] This pattern is typical of economically emerging countries: young people are predominantly affected, and the frequency of hemorrhagic stroke is higher than that described in global statistics, [12,13] as evidenced by the few studies available.

Despite the great burden generated by stroke, until a decade ago, the contribution of cardiovascular risk factors to stroke

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was not well established.[3] However, one of the most important studies to identify the risk factors for stroke was the INTERSTROKE study, which is an international multicenter case–control study that showed that 10 modifiable risk factors were associated with 90% of the risk of stroke. [14,15] Thus, we replicated INTERSTROKE in Angola, a sub-Saharan African country, with the aim of studying seven of these "classic" modifiable risk factors for stroke in patients admitted to tertiary hospitals in Luanda, Angola.

## METHODS

### Participants

This study included 314 participants from 2 public units (Américo Boavida Hospital and Cardeal Dom Alexandre do Nascimento Hospital) and 2 private units (Girassol Clinic and Multiperfil Clinic) in Luanda, Angola.

The following patients were selected arbitrarily from the outpatient and inpatient consultations of the units: 157 patients with manifestations of stroke within 5 days or who presented with such manifestations within the first 72 hours of admission and 157 patients with no history of previous stroke or transient ischemic attack. The participants were selected from October 30, 2022, to December 15, 2023.

### Procedures

Data were obtained prospectively by using physical surveys structured by the authors on the basis of the INTERSTROKE by. [14,15] Sociodemographic data and lifestyle habits were provided by patients, family members, or caregivers. The assessment of the initial physical state and the presumption of the etiology of stroke cases were defined by the doctor on duty at the emergency department or in the inpatient area and were subsequently obtained from the clinical files. Hypertension (for cases and controls) was defined as a self-reported history or a composite of self-reported hypertension and blood pressure ≥ 160/90 mmHg on admission. Diabetes was defined as a self-report or the combination of self-report and occasional serum glucose ≥ 200 mg/dL. Participants (cases and controls) underwent anthropometric assessment at the time of the interview by a senior researcher. Weight was determined using orthostatic (SECA 769) or bed-embedded (Medik YA-D8-2) scales, and waist and hip circumferences were measured in orthostatic and supine positions (patients who were not standing) by using a tape measure. Stroke cases were confirmed using computed tomography or magnetic resonance imaging (the latter was available in only one of the units). The imaging findings were described by the hospital's radiologist, with the images being completed in all cases. The degree of disability and dependence of the patients was determined using the modified Rankin Scale (mRS) one month after hospital discharge via telephone and an adapted and validated questionnaire. [16]

### Statistical analysis

The data were temporarily stored on Google Sheets and then exported and analyzed using Statistical Package for the Social Service software (IBM SPSS Statistics 24). Descriptive statistics were used, with the sample having a normal distribution according to the Kolmogorov–Smirnov test. The difference between means was calculated using Student's t-test, with a statistical significance level of 0.01. The cases and controls were matched in a 1:1 ratio according to the age of the cases.

### Ethical and administrative procedures

This research was approved by the Ethics Committee and Scientific and Postgraduate Affairs Directorate of the Faculty of Medicine of Agostinho Neto University (letter no. 77/VDACPG/FM/2022). It was conducted after prior authorization from the Pedagogical and Scientific Directorates of the hospitals of interest. Each participant/accompanying person received a copy of the free informed consent form attesting to the confidentiality of the information and the careful use of data. Participant anonymity was guaranteed in accordance with the Declaration of Helsinki on Human Research.

## RESULTS

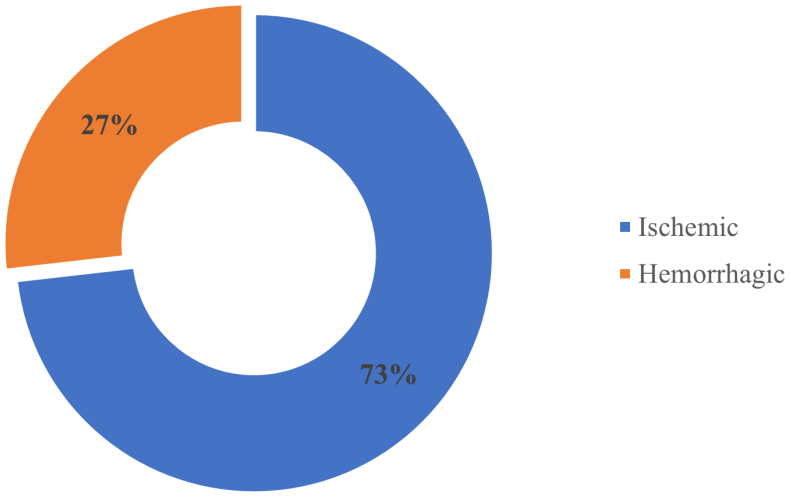
The initial population comprised 328 participants, and 14 cases were excluded mainly because of the absence of close companions. The final population comprised 314 participants (157 patients and 157 controls). The average age was 61 years (±13.9 years) for the cases, men accounted for 56.1% of the participants, and up to 59% of the cases were <65 years old (**Table 1**).

**Table 1.** Sociodemographic characterization of the cases.

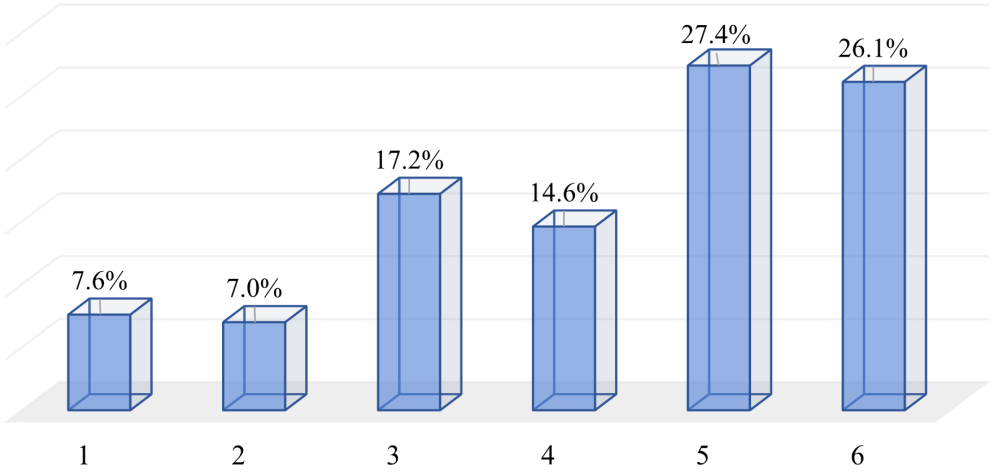
| Sociodemographic characteristics | Category | Frequency (n) | Percentage (%) |
|---|---|---|---|
| Sex | Female | 69 | 43,9 |
| | Male | 88 | 56,1 |
| | TOTAL | 157 | 100 |
| Age group | 35–44 years | 20 | 12,8 |
| | 45–54 years | 38 | 24,4 |
| | 55–64 years | 34 | 21,8 |
| | 65–74 years | 36 | 22,4 |
| | 75–84 years | 19 | 12,2 |
| | ≥85 years | 10 | 6,4 |
| | TOTAL | 157 | 100 |

Ischemic stroke was the predominant type of stroke (73%) (**Figure 1**). **Table 2** shows that 80% of ischemic strokes resulted from partial occlusion of the anterior cerebral circulation. According to the TOAST classification, 50.4% of ischemic strokes result from small-vessel atherosclerosis, and 20% had undetermined etiology mainly because of diagnostic limitations. In hemorrhagic strokes, 76.2% of the hematomas were in the nucleocapsular region, and only 19% had ventricular flooding.

**Figure 1.** Frequency distribution of cases according to the type of stroke.

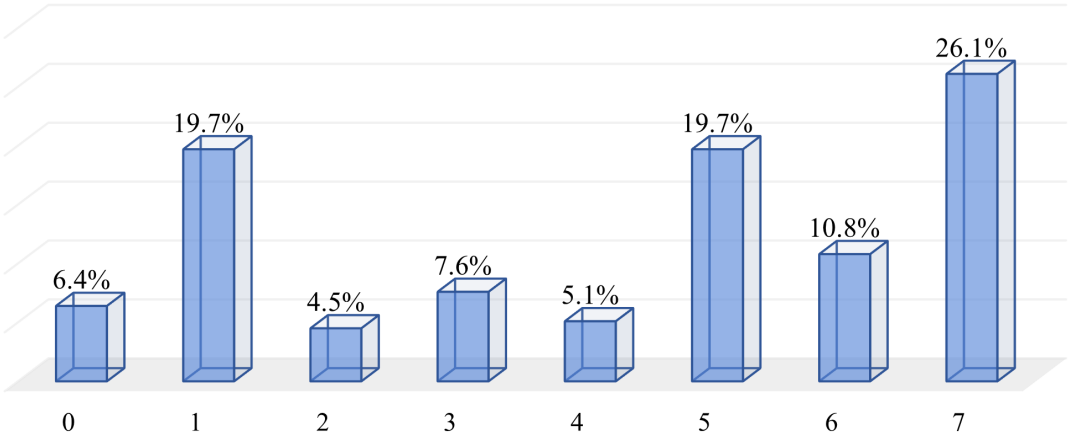



**Graph 1.** Frequency distribution of cases according to Glasgow Outcome Score.




1=Death; 2=Coma; 3= Deficit severe; 4=Moderate deficit; 5= Good recovery; 6= Unavailable.

**Graph 2.** Distribution of cases according to degree of functionality on the Modified Rankin scale (mRE) 1 month after the event.




0=Asymptomatic; 1=Symptomatic but no deficit; 2=Mild deficit; 3=Moderate deficit; 4=Moderate to severe deficit; 5=Severe deficit; 6=Death; 7=Unavailable. Note: 0-3= favorable functionality; 4-6= poor functionality.

**Table 2.** Distribution of cases according to the location and etiology of the ischemia, the location of the hematoma, and the occurrence of ventricular flooding.

| Features | Category | n | % |
|---|---|---|---|
| Location of the infarction by classification (OCSP) | Lacunar infarction (LACI) | 8 | 7,0 |
| | Total anterior circulation (TACI) | 2 | 1,7 |
| | Partial anterior circulation (PACI) | 92 | 80,0 |
| | Posterior circulation (POCI) | 13 | 11,3 |
| | TOTAL | 115 | 100 |
| Etiology of infarction by classification (TOAST) | Cardioembolism | 2 | 1,7 |
| | Large vessel occlusion | 21 | 18,3 |
| | Small vessel occlusion | 58 | 50,4 |
| | Other etiology | 11 | 9,6 |
| | Undetermined | 23 | 20,0 |
| | TOTAL | 115 | 100 |
| Location of the hematoma | Infratentorial | 2 | 4,8 |
| | Lobar | 8 | 19,0 |
| | Nucleocapsular | 32 | 76,2 |
| | TOTAL | 42 | 100 |
| Blood invasion of the ventricular system | Yes | 8 | 19,0 |
| | No | 34 | 81,0 |
| | TOTAL | 42 | 100 |

**TOAST:** Trial ORG 10172 in Acute Stroke Treatment; OCSP: Oxfordshire Community Stroke Project.

Up to 27.4% of all patients had a favorable outcome, with a tendency toward good recovery (Glasgow Outcome Scale [GOS] = 5); however, 7.6% of patients died during hospitalization (**Table 3**). One month after the event, 38.2% of the patients had favorable functionality (mRS score of zero to three). However, 26.1% of the patients were lost to follow-up (**Table 4**).

Among the seven risk factors, five were more frequent in controls than in cases (Table 5): diabetes (37.6% vs. 19.5%), current alcohol consumption (76.5% vs. 61.1%), sedentary lifestyle (98.7% vs. 78.8%), history of smoking (26.1% vs. 23.1%), and increased body mass index (BMI) (89.8% vs. 77%). All the modifiable risk factors showed a statistically significant difference between the 2 groups (**Table 5**): hypertension ($t = 42.071$, $p < 0.01$), smoking ($t = 30.992$, $p < 0.01$), increased waist-to-hip ratio ($t = 47.967$, $p < 0.01$), sedentary lifestyle ($t = 53.237$, $p < 0.01$), diabetes ($t = 55.964$, $p < 0.01$), alcohol intake ($t = 32.319$, $p < 0.01$), and increased BMI ($t = 15.813$, $p < 0.01$).

**Table 3.** Frequency distribution of cases according to Glasgow Outcome Scale.

| Glasgow Outcome Scale | Ischemic | | Hemorrhagic | | TOTAL | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| 1 = Death | 8 | 7,0 | 4 | 9,5 | 12 | 7,6 |
| 2 = Coma Coma | 10 | 8,7 | 1 | 2,4 | 11 | 7,0 |
| 3 = Severe Deficit | 20 | 17,4 | 7 | 16,7 | 27 | 17,2 |
| 4 = Moderate deficit | 18 | 15,7 | 5 | 11,9 | 23 | 14,6 |
| 5 = Good recovery | 27 | 23,5 | 16 | 38,1 | 43 | 27,4 |
| Unavailable | 32 | 27,8 | 9 | 21,4 | 41 | 26,1 |
| TOTAL | 115 | 100 | 42 | 100 | 157 | 100 |

**Table 4.** Distribution of cases according to degree of functionality on the modified Rankin Scale one month after the event.

| mRS | Ischemic | | Hemorrhagic | | TOTAL | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Asymptomatic (0) | 5 | 4,3 | 5 | 11,9 | 10 | 6,4 |
| Symptomatic but no deficit (1) | 20 | 17,4 | 11 | 26,2 | 31 | 19,7 |
| Mild deficit (2) | 5 | 4,3 | 2 | 4,8 | 7 | 4,5 |
| Moderate deficit (3) | 10 | 8,7 | 2 | 4,8 | 12 | 7,6 |
| Moderate to severe deficit (4) | 5 | 4,3 | 3 | 7,1 | 8 | 5,1 |
| Severe deficit (5) | 25 | 21,7 | 6 | 14,3 | 31 | 19,7 |
| Death (6) | 13 | 11,3 | 4 | 9,5 | 17 | 10,8 |
| Unavailable | 32 | 27,8 | 9 | 21,4 | 41 | 26,1 |
| TOTAL | 115 | 100 | 42 | 100 | 157 | 100 |

**Note:** 0–3: favorable functionality; 4–6: poor functionality

**Table 5.** Distribution and difference between cases and controls according to the frequency of modifiable risk factors.

| Risk factors | Category | Cases | | Controls | | TOTAL | | P # |
|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % | |
| Hyperten-sion | Yes | 138 | 87,9 | 69 | 43,9 | 207 | 65,9 | <0.01 |
| | No | 19 | 12,1 | 88 | 56,1 | 107 | 34,1 | |
| | TOTAL | 157 | 100 | 157 | 100 | 314 | 100 | |
| Diabetes | Yes | 30 | 19,5 | 59 | 37,6 | 89 | 28,6 | <0.01 |
| | No | 124 | 80,5 | 98 | 62,4 | 222 | 71,4 | |
| | TOTAL | 154 | 100 | 157 | 100 | 311 | 100 | |
| Regular physical exercise | Yes | 33 | 21,2 | 2 | 1,3 | 35 | 11,2 | <0.01 |
| | No | 123 | 78,8 | 155 | 98,7 | 278 | 88,8 | |
| | TOTAL | 156 | 100 | 157 | 100 | 313 | 100 | |
| Current alcohol consump-tio n | No | 61 | 38,9 | 37 | 23,6 | 98 | 31,2 | <0.01 |
| | 1-30 doses per month | 79 | 50,3 | 94 | 59,9 | 173 | 55,1 | |
| | >30 doses/month or >5 doses/week | 17 | 10,8 | 26 | 16,6 | 43 | 13,7 | |
| | TOTAL | 157 | 100 | 157 | 100 | 314 | 100 | |
| History of smoking | Never smoked | 120 | 76,9 | 116 | 73,9 | 236 | 75,4 | <0.01 |
| | Ex-smoker | 32 | 20,5 | 40 | 25,5 | 72 | 23,0 | |
| | Smoking | 4 | 2,6 | 1 | 0,6 | 5 | 1,6 | |
| | TOTAL | 156 | 100 | 157 | 100 | 313 | 100 | |
| Waist-to- hip ratio | Normal | 6 | 4,1 | 46 | 29,5 | 52 | 17,2 | <0.01 |
| | Increased* | 140 | 95,9 | 110 | 70,5 | 250 | 82,8 | |
| | TOTAL | 146 | 100 | 156 | 100 | 302 | 100 | |
| BMI | Normophobic | 23 | 23,0 | 16 | 10,2 | 39 | 15,2 | <0.01 |
| | Overweight | 52 | 52,0 | 59 | 37,6 | 111 | 43,2 | |
| | Obesity | 25 | 25,0 | 82 | 52,2 | 107 | 41,6 | |
| | TOTAL | 100 | 100 | 157 | 100 | 257 | 100 | |

# Student's t-test was used to compare the two groups.
*We consider the waist-to-hip ratio to be increased when it is ≥0.95 cm for men and ≥0.80 cm for women.
**BMI:** Body Mass Index

## DISCUSSION

Angola is a sub-Saharan African country with scarce health resources, both financial and human, with an average of 0.21 doctors per 1000 inhabitants. Most of these doctors are in the tertiary system, with an even greater shortage in the primary system. [17] Therefore, the prevention of risk factors for cerebrovascular diseases is almost non-existent.[18]

In our study population, more than half of the cases were <65 years old, thus indicating that stroke cases occurred at younger ages than global statistics. [19,20] This finding reinforces the hypothesis that stroke in economically emerging countries is characterized by a younger age of onset. [5,21] However, even in the Caucasian population, there has been a reduction in the average age of patients with stroke. [14,20] Similar to other studies in younger populations, we found a lower frequency of stroke in women, [13,22,23] with variations in the incidence of stroke in this group resulting from hormonal dynamics throughout life. [22,24]

Although we found that patients with hemorrhagic stroke tended to recover better (GOS = 5), we also found that patients with this form of stroke had higher mortality rates. These findings show that other clinical variables are probably better predictors of a patient's functional status and recovery than simply determining the type of stroke. [25–27] According to mRS, favorable functionality at one month after the event was also more common among cases of hemorrhagic stroke, and this finding corroborates the description that hemorrhagic stroke has better short-term functionality than ischemic stroke. [26,27]

In line with our findings, INTERSTROKE showed that stroke occurred in the African region at a younger age than in high-income regions, with almost one-fourth of cases being ≤45 years old and with men accounting for the majority of cases. [15,28] A predominance of ischemic stroke was also observed, but the hemorrhagic form showed a relatively higher frequency in the African region than in high-income regions. [28,29] Furthermore, regarding the contribution of risk factors among regions globally, the SIREN and INTERSTROKE studies showed that hypertension, dyslipidemia, regular meat consumption, and increased waist-to-hip ratio had a greater contribution to the occurrence of stroke among Africans, whereas physical inactivity and smoking, which are factors with an important contribution to the burden of stroke in other regions, had a lower contribution. [15,23,28,29]

In our study, the analysis of risk factors showed that a difference exists between cases and controls because these risk factors correspond to "classic" stroke factors and have been widely associated with the burden of disease in Caucasian and Black populations.[7,21,23,24] However, we found that five risk factors were more frequent among controls. This finding is extremely important because it warns of the potential increase in the incidence of stroke and other chronic non-communicable diseases in the coming years, particularly in economically emerging communities. [4,21]

## CONCLUSION

In this population, the risk factors for stroke were history of hypertension, current smoking, increased waist-to-hip ratio, sedentary lifestyle, history of diabetes mellitus, alcohol intake, and increased BMI. However, the coexistence of several risk factors in both groups indicates that these factors could serve as important targets for stroke prevention.

## LIMITATIONS

Factors such as diet and dyslipidemia were not assessed. The former was not assessed because of difficulties in adapting the dietary risk score used in INTERSTROKE to our reality, whereas the latter was not assessed because of the unavailability of tests to determine the lipid profile.

Owing to limited resources, it was not possible to create a 1:2 or higher pairing; however, we believe that 1:1 designs do not compromise the results.

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### Conflict of interest
The authors declare that they have no conflicts of interest.

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