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Disorders of Consciousness in the Acute Phase of Cerebral Infarctions in a Low-Income Country: The Case of Ouagadougou, Burkina Faso

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ABSTRACT

Introduction

Disorders of consciousness (DOC) during the acute phase of cerebral infarctions (CI) are a strong predictor of in-hospital mortality, particularly in settings like ours, where healthcare infrastructure and therapeutic resources are limited. The objective of this study was to determine the frequency and identify factors associated with DOC during the acute phase of CI through a prospective, cross-sectional, descriptive, and analytical study conducted in the university hospitals (UHs) of Ouagadougou, Burkina Faso.

Patients and Methods

This was a prospective, cross-sectional, descriptive, and analytical study involving patients aged over 18 years, admitted to the university hospitals of Ouagadougou (UH-Bogodogo, UH-Tengandogo, and UH-Yalgado Ouédraogo) for CI within less than 72 hours of onset, confirmed by brain CT scan and/or brain MRI, from January 1, 2022, to June 30, 2023, and who provided informed consent. Data were analyzed using EPI INFO 7.2.5.0 and IBM SPSS Statistics 25 to describe sociodemographic, clinical, paraclinical, and both in-hospital and post-discharge outcomes over a 3-month period. To identify factors associated with DOC, bivariate and multivariate analyses using stepwise logistic regression were performed, with a significance threshold of $p < 0.05$.

Results

A total of 278 patients were hospitalized for acute CI, of whom 84 (30.2%) presented with DOC. Patients with DOC had a mean age of 61.5 ± 18.2 years, with a male predominance (55.9%). At admission, the mean delay before hospital arrival was 41.3 hours, the mean Glasgow Coma Scale (GCS) score was 11.7, and the mean NIH Stroke Scale (NIHSS) score was 14.2. Brain imaging at admission in patients with DOC revealed massive CI in 52 patients (61.9%). The most frequently affected territories were the middle cerebral artery (MCA) in 73 patients (86.9%) and the anterior cerebral artery (ACA) in 22 patients (26.2%). Hemorrhagic transformation was observed in 5 patients (9.9%). The most common biological abnormalities at admission were hyperglycemia (46.4%), anemia (30.9%), and leukocytosis (30.9%). By the end of hospitalization, there were 29 recorded deaths (10.4%), with 25 deaths (29.8%) among patients with DOC and 4 deaths (2%) among those without DOC ($p < 0.001$). Multivariate analysis showed that an initial NIHSS score > 16 (OR = 12.78; $p = 0.000$), involvement of the MCA territory (OR = 1.26; $p = 0.044$), and massive CI (OR; $p = 0.005$) were significantly and independently associated with the occurrence of DOC.

Conclusion

Disorders of consciousness are common and associated with high mortality during the acute phase of cerebral infarctions in Burkina Faso. They more frequently complicate initially severe strokes. Early admission of stroke patients, improved availability and accessibility of diagnostic and therapeutic tools, and the implementation of intensive stroke care units (stroke units) in our hospitals could help reduce stroke-related mortality by preventing complications during the acute phase.

Keywords: Cerebral infarction; disorders of consciousness; Glasgow Coma Scale; NIHSS; Ouagadougou

INTRODUCTION

Cerebral infarctions (CI) account for approximately 80% of all strokes and are a major cause of mortality, disability, and dementia worldwide [1].

The implementation of stroke units (SUs) and recanalization therapies (intravenous thrombolysis, mechanical thrombectomy) has improved acute stroke management and optimized patient survival and functional outcomes [1].

Disorders of consciousness (DOC), assessed using the Glasgow Coma Scale or the level of consciousness items from the NIH Stroke Scale (NIHSS), appear to be frequent. DOC is a strong predictor of in-hospital mortality, particularly in settings like ours where healthcare infrastructure and appropriate therapeutic resources are limited. Indeed, several studies conducted in sub-Saharan Africa have reported high in-hospital mortality rates for CI, ranging from 17% to 29%, linked to the presence of DOC at admission [2–5].

DOC during the acute phase of CI reflects severe neurological impairment, often related to large infarcts or infarcts in strategic locations (brainstem, diffuse territories), which explains the high early mortality rate [6]. Their occurrence is promoted by the absence of stroke units or access to recanalization therapies, delayed diagnosis, and inadequate prevention of complications (aspiration, infections, prolonged immobility) [6].

In high-income countries, certain factors associated with the occurrence of DOC—such as high NIHSS, advanced age, and massive infarctions—have been identified, and their management contributes to improved patient outcomes.

In sub-Saharan Africa, the context is characterized by weaknesses in health systems, particularly delays in admission and management, which contrast with a high incidence of CI. This could contribute to increased frequency, severity, and emergence of risk factors associated with DOC during the acute phase of CI, thereby worsening patient prognosis.

This study was therefore conducted in the University Teaching Hospitals (UHs) of Ouagadougou—UH Tengandogo (UH-T), CHU Bogodogo (UH-B), and UH Yalgado Ouédraogo (UH-YO) —in Burkina Faso. Its objective was to determine the frequency and identify factors associated with DOC in the acute phase of CI, in order to help improve short-term outcomes in patients affected by CI.

PATIENTS AND METHODS

This was a cross-sectional, descriptive, and analytical study with prospective data collection. It included patients over the age of 18 who were admitted to the UHs of Ouagadougou, Burkina Faso (UH-Bogodogo, UH-Tengandogo, and UH-Yalgado Ouédraogo) for CI of less than 72 hours' duration, confirmed by a brain CT scan and/or MRI, during the period from January 1, 2022, to June 30, 2023, and who provided informed consent.

Patients who were excluded were those who died upon arrival, those admitted more than 72 hours after symptom onset, those who could not undergo a brain CT scan or MRI at admission, and those who did not consent to participate in the study.

For every patient hospitalized for stroke, admission was through the emergency department, where initial clinical evaluation was performed along with a brain CT or MRI to confirm the diagnosis of CI, an electrocardiogram (ECG), and standard blood tests. Patients were then transferred to the neurology ward for hospitalization, where daily clinical assessments were carried out, including monitoring of consciousness level using the Glasgow Coma Scale and evaluation of stroke severity using the National Institutes of Health Stroke Scale (NIHSS).

Additional etiological investigations were performed, including carotid Doppler ultrasound, transthoracic or transesophageal echocardiography, and 24-hour Holter ECG monitoring. Comorbidities and vascular risk factors (VRFs) were also evaluated, along with clinical and paraclinical complications or sequelae of the stroke.

In cases of coma (Glasgow score ≤ 8) or any life-threatening event (respiratory distress, acute severe cardiac comorbidity), patients were transferred to the intensive care unit.

At the end of hospitalization, patients were classified as either survivors or deceased. Survivors were followed up through outpatient neurology consultations after discharge and were regularly evaluated every three months using the modified Rankin Scale (mRS) to assess clinical outcomes.

Patients received care during hospitalization in accordance with the 2022 European Stroke Organization (ESO) guidelines [7].

The following variables were studied:

- Sociodemographic variables: age, sex ;
- Clinical variables at admission: vascular risk factors (VRFs), comorbidities, time to admission, blood pressure, temperature, Glasgow Coma Scale score, NIHSS ;
- Paraclinical variables at admission: brain imaging findings, biological test results (blood glucose, hemoglobin level, white blood cell count, glomerular filtration rate, serum sodium, potassium, and calcium levels)
- In-hospital outcome variables: complications including disorders of consciousness (defined as a loss of at least 1 point on the Glasgow scale), worsening neurological deficit (loss of at least 4 points on the NIHSS), other neurological complications (confusional syndrome, seizures), neuroimaging complications (hemorrhagic transformation, recurrence or extension of CI, significant cerebral edema), and general systemic (non-neurological) complications.

Consciousness level was assessed using the Glasgow Coma Scale. Patients with a Glasgow score ≤ 14 were considered to have disorders of consciousness—scores between 14 and 9 indicated DOC without coma; scores ≤ 8 indicated coma.

Initial clinical stroke severity was assessed using the NIHSS: ≤ 4: minor neurological deficit ; 5–15: moderate neurological deficit ; 15–20: severe neurological deficit ; 20: very severe neurological deficit. Massive CI was defined according to the clinical guidelines on the management of large hemispheric infarctions [9].

Data were analyzed using EPI INFO version 7.2.5.0 and IBM SPSS Statistics version 25. To identify factors associated with the presence of DOC, bivariate and multivariate analyses were conducted using stepwise logistic regression. The Chi-square test was used, and a p-value < 0.05 was considered statistically significant. Odds ratios (OR) were calculated with a 95% confidence interval (CI).

RESULTS

During the study period, out of 582 patients hospitalized for cerebral infarction (CI), 278 met our inclusion criteria. Among them, 84 patients (30.2%) presented with disorders of consciousness (DOC) during the acute phase.

For patients who developed DOC, the mean age was 61.5 ± 18.2 years (range: 18 to 94 years). There were 47 men (55.9%) and 37 women (44%), yielding a male-to-female sex ratio of 1.2. The mean time to hospital ad-

mission was 41.3 hours (±0.1), with a range from 6 to 72 hours. The average Glasgow Coma Scale (GCS) score at admission for patients with DOC was 11.7 (±2.6), ranging from 5 to 14. Nine patients (3.2%) were in a coma upon admission. Twenty-two patients (26.2%) had a severe initial neurological deficit (NIHSS >15). Brain imaging at admission revealed large CI in 52 patients (61.9%). The most commonly affected vascular territories were the middle cerebral artery (MCA) in 73 patients (86.9%) and the anterior cerebral artery (ACA) in 22 patients (26.2%). Hemorrhagic transformation was observed in 5 patients (9.9%). The most frequently observed biological abnormalities at admission were hyperglycemia in 39 patients (46.4%), anemia in 26 patients (30.9%), leukocytosis in 26 patients (30.9%), and renal failure in 21 patients (25%). The most common etiologies were atherothrombotic in 23 patients (27.4%) and cardioembolic in 19 patients (22.6%). The mean length of hospital stay was 11.4 (±7.2) days, with a range of 2 to 48 days.

Upon discharge, a total of 29 deaths (10.4%) were recorded—25 deaths (29.8%) among patients with DOC and 4 deaths (2%) among those without DOC ($p < 0.001$).

At 3 months post-stroke, a total of 44 deaths (16%) were reported among all patients hospitalized for CI, including 28 deaths (33%) in patients with DOC and 16 deaths (8.2%) in those without DOC.

Table I : Sociodemographic, Clinical, Paraclinical, and Outcome Characteristics of All Hospitalized Patients with Cerebral Infarction and Those with Disorders of Consciousness

Characteristics	All Cerebral Infarction Patients *N = 278*	Cerebral Infarction Patients with Disorders of Consciousness *N = 84*
Sociodemographic Characteristics		
Age		
< 40 years	32 (11.5%)	13 (15.5%)
40–49 years	41 (14.7%)	14 (16.7%)
50–59 years	57 (20.5%)	11 (13.1%)
60–69 years	79 (28.4%)	16 (19%)
70–79 years	50 (18%)	19 (22.6%)
≥ 80 years	19 (6.8%)	11 (13.1%)
Gender		
Male	142 (51.1%)	47 (55.9%)
Female	136 (48.9%)	37 (44.1%)
Vascular Risk Factors (VRFs)		
Hypertension	181 (65.1%)	51 (60.7%)
Sedentary lifestyle	65 (23.4%)	18 (21.4%)
Hypercholesterolemia	54 (19.4%)	16 (19%)
Diabetes	34 (12.2%)	11 (13.1%)
Tobacco use	33 (18.9%)	10 (11.9%)
Alcohol use	33 (18.9%)	9 (10.7%)
Obesity	24 (8.6%)	7 (8.3%)
History of stroke	23 (8.3%)	4 (4.8%)
Migraine	18 (6.5%)	12 (14.3%)
Stress	4 (1.4%)	2 (2.4%)
Hormonal contraception	2 (0.7%)	0 (0%)
Sickle cell disease	1 (0.3%)	1 (1.2%)
Emboligenic heart disease	6 (2.1%)	2 (2.4%)
Admission Vital Signs		
Hypertension	160 (58.2%)	46 (54.8%)
Fever	21 (7.6%)	12 (14.3%)
Oxygen desaturation	13 (4.7%)	9 (10.7%)
Time to Admission		
≤ 6 hours	0 (0%)	0 (0%)
7–24 hours	139 (50%)	39 (46.4%)
1–3 days	139 (50%)	45 (53.6%)

NIHSS Score at Admission		
Mild deficit [0–4]	47 (16.9%)	0 (0%)
Moderate deficit [5–15]	204 (73.4%)	50 (59.5%)
Severe deficit [16–20]	22 (7.9%)	23 (27.3%)
Very severe deficit > 20	5 (1.8%)	11 (13.1%)
Biological Abnormalities at Admission		
Hyperglycemia	114 (41%)	39 (46.4%)
Renal failure	50 (18%)	21 (25%)
Anemia	76 (23.3%)	26 (30.9%)
Leukocytosis	44 (15.8%)	26 (30.9%)
Hypoproteinemia	26 (9.3%)	8 (9.5%)
Hypernatremia	13 (4.7%)	6 (7.1%)
Hyponatremia	42 (15.1%)	15 (17.8%)
Hypokalemia	59 (21.2%)	16 (19%)
Hyperkalemia	9 (3.2%)	3 (3.6%)
Cerebral Infarctus Territory		
MCA (middle cerebral artery)	236 (84.9%)	73 (86.9%)
ACA (anterior cerebral artery)	36 (12.9%)	22 (26.2%)
Vertebrobasilar territory	26 (9.3%)	9 (10.7%)
AChoA (anterior choroidal artery)	4 (1.4%)	0 (0%)
Cerebral Infarction Size		
Small	89 (32%)	16 (19%)
Medium	144 (51.8%)	38 (45.2%)
Large	45 (16.2%)	30 (35.7%)
Other Neuroradiological Findings		
Old scar lesions	49 (17.6%)	21 (25%)
Early ischemic signs	52 (18.7%)	2 (2.4%)
Leukoaraiosis	98 (35.2%)	36 (42.8%)
Cerebral edema	18 (6.5%)	11 (13.1%)
Mass effect	11 (3.9%)	7 (8.3%)
Brain herniation	6 (2.1%)	6 (7.1%)
Cerebral Infarctus Etiology		
Cardioembolic	50 (18%)	19 (22.6%)
Atherothrombotic	99 (35.6%)	23 (27.4%)
Small vessel disease	15 (5.4%)	3 (3.6%)
Other	2 (1%)	1 (1.2%)
Undetermined	76 (27.3%)	38 (45.2%)
Complications (Admission & In-Hospital)		
Neurological complications		
Disorders Of Consciousness (early + late)	84 (30.2%)	—
Early Disorders of Consciousness	63 (22.7%)	—
Disorders of Consciousness without coma	59 (21.2%)	—
Coma (GCS ≤ 8)	4 (1.4%)	—
Late Disorders of Consciousness	21 (7.5%)	—
Worsening of neurological deficit	15 (5.4%)	15 (17.9%)
Seizures	2 (0.7%)	3 (3.6%)

Fever	46 (16.5%)	33 (33.3%)
Bronchopulmonary infection	36 (12.9%)	27 (32.1%)
Respiratory distress	16 (5.6%)	5 (5.9%)
Malnutrition	15 (5.4%)	6 (7.1%)
Urinary incontinence	11 (3.9%)	8 (9.5%)
Urinary infection	10 (3.6%)	7 (8.3%)
Pressure ulcers	8 (2.9%)	8 (9.5%)
Pulmonary embolism	3 (1.1%)	2 (2.4%)
Acute cardiac decompensation	2 (0.7%)	2 (2.4%)
Clinical Outcome at Discharge		
Survivors	249 (89.6%)	59 (70.2%)
Deceased	29 (10.4%)	25 (29.8%)
3-Month Clinical Outcome (mRS)		
mRS 0–2	56 (20%)	2 (3%)
mRS 3–5	178 (64%)	54 (64%)
mRS 6 (deceased)	44 (16%)	28 (33%)

After bivariate analysis, the presence of fever (p = 0.006), an initial NIHSS score ≥ 16 (p = 0.000), involvement of the middle cerebral artery (MCA) territory (p = 0.032), large infarct size (p = 0.000), presence of hemorrhagic transformation on brain imaging (p = 0.023), recurrent stroke (p = 0.037), and leukocytosis at admission (p = 0.000) were significantly associated with the occurrence of disorders of consciousness during the acute phase of cerebral infarction (Table II).

Table II: Results of Bivariate Analysis Identifying Variables Significantly Associated with Disorders of Consciousness in the Acute Phase of Cerebral Infarction

Variables	DOC: Yes	DOC: No	Odds Ratio (OR)	95% Confidence Interval	P-value
Smoking	10	23	1	[0.45–2.21]	0,991
Alcohol Use	9	24	0,85	[0.37–1.91]	0,695
History of Stroke	4	19	0,46	[0.15–1.39]	0,171
Migraine	12	66	5,22	[0.88–4.43]	0,031
Hypercholesterolemia	16	38	0,96	[0.50–1.85]	0,917
Sedentary Lifestyle	18	47	0,85	[0.46–1.57]	0,613
Obesity	7	17	0,94	[0.37–2.37]	0,907
Diabetes Mellitus	11	23	1,12	[0.51–2.41]	0,772
Sickle Cell Disease	1	0	1	NA	NA
Oral Contraceptive Use	0	2	1	NA	NA
Cardioembolic Heart Disease	2	4	1,59	[0.15–2.04]	0,082
Thrombocytosis	5	7	4,04	[1.23–13.27]	0,021
Thrombocytopenia	33	21	1,83	[0.98–3.44]	0,058
Sodium - Normal	160	62	1	Ref	Ref
Sodium - Hypernatremia	7	6	2,21	[0.71–6.84]	0,168
Sodium - Hyponatremia	27	15	1,43	[0.71–2.87]	0,31
Calcium - Normal	147	60	1	Ref	Ref
Hypercalcemia	3	1	0,81	[0.83–8.00]	0,862
Hypocalcemia	43	21	1,19	[0.65–2.18]	0,559
MCA Territory	73	163	1,26	[1.17–5.68]	0,032
ACA Territory	16	8	5,47	[2.23–13.36]	0
Vertebrobasilar Territory	10	21	0,83	[0.25–2.69]	0,759

Small Infarct	71	16	1	Ref	Ref
Large Infarct	116	52	8,92	[3.06–26.03]	0
Medium Infarct	5	16	0,61	[0.317–1.17]	0,141
Cerebral Edema	11	7	4,02	[1.50–10.78]	0,006
Mass Effect	7	4	4,31	[1.22–15.17]	0,023
Brain Herniation	6	0	1	NA	NA
Hemorrhagic Transformation	5	1	12,21	[1.40–106.23]	0,023
Old Lesions	21	28	1,96	[1.4–3.71]	0,037
Leukoaraiosis	36	62	1,59	[0.94–2.70]	0,082
Atherosclerosis	23	76	0,58	[0.94–2.70]	0,061
Microangiopathy	3	12	0,56	[0.33–1.02]	0,382
Cardioembolic Stroke	19	31	1,59	[0.15–2.04]	0,082

After multivariate analysis, an initial NIHSS > 16 (OR = 12.78; p = 0.000), involvement of the middle cerebral artery (MCA) territory (OR = 1.26; p = 0.044), and large infarct size on initial brain imaging (OR; p = 0.005) were significantly and independently associated with the occurrence of disorders of consciousness (Table III).

Variables	Odds Ratio (OR)	95% Confidence Interval	P-value
NIHSS ≤ 16	1		
NIHSS > 16	12,78	[3.72–43.92]	0
MCA Territory - Yes	1,26	[1.17–5.68]	0,044
MCA Territory - No	1		
Small Infarct	1		
Large Infarct	6,62	[1.76–24.83]	0,005
Medium Infarct	0,9	[0.39–2.08]	0,823

DISCUSSION

Early disorders of consciousness (DOC) are common among patients with acute cerebral infarction (CI). Recent studies report a wide range of prevalence rates, varying from 4% to 38% [8–11]. The rate of 30.2% reported in our study falls within this range. These frequency variations are largely due to differences in the populations studied, the criteria used to define and assess consciousness disorders, patient admission delays, and the availability of prehospital care services [8–10]. In high-income settings, earlier detection, prevention, and optimized management of DOC and other acute stroke complications are made possible by the development of stroke units and the use of recanalization therapies for acute CI (intravenous thrombolysis and mechanical thrombectomy) [12,13].

In sub-Saharan Africa, a few hospital-based studies have reported generally high frequencies of DOC during the acute phase of CI, ranging from 30% to 70% [4,14–16]. This high frequency of DOC and other complications in the acute phase of cerebral infarction in sub-Saharan Africa results from several interrelated factors: 1) delayed management, including prolonged admission times, lack of stroke units and recanalization therapies (IV thrombolysis and mechanical thrombectomy), and the absence of organized referral networks; 2) diagnostic limitations, such as the limited availability and accessibility of CT or MRI scans, insufficient diagnostic skills or awareness among healthcare providers; 3) low socioeconomic and systemic resources, including limited public awareness of stroke risk factors (VRFs), poor recognition of stroke symptoms, and the lack of perception of stroke as a medical emergency, as well as limited financial means ; pathophysiological characteristics of stroke in sub-Saharan Africa, including a high prevalence of risk factors associated with DOC.

Furthermore, this high frequency of DOC may also reflect a hospital selection bias in favor of clinically severe cases. Minor or moderate infarctions may have been managed at home or in lower-level health facilities.

Addressing these complications requires an integrated approach that combines primary stroke prevention, the implementation of stroke units, access to recanalization therapies for acute CI, the organization of efficient referral networks, and continuous training of healthcare professionals [17–19].

In our study, an initial NIHSS score > 16—indicating clinically severe CI at admission—MCA territory involvement, and large infarct size (massive or extensive infarcts on brain imaging) were significantly and independently associated with the occurrence of DOC during the acute phase of CI. These findings are consistent with previous literature.

Indeed, several factors reported in the literature are associated with the occurrence and severity of DOC during acute CI: 1) extent and location of the infarction, particularly large or bilateral cortico-subcortical cerebral infarcts, which are strongly correlated with altered consciousness; 2) stroke severity, where a high NIHSS (National Institutes of Health Stroke Scale) score is a key predictor, with elevated scores being associated with a higher probability of DOC; 3) hemorrhagic transformation or cerebral edema, as both conditions can increase intracranial pressure and lead to impaired consciousness. A severe cerebral infarction (CI) with an immediately significant neurological deficit (NIHSS >16) is often associated with extensive involvement of the middle cerebral artery (MCA) territory, typically due to proximal MCA occlusion. This frequently leads to a progressive decline in consciousness secondary to extensive cerebral edema (malignant MCA infarction) and/or hemorrhagic transformation [20–22].

Other factors commonly identified in the literature as being associated with the occurrence of disorders of consciousness (DOC) during the acute phase of CI—such as metabolic and biological disturbances (hypoxia, hypoglycemia, electrolyte imbalances, and systemic infections), advanced age (older patients more frequently experience DOC due in part to comorbidities and neuronal vulnerability), as well as factors related to medical management (early care, including intracranial pressure management and hemodynamic stabilization, can influence the recovery of consciousness)—were not identified in our study.

In our cohort, in-hospital mortality among patients with CI who developed DOC was significantly higher (29.8%) compared to those who maintained normal consciousness (2%) ($p < 0.001$), which aligns with existing literature. Indeed, several studies have shown that early decline in consciousness is a common and independent predictor of in-hospital mortality in CI patients [11,23,24].

Post-stroke complications—both neurological (e.g., cerebral edema, hemorrhagic transformation) and systemic (e.g., bronchopulmonary and urinary infections, pulmonary embolism)—which are frequent, severe, and significantly associated with DOC, likely explain this excess mortality [11,24].

Early admission of stroke patients, intensive monitoring in stroke units (SUs), and improved availability and accessibility of diagnostic and therapeutic tools (CT, MRI, and recanalization therapies) will contribute significantly to reducing mortality. This can be achieved through the prevention and mitigation of both early and late post-stroke complications, including disorders of consciousness.

Limitations of Our Study

The long delays in hospital admission for stroke patients in our context significantly reduced the number of patients eligible for inclusion and, consequently, the statistical power of this study.

Late admission and delayed management of stroke patients may also have affected the observed frequency of disorders of consciousness.

CONCLUSION

Disorders of consciousness are common during the acute phase of cerebral infarctions in the university hospitals of Ouagadougou, Burkina Faso. They occur more frequently in clinically severe infarctions at admission and, on initial brain imaging, in infarctions involving the middle cerebral artery (MCA) territory and in large (massive) infarcts.

Early admission of stroke patients—enabled by an efficient referral network—along with increased availability and accessibility of diagnostic tools (CT, MRI), therapeutic options (intravenous thrombolysis and mechanical thrombectomy), and intensive monitoring (stroke units), will contribute to reducing stroke-related mortality by preventing or minimizing complications during the acute phase.

Manuscript Submission and Approval Statement

By submitting this manuscript for publication in the present journal, the authors affirm that it has not been submitted to any other journal and has not been previously published.

We also confirm that its submission is approved by all co-authors and that, if accepted, it will not be published elsewhere in any format, including electronically, without the consent of the copyright holder.

We further certify that all necessary measures were taken to ensure strict compliance with professional confidentiality.

Conflict of Interest Statement

The authors declare no conflicts of interest related to this study.

Declaration of Use of Generative AI and AI-Assisted Technologies in the Writing Process

The authors affirm that no generative AI or AI-assisted technologies were used in the preparation of this manuscript.

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Author Contributions

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