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Research Article

Underrecognized Role of Patent Foramen Ovale in Cryptogenic Ischemic Stroke among Young Adults in Sub-Saharan Africa: A Case Series from Burkina Faso

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Abstract

Background:

Patent foramen ovale (PFO) is an uncommon cause of ischemic stroke (IS) overall but represents a frequent etiology of cryptogenic stroke in young adults. Data-t-on PFO-related stroke in sub-Saharan Africa remain scarce.

Objective:

To de scribe the clinical, radiological, and echocardiographic characteristics of ischemic strokes probably related to PFO among adults aged ≤60 years in Ouagadougou, Burkina Faso.

Methods:

We conducted a prospective, descriptive, multicenter case series from January 2021 to August 2023 in the neurology and cardiology departments of three university hospitals (UHs) in Ouagadougou (UH-Tengandogo, UH-Yalgado Ouédraogo, and UH-Bogodogo). Eligible patients were ≤60 years old with imaging-confirmed ischemic stroke and a high-risk PFO identified on contrast echocardiography (transthoracic and/or transesophageal). A Risk of Paradoxical Embolism (RoPE) score ≥4 was required for inclusion. Patients with other defined cardioembolic or atherosclerotic causes were excluded. Clinical, imaging, and echocardiographic data were analyzed using Epi Info 7.2.

Results:

Most patients were young adults with few traditional vascular risk factors. Cortical infarcts predominated on neuroimaging. Echocardiography frequently revealed large shunts or an associated atrial septal aneurysm. No in-hospital mortality was recorded, and functional outcomes were favorable in most cases (modified Rankin Scale ≤2 at discharge and follow-up).

Conclusion:

This inaugural series highlights that PFO may be an underrecognized cause of ischemic stroke in young adults in Burkina Faso. Routine contrast echocardiography and RoPE score assessment should be integrated into the diagnostic approach to cryptogenic stroke in resource-limited settings.

Key Words: patent foramen ovale; ischemic stroke; cryptogenic stroke; rope score; burkina faso

Introduction

Ischemic stroke (IS) remains a major cause of neurological morbidity worldwide. Among young adults—defined as those under 50–60 years of age—a significant proportion of IS cases are cryptogenic, meaning that no clear etiology can be identified despite a comprehensive diagnostic workup. Several studies have shown that while patent foramen ovale (PFO) is an uncommon overall cause of stroke, it represents a frequent mechanism in cryptogenic strokes among younger patients [1–3].

The most widely accepted pathophysiological mechanism is paradoxical embolism, in which a thrombus originating from the venous circulation crosses into the arterial system through a right-to-left shunt via the PFO [4,5]. Diagnosis relies mainly on transthoracic echocardiography (TTE) and, more accurately, on transesophageal echocardiography (TEE) with agitated saline contrast injection, which remains the gold standard for detecting PFO [6].

However, identifying a PFO in a patient with IS does not, by itself, establish causality. Its presence may be incidental, particularly in older patients or in those with traditional vascular risk factors, in whom other cardioembolic sources may coexist [4,7,8]. The likelihood that a stroke is attributable to PFO can be estimated using the Risk of Paradoxical Embolism (RoPE) score, which incorporates age, vascular risk factors, and stroke characteristics. A high RoPE score (≥4) indicates a strong probability that the ischemic event is PFO-related [9,10].

Moreover, certain anatomical features, such as a large right-to-left shunt or coexistence with an atrial septal aneurysm (ASA), further strengthen the plausibility of a paradoxical embolic mechanism [11,12].

In resource-limited settings, particularly in sub-Saharan Africa, the incidence of stroke in young adults is high, but the proportion of cryptogenic cases remains substantial due to limited access to specialized diagnostic investigations [13,14]. In Burkina Faso, data on PFO-associated ischemic strokes are virtually nonexistent [15].

This study—the first of its kind in our setting—aimed to describe the clinical, radiological, and echocardiographic features of ischemic strokes probably related to PFO in adults ≤60 years hospitalized in the University Teaching Hospitals of Ouagadougou.

Patients and Methods

Study design and setting:

This was a prospective, descriptive case series conducted in the Neurology and Cardiology Departments of the University Hospitals of Tengandogo (UH-T), Yalgado Ouédraogo (UH-YO), and Bogodogo (UH-B) in Ouagadougou, Burkina Faso. The inclusion period extended from January 1, 2021, to August 31, 2023.

Study population and inclusion criteria:

We included patients under 60 years of age who were hospitalized or followed up for ischemic cerebral infarction (IC) confirmed by brain computed tomography (CT) and/or magnetic resonance imaging (MRI), in whom a high-risk patent foramen ovale (PFO) was demonstrated on contrast echocardiography (transthoracic and/or transesophageal). Inclusion required a Risk of Paradoxical Embolism (RoPE) score ≥4, indicating a high likelihood of a causal relationship between the PFO and the ischemic stroke. Other cardioembolic, atherosclerotic, or lacunar causes were excluded after a comprehensive etiological workup, including brain and supra-aortic MRI angiography, carotid and vertebral Doppler ultrasound, ECG or 24-hour Holter monitoring, lipid profile, and standard laboratory tests.

Exclusion criteria:

Patients aged ≥60 years, those with a low-risk PFO (RoPE score <4) [5,16], ischemic stroke related to another high-risk cardioembolic source, or incomplete etiological workup were excluded.

Variables included in the RoPE score (0–10 points):

Characteristic	Points
Age 18–29 years	5
Age 30–39 years	4
Age 40–49 years	3
Age 50–59 years	2
Age 60–69 years	1
Age ≥70 years	0
No hypertension	1
No diabetes	1
No prior stroke/TIA	1
Non-smoker	1
Cortical infarct location on imaging	1
Maximum score	10
Minimum score	0

Interpretation:

A RoPE score of 7–10 (high) suggests a strong likelihood of PFO causality (~80–90%), whereas a score of 0–3 (low) indicates a low probability.

Diagnostic procedures:

Transthoracic (TTE) and/or transesophageal echocardiography (TEE) was performed by an experienced cardiologist. PFO diagnosis was based on either direct anatomical visualization or the passage of ≥3 microbubbles into the left atrium within 3–5 cardiac cycles following right atrial opacification.

A high-risk PFO was defined by a large right-to-left shunt (≥20 microbubbles), a wide opening (≥2 mm), or the presence of an associated atrial septal aneurysm (ASA).

Variables studied:

Collected data included sociodemographic characteristics (age, sex, occupation, medical history), vascular risk factors (hypertension, diabetes, smoking, dyslipidemia, prior stroke/TIA), clinical presentation

(onset circumstances, Glasgow Coma Scale, NIHSS at admission), brain imaging (location, size, and topography of the infarct), echocardiographic features (PFO size, shunt grade, associated ASA), therapeutic management, and outcomes (treatment received, complications, and modified Rankin Scale [mRS] score at discharge and 6 months).

Ethical considerations:

The study was conducted after obtaining administrative authorization from all three university hospitals. Verbal informed consent was obtained from each patient or their legal representative. Anonymity and data confidentiality were strictly maintained throughout the study.

Results

During the study period, 42 cases of ischemic stroke (IS) associated with a patent foramen ovale (PFO) were identified. Among them, 30 cases (71%) were considered *probably attributable to the PFO*, based on a strong causal relationship (RoPE score ≥ 4), while 12 cases (29%) had a weak causal link (RoPE < 4).

The median age of patients was 35 years (IQR 12; range 20–60 years). The most represented age groups were 15–40 years and 41–50 years, with 11 patients each (37%), followed by 51–60 years (8 patients, 26%). There were 22 men (73%) and 8 women (27%).

The most common vascular risk factors (VRFs) were migraine (14 cases, 35%) and hypertension (6 cases, 20%). A venous thromboembolic event was present in 4 patients (13%), including 3 cases of deep vein thrombosis (10%) and 1 pulmonary embolism (3%).

The median Glasgow Coma Scale (GCS) score on admission was 13 (IQR 2; range 9–15); 9 patients (30%) had impaired consciousness, and 17 (57%) presented with moderate neurological deficits (NIHSS 6–15). The middle cerebral artery (MCA) territory was the most frequently involved (28 patients, 93%), followed by the anterior cerebral artery (ACA) territory (7 patients, 23%). The most common infarct size was medium (12 patients, 40%). Associated neuroimaging findings included old ischemic scars (4 cases, 13%) and leukoaraiosis (3 cases, 10%).

On contrast transesophageal echocardiography (TEE), a large shunt PFO was found in 13 patients (43%), a moderate shunt in 12 (40%), and a small shunt in 5 (17%). An atrial septal aneurysm (ASA) was associated in 18 patients (60%) (Table I).

Evaluation of the causal relationship between PFO and IS using the RoPE score showed that 18 patients (60%) had a *very strong association* (RoPE = 10), while 12 patients (40%) had a *strong association* (RoPE = 4–9).

The median hospital stay was 13 days (IQR 3; range 3–60 days). All patients received long-term antiplatelet therapy (aspirin 160 mg/day or clopidogrel 75 mg/day).

At 6-month follow-up, 1 patient (3%) had died, and 4 (13%) experienced recurrent ischemic stroke. Among the 8 patients with prior or recurrent IS (including 1 death), 3 patients (10%) underwent percutaneous PFO closure abroad (France or Morocco) within a median of 23 months (IQR 8; range 16–38 months), funded by the Burkinabe government. Post-procedure outcomes were uneventful, with no recurrent cerebrovascular events reported.

At the end of follow-up, 22 patients (73%) were functionally independent (mRS 0–2), 7 (24%) had moderate disability (mRS 3), and 1 patient (3%) had died (mRS 6). (see Table I).

Variables	n	%
Vascular risk factors		
Migraine	14	35
Hypertension	6	20
Obesity	1	3
Diabetes mellitus	2	6
Previous stroke	4	13
Oral contraception	1	3
Dyslipidemia	2	6
Smoking	3	10
Alcohol use	2	6
Physical inactivity	1	3
Level of consciousness (Glasgow Coma Scale)		
Normal (GCS = 15)	21	70
Altered (GCS = 14–9)	9	30
Stroke severity at admission (NIHSS)		
Minor (≤ 5)	12	40
Moderate (6–15)	17	57
Severe (≥ 16)	1	3
Venous thromboembolic event at admission	4	13
Deep vein thrombosis	3	10
Pulmonary embolism	1	3
Infarct territory (MRI/CT)		

Variables	n	%
Middle cerebral artery (MCA)	28	93
Superficial ± deep	26	86
Deep only	2	6
Anterior cerebral artery (ACA)	7	23
Anterior choroidal artery	1	3
Posterior cerebral artery (PCA)	2	6
ACA–MCA borderzone	1	3
Infarct size		
Medium	12	40
Small	11	37
Large	7	23
Associated neuroimaging findings		
Old ischemic scars	4	13
Leukoaraiosis	3	10
Hemorrhagic transformation	3	10
Cerebral edema	2	6
Mass effect	2	6
Contrast transesophageal echocardiography findings		
Large shunt PFO	13	43
Moderate shunt PFO	12	40
Small shunt PFO	5	17
Associated atrial septal aneurysm (ASA)	18	60

Table I: Clinical, neuroimaging, and echocardiographic characteristics of patients with ischemic stroke attributed to a patent foramen ovale (strong causal link, RoPE ≥ 4) (n = 30)

Legend:
GCS = Glasgow Coma Scale; NIHSS = National Institutes of Health Stroke Scale; PFO = Patent Foramen Ovale; MCA = Middle Cerebral Artery; ACA = Anterior Cerebral Artery; PCA = Posterior Cerebral Artery; ASA = Atrial Septal Aneurysm.

Discussion

Over the past two decades, the association between patent foramen ovale (PFO) and cryptogenic ischemic stroke (IS)—which accounts for 30–40% of all IS—has been firmly established [6,17]. Case–control studies have shown that PFO is a frequent cause of cryptogenic IS, most likely through paradoxical embolism from the venous to the arterial system via a right-to-left shunt [4,5]. However, attributing an IS to a PFO remains challenging, given the high prevalence of PFO in the general population (≈25%) and the frequent incidental nature of its discovery (about one-third of cases) [18,19, 20]. This highlights the need for a systematic etiological workup to exclude other potential causes and to retain only cryptogenic IS associated with PFO, as recommended by the French Society of Vascular Neurology (SFNV) and the French Society of Cardiology (SFC) in 2019 [21]. In line with these recommendations, our study identified 42 cases of IS associated with PFO over a 32-month period among 1,455 cryptogenic IS cases recorded in the University Teaching Hospitals of Ouagadougou in patients aged ≤60 years. The Risk of Paradoxical Embolism (RoPE) score was then applied to assess the probability of a causal relationship between PFO and IS. This 10-point score incorporates factors such as young age, cortical infarction, and the absence of traditional vascular risk factors (hypertension, diabetes, prior stroke/TIA, smoking), atherosclerosis, or left ventricular hypertrophy [3]. Higher RoPE scores correspond to a greater likelihood that the IS is PFO-related. Indeed, the prevalence of PFO increases from 23% (95% CI: 19–26%) among patients with RoPE scores of 0–3 to 73% (95% CI: 66–79%) among those with scores of 9–10, with an attributable fraction ranging from 0% to 90% [9]. In our series, 30 of 42 IS cases (71%) were considered probably attributable to PFO (RoPE ≥4), while 12 (29%) showed a weak causal relationship (RoPE <4).

Among patients with PFO-related IS, coexistence of PFO with an atrial septal aneurysm (ASA) is common, with reported prevalence ranging from 32–33% [11] to as high as 60–70%, significantly increasing the risk of IS recurrence [22]. Epidemiologically, PFO prevalence is similar in both sexes, though differences exist across races and ethnicities [3,10,23]. Cryptogenic IS is more frequent in younger individuals, and the association between PFO and cryptogenic IS in this population has been confirmed by several case–control studies using contrast transthoracic or transesophageal echocardiography [24], consistent with our findings. Clinically, PFO-related cryptogenic IS tends to be less severe, as confirmed in our cohort, where 97% of patients had minor to moderate deficits at admission, and 77% had small to medium infarcts on neuroimaging. Deep vein thrombosis (DVT) is inconsistently reported in these patients due to the limited sensitivity of standard venous Doppler ultrasound, which cannot detect pelvic vein thromboses, a common source of paradoxical embolism [6,25]. In our study, DVT of the lower limbs was identified in 3 patients (10%), though no pelvic vein imaging was performed. Migraine was found in 46% of our cases, consistent with reports of a higher prevalence of migraine among PFO patients [26,27].

This association is thought to be bidirectional, particularly for migraine with aura [26]. Studies have shown that migraine is more frequent among patients with PFO-related cryptogenic IS (27.3%) than among those without PFO (14.0%) [21]. It has been hypothesized that PFO allows vasoactive substances and microthrombi to bypass the pulmonary filter and reach the systemic circulation in sufficient concentrations to trigger migraine attacks [21,26]. All our patients received antiplatelet therapy, in accordance with evidence-based guidelines from major clinical trials [11,12,28,29]. Only three patients (10%) underwent percutaneous PFO closure abroad (France or Morocco) after a median delay of 23 months, reflecting limited local access to interventional cardiology. Recent randomized controlled trials—CLOSE [9], REDUCE [12], DEFENSE-PFO [29], and the extended RESPECT study [16]—have demonstrated the superiority of PFO closure over medical therapy in preventing recurrent IS. Current indications target patients aged ≤60 years with recent IS (≤6 months), a high-risk PFO (large shunt ≥20 microbubbles or ≥2 mm, or associated ASA >10 mm), and a strong causal link after comprehensive etiologic evaluation [11,12,16,29]. The low rate and long delay of closure in our series reflect the absence of interventional cardiology infrastructure and the high cost of specialized care in our setting.

Conclusion:

Diagnosing PFO-related ischemic stroke with a strong causal link remains challenging in Ouagadougou due to the limited availability and accessibility of appropriate diagnostic and etiologic investigations. These strokes are characterized by young age at onset, low prevalence of traditional vascular risk factors, cortical infarct localization, coexistence of ASA and large shunt, high recurrence rate, and very limited access to PFO closure. Improving access to advanced etiologic investigations and to interventional cardiology services in sub-Saharan Africa would enhance the availability of percutaneous PFO closure, currently the treatment of choice for preventing PFO-related stroke recurrence.

Keywords:

Cryptogenic ischemic stroke; age ≤60 years; patent foramen ovale; RoPE score; atrial septal aneurysm

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