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Tracking Atrial Fibrillation by 24-Hour Holter ECG in Ischemic Stroke of Unclear Origin, an Experience of the Cardiology Department of the University Hospital of Marrakesh

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Abstract **Original Research Article**

Background: Stroke is a worldwide growing health problem; a significant proportion of acute ischemic strokes occur as the first manifestation of atrial fibrillation. We sought to evaluate the performance of 24-hour rhythm monitoring in detecting paroxysmal atrial fibrillation. ***Methods:*** This was a cross-sectional study conducted at the University Hospital of Marrakech, in 174 selected patients with ischemic stroke without clear etiology at baseline subjected to ambulatory Holter monitoring. ***Results:*** The overall detection rate for atrial fibrillation was 4.1%, allowing the initiation of anticoagulant therapy in selected patients. Nevertheless, although some degree of success in detecting AF in a short period of monitoring was achieved, it is believed that the prevalence of AF is still underestimated by this screening modality. ***Conclusion:*** Tracking atrial fibrillation is a fundamental element in the secondary prevention of stroke; the development of new digital technologies now makes the possibility of long-term heart rhythm monitoring accessible. Numerous ECG recording solutions have been scientifically proven reliable, some are already recommended for the detection of cardiac arrhythmias. The choice of the screening method must be tailored to each individual case.

Keywords: Holter monitoring, Ischemic stroke, atrial fibrillation, Screening.

INTRODUCTION

Stroke is a global health problem, particularly in developing countries(Feigin *et al*., 2014), It comes second only to ischemic heart disease as a cause of death, accounting for 11% of all deaths(Wang *et al*., 2016), and is a major contributor to disability worldwide.

Around 80% of all strokes are ischemic(Donnan, Fisher, Macleod, & Davis, 2008); there are two types of ischemic strokes, thrombotic strokes due to atherosclerosis and embolic strokes caused primarily by atrial fibrillation(Allen & Bayraktutan, 2008).

The prevalence of AF, the most common arrhythmia in the general population, is currently estimated at 2% to 4% and is steadily increasing. The risk of stroke is substantial whether AF is paroxysmal, persistent, or permanent. In fact, AF puts patients 5-fold increased risk of stroke, depending on the presence of specific risk factors for stroke summarized in the CHA2DS2-VASc scale (Hindricks *et al*., 2021).

Although the benefit of oral anticoagulants in reducing the risk of stroke occurrence and recurrence in AF is well established, the first step is to document AF. Authentication can be challenging, as it tends to be asymptomatic and paroxysmal and thus not detected by conventional ECG tracing; various approaches for AF detection are being employed, including Holter ECG and continuous monitoring, with variable sensitivity and specificity.

In order to improve the management of stroke patients in Marrakech, we conducted this study to evaluate the usefulness of Holter monitoring in the detection of rhythmic disorders in cerebral infarction, particularly atrial fibrillation.

AIM OF THE STUDY

The objective of this study was to determine the clinical utility of ambulatory Holter monitoring in detecting paroxysmal AF in patients with ischaemic stroke.

PATIENTS AND METHODS

This is a cross-sectional study at the University Hospital of Marrakech, between November 2017 and November 2021; (N = 174) patients were enrolled for ambulatory monitoring.

Inclusion criteria

- Ischemic stroke documented by MRI/CT scan
- Resting 12-lead ECG showing sinus rhythm

Exclusion criteria

- Transient (TIA) or undocumented stroke.
- Atrial fibrillation or other previously diagnosed arrhythmia or other identified stroke etiology.

The devices employed in our study were the Mortara H12+™ Holter monitor, providing continuous (24-48h) 12-lead recording, and CompactFlash (DEKLINDEVICES) as storage media. Patient identifiers were entered and data analyzed by a computer using the Mortara HScribe 5 Holter Analysis System.

Demographic and clinical data were collected from the cardiology department's explorations register.

The variables studied were age, sex, cardiovascular risk factors, and Holter findings. The main end point was to enumerate the number of newly diagnosed AF cases during Holter monitoring in order to assess its diagnostic utility.

RESULTS

174 Holter recordings were performed, the third most common indication for ambulatory rhythmic monitoring in the Cardiac Exploration Department, after the assessment of palpitations and extrasystoles (premature heart contractions). The demographic and clinical characteristics of the patients are listed in Table 1. Among the 174 patients, 95 were men and 79 were women, with an average age of 56 ± 1 year (extremes: 22 and 87 years); patients aged less than 50 years accounted for 51 cases (29.3%). The main cardiovascular risk factors identified were hypertension (HTN) in 65 cases (37.4%), followed by smoking, diabetes mellitus, and obesity in order of frequency.

The Holter ECG was normal in 139 cases (81%) and uninterpretable in 4 cases, with an average recording time of 22 hours; After analysis, main findings (Table2) were extrasystoles (ventricular, junctional, or supraventricular) in 18 cases (10.6%), paroxysmal atrial fibrillation (AF) in 7 cases (4.1%), atrial flutter in 1 patient, and 5 cases of atrioventricular block (4 first-degree and 1 complete AVB).

Table-1: Patient Characteristics

Patient Characteristics	N
Age (years) <50 (n) ≥50 (n)	56±1 51 (29,3%) 123 (70,7%)
Sex F. M	79 (45,4%) 95 (54,6%)
HTN	65 (37,4%)
Smoking	31 (17,8%)
Obesity	23 (13,2%)
D.M	28 (16%)

Table-2: Holter findings

HOLTER findings	N
Mean time (hours)	22,2
Non-Interpretable	4
Normal	139 (81%)
A. Fibrillation	7 (4,1%)
A. Flutter	1
Premature heart beats	18 (10,6%)
1st degree AV block	4
Complete AV block	1

DISCUSSION

The first point to note in this series is that the vast majority of patients have one or more cardiovascular risk factors. The aggregation of these risk factors increases both the incidence of ischemic stroke as well as AF. The management of these risk factors remains extremely important in secondary prevention, with therapeutic objectives adapted to each patient ; In fact, five factors: hypertension, unhealthy diet, physical inactivity, smoking, and abdominal obesity, accounted for 82% of the population-attributable risk of ischemic stroke in the INTERSTROKE study(O'Donnell *et al*., 2010).

In the design of the study, the primary objective was to screen for underlying paroxysmal AF, and for this we excluded patients with a clear etiology for their ischemic stroke at baseline and only selected patients in sinus rhythm on the resting ECG.

The TOAST classification (Adams *et al*., 1993) denotes five subtypes of ischemic stroke: A) large vessel atherosclerosis, B) cardio-embolism, C) small-vessel occlusion, D) stroke of other unsual etiology (i.e dissection, arteritis), and E) stroke of undetermined etiology (cryptogenic stroke). This classification identifies atrial fibrillation as a high-risk source of cardio-embolism.

The 2021 Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack(Kleindorfer *et al*., 2021) writing group has a conceptually similar representation of ischemic stroke subtypes: Lacunar stroke; Stroke Due to Small Vessel Disease; Cardioembolic Stroke; Cryptogenic Stroke; and Stroke Caused by Large Artery Atherosclerosis.

The intrinsic mechanism of ischemic stroke is unclear in 20% to 40% of patients(Hindricks *et al*., 2021) ; Cryptogenic stroke is defined as an imaging-confirmed stroke of unknown origin after a thorough diagnostic evaluation(Yaghi, Bernstein, Passman, Okin, & Furie, 2017). Several possible scenarios have been proposed, such as undiagnosed atrial fibrillation and atrial cardiomyopathy.

Since 2014, the concept of ESUS (Ntaios, 2020) (embolic stroke of undetermined source) has evolved to describe patients with non-lacunar ischemic stroke lacking a definitive etiology; This terminology is distinct from cryptogenic stroke because it implies that the stroke is embolic in origin, but somewhat similar to the Causative Classification System(Ay *et al*., 2005) definition of Cryptogenic embolism.

ESUS is estimated to account for 17% of ischemic strokes and its diagnosis is based on cerebral and supra-aortic trunk imaging (ruling out >50% stenosis), resting and 24-hour ECG recordings, and transthoracic or even transoesophageal echocardiography to rule out a major cardiovascular explanation.

Atrial fibrillation may be causal, coincidental, or neurogenically induced by a stroke ; Ischemic strokes occurring in AF are nearly twice as apt to be fatal as non-AF strokes, according to the Framingham study(Allen & Bayraktutan, 2008), with more frequent relapses and greater functional deficits in survivors, whereas the rest of patients with ESUS tend to be younger, have mild strokes, and have an annual recurrence rate of 4% to 5%. The minimum time in AF that carries a significant risk of stroke remains unknown.

The escalating prevalence of AF (specifically asymptomatic AF), the detection of AF in approximately 10% of all ischemic strokes, the possibility of preventing AF-related strokes with appropriate treatment, and the expanding availability of AF detection tools are all prompting international initiatives to implement AF screening in clinical practice(Hindricks *et al*., 2021), in conjunction with the WHO criteria for screening.

Population-level AF screening has been the focus of recent studies, the European Society of Cardiology recommends "opportunistic" AF screening in patients older than 65 years and "routine" screening in those older than 75 years or at high risk for stroke (Hindricks *et al*., 2021).

There is no proven benefit to treating patients with embolic stroke of uncertain origin empirically with anticoagulants(Kleindorfer *et al*., 2021), nor is the treatment of atrial myopathy without detected AF.

ECG is a simple, non-invasive tool for the diagnosis of AF. It is recommended in patients suspected of having a stroke or TIA, to screen for AF, atrial flutter, and to assess other concomitant cardiac conditions that may have therapeutic implications (Hindricks *et al*., 2021; Kleindorfer *et al.*, 2021).

"Covert" atrial fibrillation in stroke patients is an unsettled issue. Tracking AF has been limited to electrocardiographic monitoring for a relatively short period of time, lacking the sensitivity to detect paroxysmal atrial fibrillation; Ambulatory ECG monitoring (Holter) uses relatively compact devices to continuously record ECG signal over a defined period. It is simple to use, allows detection of asymptomatic events, and some more modern devices have patient-activated event cueing to allow symptom-rhythm correlation.

The ideal is to extend the Holter ECG monitoring as long as possible, but due to cost and logistical constraints, we opted for a 24-hour protocol, the Holter recording is usually the first test performed to detect paroxysmal AF, despite relatively poor diagnostic efficiency. The 2016 ESC Guidelines for the management of atrial fibrillation, recommend screening for AF in patients with TIA or ischaemic stroke, by short-term ECG recording followed by continuous ECG monitoring for at least 72hour (Class I, LOE B).

The AF detection rate in the present series (4.1%) is close to that described in the literature for a 24- to 48-hour rhythm Holter; however, even though a proportion of patients were put on anticoagulation, this result is not at all satisfactory, because subclinical AF has a much higher prevalence.

In patients with cryptogenic stroke who do not have a contraindication to anticoagulation, long-term rhythm monitoring by mobile ambulatory cardiac telemetry, implantable loop recorder, or other approaches capable of detecting atrial high rate events (AHRE) is reasonable to detect intermittent AF (Hindricks *et al*., 2021; Kleindorfer *et al*., 2021) ; The diagnosis of AF in positive screening cases is made definitively only when a physician reviews the ≥30s single-lead ECG or 12-lead ECG recording and confirms that AF is present.

In 2014, a randomized trial(Gladstone *et al*., 2014) of 572 patients free of known atrial fibrillation who had a cryptogenic ischemic stroke or TIA within the previous 6 months were randomized to undergo

non-invasive ambulatory ECG monitoring with either continuous recording over 30 days (intervention group) or a conventional 24-hour monitor (control group). AF of a minimum of 30 seconds was detected in 16.1% of patients in the intervention group, 5 times more than in the control group (3.2%) with, consequently, an almost doubled rate of anticoagulant treatment in the intervention group compared with standard short-term ECG monitoring practice.

The FIND-AF study was one of the first to show that the probability of detecting a paroxysmal AF episode after stroke was proportionally correlated with the duration of the recording (Stahrenberg *et al*., 2010); with implantable cardiac monitors, the detection rate is approximately 16% at 30 days and 30% after 3 years according to the CRYSTAL-AF and EMBRACE studies.

A tiered focus on AF tracking using resting ECG, then Holter monitoring, followed by a 7-day external loop recorder, and ultimately more prolonged monitoring in patients at increased risk for AF has been proposed(Schnabel *et al*., 2019).

There is a wide range of devices and methods for AF testing, from blood pressure monitors, smart -phones, and -watches to wearable belts, adhesive patch devices, and implantable loop recorders; Whereas the most cost-effective approach to cardiac monitoring remains to be determined, it may be reasonable to start with medium- to long-duration non-invasive cardiac monitoring, particularly in patients with a high index of suspected AF and a high likelihood of compliance during the set period.

CONCLUSION

The relationship between AF and the risk of ischemic stroke is well established and is incorporated into management recommendations; the main challenge is to authenticate the presence of AF.

This study showed that atrial fibrillation is relatively rare in cryptogenic infarcts in Marrakesh, its prevalence is most likely underestimated, indeed, it must be admitted that detection rates are not satisfactory with current traditional recordings such as the 24-hour ECG Holter. Prolonged monitoring is likely to maximize the detection of paroxysmal AF episodes, regardless of the tool used.

With the development of implantable devices and new digital diagnostic tools, a significant improvement in the detection of paroxysmal AF is emerging.

The optimal strategy for AF detection and the precise duration of monitoring are still not defined, and expected recommendations will depend on cost-effectiveness, patient acceptance and adherence, legal considerations, and demonstration of higher stroke risk reduction by a specific approach.

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