

Automatic Cardiac Event Recorders Reveal Paroxysmal Atrial Fibrillation after Unexplained Strokes or Transient Ischemic Attacks

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Background: The etiology of stroke or transitory ischemic attack (TIA) remains frequently unknown. While paroxysmal atrial fibrillation (PAF) is often suspected, its presence remains difficult to establish. Therefore, we investigated the occurrence of PAF episodes in such a population using a long-term automatic cardiac event recorder.

Methods: We prospectively investigated 60 consecutive subjects admitted in our university hospital for stroke (n = 44) or TIA (n = 16), adding long-term automatic cardiac event recorders, with a target duration of 4 days, to standard investigations, which included 12-lead ECGs and 24-hour Holter recordings.

Results: In 28 patients no etiology was found for their stroke or TIA. However, one or more than one PAF episode was found in 4 of them (14.3%) using the long-term automatic event recorder. In the 32 remaining patients, 8 presented with PAF, and this was considered as the cause of their stroke. In both groups, AF was paroxysmal. The PAF episodes' duration went from 1 to 96 hours (mean \pm standard deviation, 18 hours and 30 minutes \pm 30 hours).

Conclusions: Patients suffering PAF episodes after ischemic stroke or TIA were statistically less often recognized using the 24-hour Holter ECG recording alone than the R-Test Evolution alone.

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ischemic stroke; transitory ischemic attack; atrial fibrillation; paroxysmal ambulatory ECG monitoring

The global burden of an ischemic stroke is rapidly increasing, with more than 1,500,000 new cases each year in developed countries.¹ It is the second largest cause of mortality, and is responsible for almost as many deaths (70%) as ischemic heart disease.²

Atrial fibrillation (AF) is shown to be a major determinant of ischemic stroke.³⁻¹⁶ In the presence of AF, the odds ratio for an ischemic stroke reaches 5.6^{13,17,18} while the Framingham study revealed that 14.7% of all strokes were directly linked to AF; that percentage increases with advancing age, from 6.7% at age 50 to 36.2% at age 89.^{14,17,19-23}

The relative risk of stroke in the presence of AF is as high as 5.6.²² Furthermore, after the occurrence of stroke, the presence of AF increases short-term, as well as long-term, mortality.^{4,5,24,25} More importantly, the type of AF, permanent or intermittent, does not modify the risk of stroke.¹⁰ However, that risk could be increased by prolonged episodes of paroxysmal AF.

In this context, the detection of AF is an important step for the etiological diagnosis, as well as prognosis, of ischemic stroke. That detection is usually performed by recording a full 24-hour period, using an ambulatory Holter ECG. Some studies,

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however, have underlined the shortness of the 24-hour period, when looking for paroxysmal cardiac arrhythmias.²⁶ Cardiac event recorders have broken the 24-hour barrier for symptomatic arrhythmias^{27,28} and the introduction of added automaticity has also allowed the test for asymptomatic cardiac arrhythmias,²⁹ which are at least as frequent as symptomatic ones.²⁷⁻²⁹

We used one such long-term automatic event recorder, R-Test Evolution (R-TE), in a population suffering of ischemic stroke, to detect the presence, duration, and density of AF episodes that would not have been detected using conventional evaluations, including a 24-hour Holter ECG.

MATERIAL AND METHODS

The study group consisted in 60 consecutive patients, of whom 33 (55%) were male. They were aged 64 ± 14 years old (range 27-89 years), and had been admitted to our university hospital from January to December 1998 either because of a durable ($n = 44$) or because of a transient ischemic attack (TIA) ($n = 16$).

TIA was defined as an acute loss of ocular or focal cerebral function, lasting less than 24 hours; any other transitory neurological pathology, such as metabolic abnormality, epilepsy or migraine, was excluded. Stroke was defined as a durable (>24 hours) ocular or neurological deficit and was clinically assessed and cerebral damage was systematically documented through brain imaging.

All patients underwent physical and neurological examinations. Systematic work-up included head computerized tomographic scan to assess and localize the ischemic cerebral damage, 12-lead ECG performed in the emergency room and again upon admission to the neurology department, chest radiography, 24-hour Holter ECG recording, carotid ultrasound, transthoracic echocardiography supplemented by a transesophageal echocardiography in 21 cases, and routine blood tests that included complete blood cell count, fasting glucose, cholesterol levels, and serologic status for syphilis. Additional investigations were sometimes necessary to confirm the vascular origin of the stroke. Thus, MRI of the head was performed in 40 cases, MRI angiography in 32 cases, and conventional angiography in 11 cases. MRI of the head consisted in conventional sagittal and transverse T1- and T2-weighted images, with 5-mm-thick slices.

In 28 cases, no obvious explanation as assessed was found in spite of a clinical suspicion of embolic events. All cases ($n = 60$), underwent automatic event recording by means of the R-TE (Novacor, Rueil-Malmaison, France), beginning 10 ± 2 days after the occurrence of stroke or TIA, and during a mean period of 70.1 ± 30.9 hours, to search for infrequent arrhythmias. The R-TE combines, in a small box weighing 42 grams, analysis and storage of electrocardiographic events, with an autonomy of up to 7 days. Arrhythmia detection is based on automatic continuous analysis. The arrhythmic events are recorded in a solid-state memory, and each time an event is encountered, an individualized counter is incremented. The patient-triggered ability was not used in the study. The R-TE is programmed to recognize 10 categories of arrhythmic events. A heart rate trend covering the whole recording period is memorized as well. The event recorder was connected to the patient using two electrodes, one on the sternum, and the second at the apex position, which gives a lead close to a CM5 configuration.

Only sustained (≥ 30 seconds) episodes of paroxysmal Atrial Fibrillation were considered for this analysis. PAF was defined as fine oscillations in the baseline ECG (fibrillatory waves), associated with an irregular ventricular response ratio and lasting at least 30 seconds. The 30-second limit was based on the fact that this duration is generally admitted at the ventricular level as a criterion for sustained events. For an event of any length, sinus rhythm was considered restored after five consecutive sinus beats had been observed.

Statistical analysis compared the percentage of PAF recognition by either a 24-hour Holter ECG or the R-TE using a contingency table. A P value of less than 0.05 was considered as statistically significant.

RESULTS

Patients

In 32 patients, the etiology was identified as follows: intracranial atherosclerotic vascular disease (4 cases); extracranial supraaortic atherosclerotic vascular disease (9 cases); hypercoagulable states (4 cases); vascular encephalopathy or lacunar infarction related to hypertension (4 cases); non-rheumatic atrial fibrillation (6 cases); cardiac embolism from an origin other than atrial fibrillation

Table 1. Epidemiological Characteristics and Risk Factors of the Two Groups of Patients

	Established Etiology of Stroke N = 32	Negative Work-Up of Stroke N = 28
Male (%)	17 (52)	16 (57)
Mean age ± SD (y)r	64.7±13.4	64.0±16.3
TIA/stroke	7/25	9/19
Diabetes (%)	7 (21.9)	3 (10.7)
Hypertension (%)	17 (53.1)	13 (46.4)
Dyslipidemia (%)	20 (62.5)	10 (35.7)
Tabagism (%)	13 (40.6)	9 (32.1)
Family history of CV disease (%)	19 (59.4)	15 (53.6)
Aspirin therapy (%)	7 (21.9)	5 (18.5)

(4 cases); and arterial dissection due to fibromuscular dysplasia (1 case). Among the 32 patients with an established etiology, 25 had a final diagnosis of durable stroke or TIA.

Among the 28 patients with a negative work-up, 19 had a final diagnosis of durable stroke and 9 of TIA. The epidemiological data and the risk factors of these two groups of patients are listed in Table 1.

Detection of Atrial Fibrillation

Among the 60 consecutive patients, 12 (20%) of them demonstrated atrial fibrillation. The mean ±SD duration of PAF episodes was 18 hours and 30

minutes ± 30 hours (range: 10 minutes–96 hours) (Fig. 1).

For the 32 patients with an established etiology, 8 of them presented with AF as diagnosed by standard investigations, namely either the 12-lead electrocardiogram recorded in the emergency room or in the neurology department, or the 24-hour Holter recording (Table 2); among these 8 patients, the R-TE, was positive in 5 but remained negative in 3 of them.

For the 28 patients without an established etiology after their strokes, the R-TE revealed the presence of PAF in 4 (14.3%) of them (Table 2), during the whole recording in 2 cases, and as repeated episodes, of 30 minutes to 14 hours 30 minutes

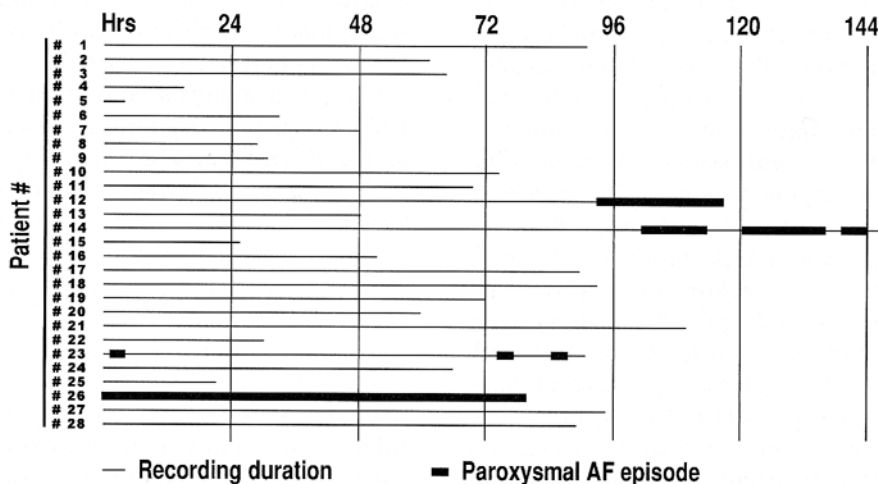


Figure 1. Episodes of paroxysmal atrial fibrillation (thick lines) are represented along the recording (thin lines) for each of the 28 patients having negative investigations after ischemic stroke or transient ischemic attack. One episode is permanent (patient 26) while the others are paroxysmal (patients 12, 14, and 23).

Table 2. Presence (AF) or Absence (–) of Episodes of PAF According to the Test Used

Age (Yrs)	12-lead Electrocardiogram		24-hour Holter	R-TE	R-TE Duration (Hours)	R-TE Characteristics of PAF Episodes
	Emergency Room	Neurology Unit				
Patients with negative etiological investigations (4 of 28 patients)						
12	77	–	–	AF	69	1 episode, 24 hours
23	87	–	–	AF	162	3 episodes, 30 minutes each
14	78	–	–	AF	93	3 episodes, 4 hours and 30 minutes to 14 hours and 30 minutes
26	85	–	–	AF	90	Permanent
Patients with positive etiological investigations (8 of 32 patients)						
30	68	–	AF	–	95	–
34	62	–	AF	AF	96	Permanent
42	89	–	AF	–	71	–
49	66	–	AF	AF	69	Multiple episodes, 15 to 120 minutes
51	83	–	AF	AF	94	Permanent
56	73	AF	–	–	24	–
57	75	–	AF	AF	81	Multiple episodes, 10 minutes each
58	70	–	AF	AF	93	Multiple episodes, 10 minutes each

duration, for the 2 remaining cases. Only 1 of the 4 patients had symptoms during the recording that could be related to arrhythmia, the three others being totally symptom-free. In 2 patients, AF was revealed only on the fifth day.

The patients suffering PAF episodes were statistically less often recognized ($P = 0.045$) using the 24-hour Holter ECG recording alone (6/12) than the R-TE alone (9/12).

DISCUSSION

Our study revealed that among the 28 patients who suffered a recent ischemic stroke without etiological explanation after standard work-up investigations, prolonged R-TE automatic recording revealed PAF in 4 (14.3%) of them.

However, the study presented here does not fully ascertain the link between the AF episodes and stroke. It underlines only that approximately 33% of AF episodes are missed in spite of thorough classical ECG and Holter investigations. More importantly, 15% of patients with negative investigations after ischemic stroke or TIA present PAF episodes revealed by prolonged monitoring.

Intermittent AF episodes are thought of as threatening as permanent ones.¹⁰ It is very important to detect them. As a matter of fact, hemodynamic studies reveal a prolonged left ventricular dysfunction after an AF episode.³⁰ Prolonged low cardiac output, particularly marked in some subjects, was

confirmed using Doppler echocardiography and was associated with a very high risk of thromboembolic events.³¹ A significant point lies in the fact that, compared to the results of usual ECG investigations, none of our patients presented a true *chronic AF* as a period of sinus rhythm was always observed in at least one type of recording. However, the interpretation of 24-hour Holter ECG recordings or of the R-TE could have concluded a *chronic AF* in 1 and 4 cases, respectively. From these data, the length of ECG monitoring should be prolonged to improve the identification of sustained supraventricular arrhythmias. In our setting, the cost of prolonged duration monitoring using the R-TE equals that of a standard 24-hour ECG monitoring. Thus, considering the yield of such recordings, this diagnostic strategy appears more cost-effective, saving 50% of the time spent on standard 24-hour ECG monitoring interpretation. These arguments have made R-TE a systematic screening test in unexplained ischemic stroke and is now routinely used in our hospital.

The only case where AF was recognized in the emergency room may be interpreted as a consequence of an extended right hemispheric damage instead of the etiology of the stroke. As a matter of fact, the occurrence of such transient arrhythmias in the acute phase of stroke has been related by some authors as a complication of stroke. From our experience, ECG monitoring should probably be more pertinent to an independent atrial electrical

instability if delayed 10 days after the initial cerebral accident.

When exploring unexplained palpitations, a two-week recording duration has been suggested using patient-triggered event recorder.²⁷ Thus, event recorders should represent a better choice. However, most of AF episodes being asymptomatic, those concerning 3 of the 4 cases are disclosed by R-TE only. An automatic event recorder is able, in such a case, to address both the necessary recording length and the required detection automaticity, with high feasibility. Even so, the appropriate length of recording to ensure an efficient AF detection remains difficult to establish. Atrial fibrillation episodes recorded in this study are remarkably long, with a mean duration of 18 hours and 30 minutes, which should help the detection process. As a matter of fact, the episodes can be scattered, as 3 of the patients' group have demonstrated that AF on the classical ECG investigation did not show the recurrence of this supraventricular arrhythmia on the R-TE recording, in spite of the recording duration of up to 96 hours.

CONCLUSION

Better knowledge of the relationship between AF and ischemic stroke would clearly need a larger prospective cohort study. This would allow the establishment of the relevance of preventive measures. However, considering the ease of use, the high acceptability rate of automatic event recorders, the already important number of new PAF cases disclosed in our study, R-TE monitoring should be systematically proposed in order to look for spontaneous PAF episodes in patients with unexplained ischemic stroke or TIA.

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