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ORIGINAL COMMUNICATION

Diagnostic yield of external loop recording in patients with acute ischemic stroke or TIA

Gerben J. J. Plas · Jorieke Bos · Bob Oude Velthuis · Marcoen F. Scholten · Heleen M. den Hertog · Paul J. A. M. Brouwers

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Abstract Atrial fibrillation (AF) is a strong risk factor for first-ever stroke and stroke recurrence. The detection rate is low and detection is often costly and time-consuming. We evaluated the diagnostic yield of an external loop recorder (ELR) in patients with acute ischemic stroke or TIA, and assessed factors that are associated with AF detection. We prospectively studied patients admitted to the stroke unit with ischemic stroke or TIA, without a history of AF, and no AF on routine-ECG and 24-h telemetry. Patients received an ELR for another 24-h registration. Rhythm registration with an ELR was performed in 94 patients. AF was identified in 5 patients (5 %). AF was associated with cryptogenic stroke and cortical or subcortical involvement. If ELR was limited to patients with cryptogenic stroke in combination with cortical or subcortical involvement, the detection rate increased to 17 %. Automated recording with ELR was easy to use in the acute setting of ischemic stroke or TIA and seems promising to detect AF or atrial flutter, in particular in patients with cryptogenic stroke in combination with cortical or subcortical symptoms.

Keywords Ischemic stroke · Transient ischemic attack · Atrial fibrillation · External loop recording · Rhythm observation · Detection rate

G. J. J. Plas (✉) · H. M. den Hertog · P. J. A. M. Brouwers
Department of Neurology, Medisch Spectrum Twente, Haaksbergerstraat 55, 7513 ER Enschede, The Netherlands
e-mail: g.plas@mst.nl

J. Bos · B. O. Velthuis · M. F. Scholten
Department of Cardiology, Medisch Spectrum Twente, Enschede, The Netherlands

Introduction

Persistent or intermittent atrial fibrillation (AF) is a strong risk factor for first-ever stroke and stroke recurrence [1–4]. Ischemic stroke in patients with AF is associated with unfavorable functional outcome and increased case fatality [1, 4–6]. Oral anticoagulation therapy with vitamin K antagonists or novel oral anticoagulants is very effective to prevent ischemic stroke in these patients [1, 3, 6].

Current stroke guidelines recommend at least 24 h of electrocardiographic (ECG) monitoring besides a routine 12-channel ECG on admission [3]. However, since AF is often transient in nature, diagnosis may be missed with this approach. Detection rates in previous studies are low, ranging from 2 to 13.5 % [5, 7–11]. Some AF episodes are probably missed due to insufficient trained nurses, the absence of automated detection algorithms, or short duration of ECG registration. Previous studies suggest that AF detection might be improved by early and prolonged monitoring. In addition to routine ECG on admission and 24-h ECG monitoring at the stroke unit, Holter registration during 24–48 h is the most commonly used method to detect AF. However, there is considerable controversy regarding the use of routine Holter registration, because of its low detection rates and cost-effectiveness. The external loop recorder (ELR) is a small device with two leads that are attached to electrodes on the chest. It can be worn for several weeks. This non-invasive way of monitoring may have a higher detection yield, is less time-consuming, less expensive, and allows longer cardiac rhythm monitoring compared to Holter registration. Therefore, it might be a good alternative [2, 8, 10, 12–20].

Two studies assessed the diagnostic yield of ELR in the non-acute setting of stroke, and found detection rates

ranging from 5 to 14 % dependent on the registration time [12, 18].

In this study, we evaluated the diagnostic yield of a 24-h automated ELR for detection of AF in consecutive patients with acute ischemic stroke or TIA, without a history of AF, and in the absence of AF on routine-ECG and 24-h ECG monitoring. In addition, we identified factors that are associated with AF detection to improve the diagnostic yield.

Methods

We prospectively studied consecutive patients with presumed diagnosis of ischemic stroke or TIA, who were admitted to our stroke unit between July and October 2011. Ischemic stroke was defined as focal neurological deficit of presumed vascular origin, lasting 24 h or more, with acute brain imaging showing typical signs of recent brain infarction or no abnormalities in this early stage. TIA was defined as a focal neurologic deficit of sudden onset lasting less than 24 h, with or without signs of recent infarction on acute brain imaging. Patients with a pacemaker, with a history of AF, and with AF detected on admission ECG or during standard 24-h ECG monitoring at the stroke unit were excluded.

The study was in line with the procedures of our local Medical Ethics Committee. All patients or their legal representatives gave their written informed consent.

We recorded data on vascular history, risk factors, and event characteristics. All patients underwent a standard workup, including X-thorax, routine laboratory assessments, brain CT or MRI, and imaging of the carotid arteries by Doppler ultrasonography, CT-angiography or MR angiography. Stroke severity was assessed with the NIH Stroke Scale and the cause of the stroke was classified according to the Trial of ORG 10172 in Acute Stroke Therapy (TOAST) classification [21]. Ischemic stroke and TIA were subdivided in cortical, subcortical and lacunar stroke based on the combination of clinical and imaging findings. The difference between subcortical and lacunar stroke on imaging was made by diameter of the infarction (<1.5 cm lacunar). At the emergency room, all patients had an ECG and were asked for palpitations. Palpitations were defined as the awareness of increased heart rate at rest, not directly after exercise or during emotional stress. At the stroke unit, all patients were monitored with ECG for 24 h. If telemetry identified no AF, patients received an ELR for another 24 h of registration (3100 BT, Vita systems GmbH, Chemnitz, Germany). The ELR had an automated AF detection algorithm; the R–R interval pattern was analyzed for irregularity within the last 14 R–R intervals. An episode was classified as AF by the ELR if 6 out of 14 intervals matched $RRx - RRy > RRx/8$ and $RRx - RRy < 2 \times RRx$. We adjusted the tachycardia setting to 140 beats per minute to allow flutter detection with a 1:1 or 2:1 conduction. The length of the ECG recording was set 30 s before and 60 s after the event. AF was defined as a sequence of at least 30 s irregular R–R intervals and the presence of fibrillation P waves [22]. Atrial flutter was defined by clear flutter waves with regular or irregular ventricular rate lasting at least 30 s [22]. All recordings were independently analyzed by two residents in cardiology. If consensus could not be reached a cardiologist with expertise in electrophysiology was consulted.

All statistics were calculated with SPSS 17.0 (Statistical Package for the Social Sciences, Version 17, SPSS, Chicago, IL). Categorical variables were compared with a Chi-square test and continuous variables were compared with a two-tailed *T* test. A significance level of 0.05 was used.

Results

Between July and October 2011, 153 patients with presumed diagnosis of ischemic stroke or TIA were admitted to our stroke unit. Twenty-five patients were excluded from ELR because of a medical history of AF or atrial flutter ($n = 20$), or the detection of AF or atrial flutter on the admission ECG or during standard telemetry ($n = 5$). ELR was performed in 128 patients. Another 34 patients were subsequently excluded from further analysis since the final diagnosis was a stroke mimic ($n = 33$), or the ELR registration was incomplete ($n = 1$) (Fig. 1). The remaining 94 patients were studied and patient characteristics are shown in Table 1. ELR was easy to use and adverse events in association with ELR were not reported.

Mean age was 69 ± 11 years and 50 patients (53 %) were male. Of the 94 patients, 79 (84 %) had ischemic stroke and 15 (%) patients had a TIA. According to the TOAST classification, without knowledge of the ELR results, 40 (43 %) patients had stroke with an unknown etiology despite complete workup (cryptogenic stroke), 23 (25 %) patients had small vessel disease, 9 (10 %) patients had a cardio-embolic cause, 10 (11 %) patients had large vessel disease, and 10 (11 %) patients had an incomplete workup. Thirty-two patients (34 %) had a cortical infarction or TIA, 17 (18 %) had a subcortical infarction or TIA, and 45 (48 %) patients had a lacunar infarction or TIA. Median time between ELR and stroke onset or hospital admission was 43 h (IQR 24–71 h) and 31 h (IQR 16–38 h), respectively.

The 24-h automated ELR revealed paroxysmal AF in 4 patients (4 %) and paroxysmal atrial flutter in 1 patient (1 %). These 5 patients were initially classified as cryptogenic stroke. Specific characteristics of these 5 patients are presented in Table 2.

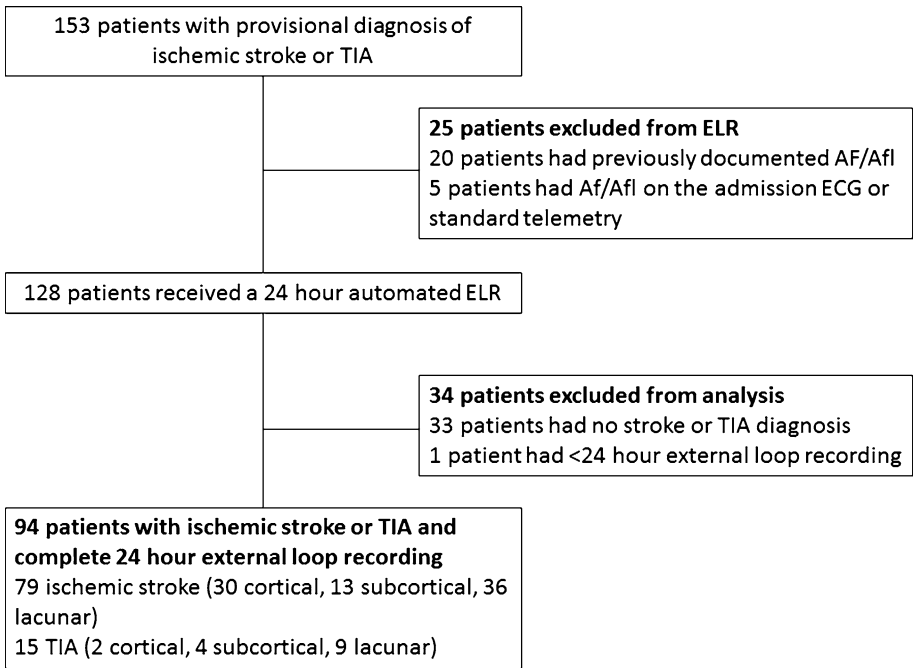

Fig. 1 Flowchart inclusion

Patients with newly diagnosed paroxysmal AF of atrial flutter during ELR were more often women, were older, had more cortical involvement, and more often had palpitations, than patients without paroxysmal AF or atrial flutter.

If automated rhythm observation had been limited to patients with cryptogenic stroke, the yield to detect paroxysmal AF would have been 13 % (5 of 40 patients), and if ELR had been limited to patients with a cryptogenic stroke in combination with cortical or subcortical symptoms, the yield of ELR improved to 17 % (5 of 29 patients).

Discussion

In this prospective study with unselected patients with acute ischemic stroke or TIA, 24-h automated rhythm observation with an ELR revealed paroxysmal AF and atrial flutter in 5 % beyond routine ECG and 24-h ECG telemetry. We found that if ELR was limited to patients with cryptogenic stroke in combination with cortical or subcortical symptoms, the diagnostic yield of ELR to detect patients with paroxysmal AF improves to 17 %.

Six previous studies have evaluated ELR to detect AF after ischemic stroke or TIA beyond routine ECG and 24-h ECG telemetry in unselected patients, but comparison of their findings with ours is hampered by different study designs (Table 3). Nevertheless, the findings in these studies are in line with our results. In a study with 60 consecutive patients with ischemic stroke, 28 of them had stroke or TIA of unknown etiology after standard stroke workup and Holter monitoring. Event recorders detected AF in 14 % of these 28 patients after 24–162 h of registration [12]. In a retrospective study, 56 patients with cryptogenic stroke or TIA were studied with a Mobile Cardiac Outpatient Telemetry device. AF was found in 23 % after 21 days of monitoring [23]. In two other retrospective studies with 20 and 256 patients with cryptogenic stroke or TIA, a thirty-day cardiac event monitor detected AF in 20 and 17 %, respectively [14, 24]. In a randomized study among 572 patients with a recent cryptogenic stroke or TIA who were 55 years of age or older, atrial fibrillation lasting 30 s or longer was detected in 16 % of patients with a 30-day event-triggered recorder compared to 3 % with 24-h Holter registration [15]. All patients underwent standard 24-h ECG monitoring before randomization. Finally, only one study assessed the diagnostic yield of an event recorder in the acute phase of TIA or ischemic stroke. In 149 patients with normal baseline ECG and 24-h Holter monitoring, AF was detected in 5.7 % within 7 days of monitoring [18].

In line with previous studies, patients detected with AF were older and more often women [25]. Furthermore, AF was more frequently associated with cortical involvement and not with lacunar infarcts [26, 27]. In our study, palpitations were more frequently reported in newly diagnosed AF patients than in patients without AF. Although palpitations are associated with a high risk of future AF [28], it has not shown to be a very specific predictor of cardiac arrhythmia [29].

Table 1 Characteristics between groups with and without AF detection on ELR

Patient characteristics	Without paroxysmal AF ($n = 89$)	With paroxysmal AF ($n = 5$)	P
Age, mean (SD)	68.6 (11.3)	74.6 (3.8)	0.020
Male, *n* (%)	50 (56 %)	0 (0 %)	0.020
Hypertension, *n* (%)	54 (61 %)	4 (80 %)	0.646
Hyperlipidemia, *n* (%)	74 (83 %)	5 (100 %)	1.000
Diabetes Mellitus, *n* (%)	20 (23 %)	2 (40 %)	0.333
Smoking, *n* (%)	27 (30 %)	1 (20 %)	1.000
Coronary heart disease, *n* (%)	11 (12 %)	1 (20 %)	0.503
Previous stroke, *n* (%)	8 (9 %)	1 (20 %)	0.402
Previous TIA, *n* (%)	10 (11 %)	0 (0 %)	1.000
Previous peripheral artery disease, *n* (%)	7 (8 %)	2 (20 %)	0.70
Body mass index >30, *n* (%)	24 (27 %)	0 (0 %)	0.324
Positive family history, *n* (%)	21 (22 %)[a]	2 (20 %)	0.594
Palpitations, *n* (%)	13 (15 %)[b]	3 (60 %)[a]	0.022
Cortical involvement, *n* (%)	28 (32 %)	4 (80 %)	0.044
Subcortical involvement, *n* (%)	15 (17 %)	1 (20 %)	1.000
TOAST			
Large-artery atherosclerosis	10 (11 %)	0 (0 %)	1.000
Cardioembolism	9 (10 %)	0 (0 %)	1.000
Small vessel-occlusion	23 (26 %)	0 (0 %)	1.000
Stroke of other determined etiology	4 (5 %)	0 (0 %)	1.000
Stroke of undetermined etiology	35 (39 %)	5 (100 %)	0.012
More than one etiology	2 (2 %)	0 (0 %)	1.000
Incomplete workup	6 (7 %)	0 (0 %)	1.000

[a] 1 missing value

[b] 11 missing values

Table 2 Characteristics of patients with paroxysmal atrial fibrillation or atrial flutter during automated recording

Patient	1	2	3	4	5
Age	70	73	73	79	78
Sex	Female	Female	Female	Female	Female
Ischemic stroke/TIA	Subcortical	Cortical	Cortical TIA	Cortical	Cortical TIA
Cardiac rhythm	Atrial fibrillation	Atrial fibrillation	Atrial flutter	Atrial fibrillation	Atrial fibrillation
Event recording	1	2	1	3	8
Body mass index	25–30	25–30	<25	<25	<25
Hypertension	Yes	Yes	No	Yes	Yes
Diabetes mellitus	No	No	No	Yes	Yes
Previous stroke/myocard infarct	No	No	No	MI	Stroke
Peripheral arterial disease	No	No	Yes	No	Yes
Congestive heart failure	No	No	No	Yes	No
Palpitations	Yes	Yes	No	Unknown[a]	Yes
CHADS2VA2SC	5	5	4	8	7

[a] Unknown due to aphasia

Strong points of our study are the unselected population of ischemic stroke and TIA patients and detailed clinical data. Some methodological issues have to be discussed. Generalizability of this study is limited by the relatively small sample size reflected by wide confidence intervals, and its single center study design. This limitation is

Table 3 Characteristics and results of previous comparable studies

Reference	Stroke population	ELR duration	Total number of patients	Percentage of atrial fibrillation found with ELR registration, %
Sposato et al. [5]	Unselected patients	5 days	155	13.5
Rizos et al. [9]	Unselected patients	64 h	496	5.4
Barthelemy et al. [12]	Unselected patients	70 ± 30 h	28	14.3
Higgins [17]	Unselected patients	14 days	50	18
Jabaudon et al. [18]	Unselected patients	7 days	88	5.7
Elijovich et al. [14]	Cryptogenic stroke	30 days	20	20
Gladstone et al. [15]	Cryptogenic stroke	30 days	280	16.1
Tayal et al. [23]	Cryptogenic stroke	21 days	56	23
Miller et al. [24]	Cryptogenic stroke	30 days	156	17.3

minimized by the fact that our stroke unit is an accredited and quality-controlled stroke unit and thereby representative for most stroke units in the Netherlands. Secondly, the duration of the ELR registration in this study was short, and prolonged registration would have probably increased the detection rate of AF [12, 17]. Thirdly, of the 80 patients with ischemic stroke, 74 (82 %) had a recent cortical, subcortical or lacunar infarction on a second brain CT or MRI. In the other 20 patients, type of ischemic stroke or TIA was based on clinical symptoms and results from the stroke workup without secondary imaging, and therefore some might have been misclassified.

Furthermore, we documented episodes of accelerated atrial activity lasting less than 30 s in 12 patients. It is unknown whether these brief bursts are as potent a risk factor for stroke compared to more prolonged episodes, or whether the benefits of anticoagulation can be extrapolated to these patients. More likely, they could be markers of periods of AF occurring outside the recording period or indicative for future AF. At this moment, it is not clearly established what duration or frequency of paroxysmal atrial fibrillation should be treated with oral anticoagulation therapy. Current guidelines advise to start anticoagulation in atrial fibrillation lasting 30 s or longer [22, 30–32]. The expert opinions vary, but in our opinion these guidelines should be followed until future studies have established more evidence.

Adequate signal processing and event triggering largely depend on the quality of the algorithm. Our device utilizes a non-disclosed algorithm based on R–R interval dynamics to distinguish between AF and other rhythms. R–R interval dynamics make the algorithm vulnerable for supraventricular or ventricular extrasystoles and sinus arrhythmias or SA blocks. Furthermore, the ELR memory does not store the whole episode of paroxysmal AF. In our hands, ELR was easy to use and no adverse events were observed.

The 5 % detection rate of AF in this study is comparable with the diagnostic yield of routine 24-h Holter found in previous studies [33], which is the most commonly used method for the detection of AF nowadays.

Prolonged duration of monitoring may increase rates of detection of AF. The detection rate of newly diagnosed AF with ELR varies between 5 and 18 % dependent on registration duration ranging from 64 h to 30 days [9, 12, 17, 18]. In Holter ECG for up to 7 days, AF was detected in 13 % of patients with stroke [20]. However, prolonged Holter registration is time-consuming and uncomfortable for patients. Moreover, Holter registration in comparison to ELR is more expensive in search for diagnosis in patients with palpitations [34]. But there are no studies that compare cost-effectiveness between these two systems to identify atrial fibrillation in stroke patients. We did not compare directly between Holter monitoring and ELR, therefore we cannot conclude that one method is superior to the other. Implantable loop recorders allow continuous cardiac monitoring for up to 3 years. Two recent studies showed that the diagnostic yield was 10–26 % in patients with cryptogenic stroke when patients were monitored for at least 50 days [35, 36]. Disadvantages may include the need for a minor surgical procedure, the presence of under- or over-sensing that may exhaust the memory of the implantable loop recorder, and the high costs of the device. In particular, the latter suggests that this invasive way of monitoring should be left to a much selected group of patients.

In conclusion, early ELR in the acute setting of stroke or TIA seems promising to detect AF or atrial flutter and is of additional value to routine ECG on admission and 24-h ECG at the stroke unit. If the registration is limited to patients with cryptogenic stroke or TIA in combination with subcortical or cortical symptoms, the diagnostic yield of ELR to detect patients with paroxysmal AF improves to 17 %. In other words, theoretically, 29 ELR registrations instead of 94 would have been enough to diagnose the same number of patients with AF in this study. The results of our study require further validation in a larger cohort study with prolonged registration.

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical standards The authors declare that this study has been approved by the institutional ethics committees and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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