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Atrial fibrillation detected by external loop recording for seven days or two-day simultaneous Holter recording: A comparison in patients with ischemic stroke or transient ischemic attack

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Abstract Atrial fibrillation (AF) is the most common cardiac cause of ischemic stroke and transient ischemic attack (IS/TIA).

Aim: To compare the diagnostic value of seven-day external loop recording (ELR) and two-day Holter recording for detecting AF after IS/TIA.

Methods: 191 IS/TIA patients without AF history. Endpoint was AF >30 s. We started two-day Holter recording and seven-day ELR simultaneously.

Results: Seven-day ELR and two-day Holter recording detected the same three AF patients. ELR detected another six patients with AF adjudicated by cardiologists, four detections after Holter (3 vs. 7, p = 0.125) and two false-positive detections during Holter. Seven-day ELR automatically classified 50/191 patients (26%) with AF, but only 7/50 (14%) were confirmed as AF by cardiologists.

Conclusion: Seven-day ELR did not detect significantly more patients with AF than two-day Holter recording. 86% of patients with ELR-classified AF were false positives, indicating a poor performance of the automatic AF detection algorithm used.

Keywords: Atrial fibrillation; Ischemic stroke; External loop recorder; Holter monitor recorder; Transient ischemic attack; Validation

Introduction

Stroke constitutes a major global health problem and is the second leading cause of death and disability worldwide after ischemic heart disease [1]. The World Health Organization (WHO) estimates that 15 million people have a stroke each year.

Atrial fibrillation (AF) is the most common cardiac arrhythmia affecting %1–2% of the world's population and 9% of people over 80 [2]. In 2010, 33.5 million (20.9 million males and 12.6 million females) globally were estimated to have AF, characterized as a "growing epidemic" by WHO [3]. AF increases mortality in general, and it is associated with a fivefold increased risk of stroke [4].

Up to 30% of all ischemic strokes and transient ischemic attacks (TIA) are cardioembolic [5], with AF counting for at least half of these instances. Strokes related to AF have increased rates of mortality, a higher degree of disability and longer periods of hospitalization compared to other types of strokes [6]. A challenge with AF is that about half of the cases are paroxysmal (PAF) and it is often asymptomatic and undiagnosed, and yet it still increases stroke risk [7]. When AF is detected, anticoagulation therapy reduces thromboembolic risk by two-thirds and lowers mortality significantly [8]. Usually, stroke/TIA patients receive platelet inhibitors as part of standard stroke treatment. Anticoagulation therapy reduces recurrent stroke risk from 10% to less than 4% per year compared to aspirin only [9], and it reduces mortality and stroke severity if stroke does occur [10]. However, anticoagulation therapy is associated with a risk of intracranial bleeding, especially in patients with previous stroke and TIA [11]. AF detection therefore needs to be reliable.

The best method for detecting AF in stroke/TIA patients is yet to be determined.

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External loop recorders (ELRs) are new devices that promise non-invasive, automatic AF detection, up to 32-day recording time and high patient comfort. In comparison, Holter recording has been used for decades, and it is often referred to as the gold standard in arrhythmia detection.

The aim of this study is to compare the diagnostic value of seven-day ELR recording and two-day Holter recording with regard to the detection of AF in consecutive patients with ischemic stroke/TIA and no previously diagnosed AF.

Methods

The research design is a prospective observational study. We recruited consecutive patients who had presented with ischemic stroke or TIA within the previous week from the Department of Neurology in Regional Hospital West Jutland in Denmark during April 2014 to January 2015.

Inclusion criteria were stroke/TIA within one week, age ≥ 60 years, no AF on admission 12-lead ECG and no history of AF according to ICD-10 codes from hospitalizations or outpatient clinical visits and thorough review of medical records, no pacemaker, no active cancer or expected low compliance, no previous participation in the study and written informed consent. TIA was defined as stroke-like symptoms lasting shorter than 24 h. Neurologists validated the diagnosis of stroke or TIA, and cerebral imaging (CT or MRI) was obtained for all patients.

Each patient's blood pressure was measured in the supine position at rest, and a nurse entered baseline data onto a datasheet.

We started Holter recording and ELR recording simultaneously. After 48 h, the Holter recorder was removed while the ELR recording was continued for an additional five days.

AF was defined according to the guidelines, i.e. an atrial arrhythmia with irregular intervals between R waves, without detectable normal P waves and lasting more than 30 s [12].

For Holter recording, we used a Life Card CF digital Holter recorder from Spacelabs Healthcare Diagnostic Cardiology (Washington, United States). Specially trained nurses analyzed the 48-h Holter recordings blinded to the results of the ELR monitoring. A cardiologist, also blinded to the ELR monitoring results, examined and approved all Holter recordings with suspected arrhythmia. The Holter recording results were used for both daily clinical purposes and for comparison with ELR monitoring.

The R.Test Evolution 4® (NorDiaTech, Paris, France) was used for ELR monitoring. ELR AF-detecting software was tested in prior studies [13,14] using the previous generation R.Test Evolution 3®. We adjusted the devices according to the manufacturer's recommendations. This type of ELR is non-invasive and uses a loop recording system that continuously monitors and automatically analyzes the heart rhythm through two electrodes attached respectively at the cardiac apex and the sternum. In case of an arrhythmic event, the device automatically triggers and records. The ELR saves arrhythmia recordings in its 60 min total memory capacity, eventually overwriting older tracings but keeping the most characteristic episodes if the memory capacity is exceeded. The device defines the most characteristic AF episodes as the fastest, based on maximum heart rate during an event. In this study, we adjusted the device to save one-minute recordings per AF episode, thereby allowing up to 54 AF recordings per patient, while 6 min' recording time was left to detect pauses in the heart rhythm and other tachyarrhythmia. The ELR algorithm analyzes the length of RR intervals as well as the temporal stability between regular and irregular periods. The ELR analyzes 64 consecutive RR intervals at a time and categorizes the rhythm as AF when approximately two-thirds of the 64 RR intervals are irregular, which, depending on the heart rate, correspond to approximately 25 s. Thereby, the ELR automatically is able to categorize AF episodes of approximately 30 s in duration and longer.

Three members of the research group assessed all episodes automatically classified by ELR as AF. All analyses of the ELR recording results were blinded to the evaluators of the Holter recording results.

Statistics

Based on prior studies [15,16], we assumed two-day Holter recording to detect AF in approximately 3% and seven-day ELR in 9% of patients. We assumed that two-day Holter recording would detect AF in 0.5% of the cases not caught by seven-day ELR monitoring, and that seven-day ELR monitoring would detect AF in 6.5% of cases not caught by the two-day Holter recording. As a result the two methods would disagree on the outcome of AF or no AF in 7% of the study participants. Based on these assumptions, the minimum sample size was calculated at 142 patients, with a power of 84% to conclude with a type-1 error of 0.05 that seven-day ELR detects AF in more patients compared to two-day Holter recording.

Baseline and follow-up data were presented as absolute numbers (percentages) and as means (SD) if normally distributed; otherwise as median (interquartile ranges (IQR)).

As the patients wore both recording devices at the same time and recordings were started simultaneously, data were analyzed as paired data, with the detection or categorization of AF-episodes as the binary outcome. The hypothesis of no difference in the number of positive AF findings between the two devices was tested with an exact McNemar's test.

All statistical analyses were done using STATA from StataCorp LP (Texas, United States).

Ethics

The Central Denmark Region Committees on Health Research Ethics (approval number 35620) and the Danish Data Protection Agency (case number 1-16-02-351-14) gave study permissions. The study was registered in ClinicalTrials.gov (NCT02155907).

Results

We consecutively included 191 patients in the study, 118 (62%) with ischemic stroke and 73 (38%) with TIA. Mean (SD) age was 71.1 (7.6) years and 109 (57%) were males. Table 1 presents baseline data. Total recording time for the ELR monitoring was 145 (47) h, range (0.2–356) with a