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Prevalence of unknown atrial fibrillation in patients with risk factors

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Aims Atrial fibrillation (AF) is the most common cardiac arrhythmia. 'Silent', undiagnosed AF is often only detected with the first complication, e.g. a stroke. Detection of 'silent' AF prior to the first cerebrovascular event would be valuable to institute adequate therapy and prevent complications related to AF. We performed a simple electrocardiography (ECG) screening for silent AF in patients at risk for AF.

Methods and results One hundred and thirty-two adult patients (76 male; age: 64 ± 14, mean ± SD) without known AF presenting to the diabetes, hypertension, and dyslipidaemia clinics (76 outpatients in the different clinics), or to the stroke unit (56 stroke survivors) at the University Hospital Muenster were screened for unknown AF using a simple patient-operated, single-channel ECG recorder (Omron hcg-801-e, Germany). Silent AF was found in 7/132 patients (5.3%; four stroke survivors, two diabetics, one patient with hypertension, median CHADS2 score: 2 (25–75 quartiles 1–3). The prevalence of AF was higher in patients with multiple risk factors for stroke and AF: AF was found in 3% (1/32) patient with hypertension and no other risk factors for AF, but in 7% (5/71) patients with two risk factors including stroke patients (diabetes and hypertension, stroke, or stroke and hypertension), and in 11% (1/9) with stroke, hypertension, and diabetes. Standard ECG did not detect further patients with AF.

Conclusion A simple ECG screening could help to detect 'silent' AF prior to the first cerebrovascular events, especially in patients with multiple cardiovascular conditions. Larger studies of such a screening are warranted.

Keywords Atrial fibrillation • Diagnosis • Screening • 'Silent' atrial fibrillation • Stroke prevention

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting at least 1% of the population.[1] Approximately every fourth person over 40 years will suffer from AF in his or her life.[2] Changes in the age structure of Western populations suggest that the number of affected patients will duplicate or even triplicate in the next 30 years. Atrial fibrillation often presents with no or only few symptoms and is therefore often undiagnosed. 'Silent', hitherto undiagnosed AF is often only diagnosed when severe AF-related complications such as stroke or heart failure occur. Atrial fibrillation is a major cause for ischaemic stroke, and strokes caused by AF are often more severe with a higher number of irreversible organic damages or deaths than strokes caused by other aetiologies.[3–6] Effective oral anticoagulation therapy can prevent 2/3 of strokes in AF, and several studies have shown that prolonged electrocardiography (ECG) monitoring after a stroke will increase AF detection rates.[7–10] In principle, it would be even more desirable to initiate anticoagulant therapy prior to the first cerebrovascular event, urging for timely, early diagnosis of 'silent' AF.

Standard 12-channel ECG still is the most important tool in the diagnosis of AF, but it is only available within health care settings, and professional staff for measurement and appraisal is obligate. There is good evidence, especially in large AF trials that a patient-

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What's new?

- 'Silent', hitherto undiagnosed atrial fibrillation (AF) is one of the most common causes for severe complications such as stroke or heart failure.
- While detection of 'silent' AF has been studied in several cohorts of stroke survivors, it would be preferable for the patients to detect AF prior to the first cerebrovascular event ('primary prevention').
- We used a patient-operated electrocardiography (ECG) screening system to evaluate the prevalence of AF in patients with risk factors for stroke and AF.
- We found an important prevalence of 'silent', undiagnosed AF in this population.
- This paper suggests that a simple ECG-based screening for AF could be of value in high-risk populations. Further studies in larger patient populations are warranted.

activated short-term ECG, recorded with simple ECG systems, increases the diagnostic yield of ECG monitoring in such patients.[11–13] Nevertheless, most of these ECG devices require telemetric transmission systems and a central analysis platform. A simple alternative to these systems is for example the OMRON HCG 801® ECG recorder, a patient-operated leadless single-channel ECG recorder which has been validated for AF detection. Kaleschke *et al.*[14] reported sensitivity of 99% and specificity of 96% for detection of AF using this device.

Fortunately, the risk factors for AF and the risk factors for stroke in AF largely overlap.[15–17] Risk factors for AF and for stroke in AF include advanced age, male sex, heart failure, hypertension, diabetes mellitus, survived myocardial infarction, and valvular heart disease. New, less-validated risk factors comprise vascular disease, obesity, sleep apnoea, alcohol abuse or other drug intoxications, excessive sport practice, latent hypertension, genetic factors or inflammation.[18]

To improve the detection of silent AF in patients at risk for AF and AF-related stroke, we performed a simple ECG screening for unknown AF using a fully patient-operated, leadless ECG system in patients with risk factors for AF who were seen for management of diabetes, hypertension, or stroke at the University Hospital Muenster.

Methods

Patient-operated electrocardiographic system

Here, we used the Omron HeartScan 801® patient-operated ECG recorder which has been validated for the diagnosis of AF[14] (*Figure 1*). Electrocardiography device was placed between the index finger of patient's right hand and the skin of patient's torso under the left acromastium; in the area of standard chest lead C4. When activated, the system records a 30 s single-channel ECG, followed by an acoustic signal. All recordings were automatically analysed by the system immediately after recording; results were visualized on the liquid crystal display. The whole bedside procedure of ECG recording and semi-automated data analysis took <2 min. Whenever the patient-operated ECG suggested AF, a 12-channel ECG was recorded to confirm the diagnosis. All recorded ECGs were digitally stored on a memory card and offline analysed by two experienced cardiologists using a personal computer-based software tool (ECG viewer) (*Figures 2A* and *B*).

Patients

We enrolled 132 consecutive patients aged ≥18 years, without a known history of AF and with at least one of the following risk factors: hypertension, diabetes mellitus (treated by drugs or insulin), left ventricular hypertrophy, prior myocardial infarction, C-reactive protein >3 mg/dL, peripheral vascular disease, kidney disease [Modification of Diet in Renal Disease (MDRD) III or higher with a glomerular filtration rate <60 mL/h], heart failure [New York Heart Association (NYHA) III/IV or EF < 50%], ischaemic stroke, or transient ischaemic attack (TIA). All patients gave written informed consent to the screening. After a short instruction in the use and handling of the ECG system, patients performed the ECG recording without supervision.

Statistical analysis

Differences of metric target variables between groups were assessed by non-parametric analysis of variance with *posthoc* testing adjusted for multiplicity applying the closed test principle. In case of binary target variables, the χ^2 test was used. *P* values ≤0.05 were regarded significant. Statistical analyses were performed using IBM SPSS Statistics (version 20 for Windows, IBM Corporation, Somers, NY, USA).

Results

One hundred and thirty-two patients were enrolled in our study. Seventy-six outpatients were screened during visits at gastroenterology or hypertension clinics, and during a visit of the annual 'diabetes day' at our hospital. Fifty-six patients were screened after presenting with an ischaemic stroke ($n = 36$) or TIA ($n = 20$). Patient characteristics are shown in *Table 1*. The automated ECG analysis function suggested successful and immediate repetition of ECG recording in 3/132 patients due to recording artefacts. These failures were not related to specific patient characteristics. All other ECG recordings were analysable after a single

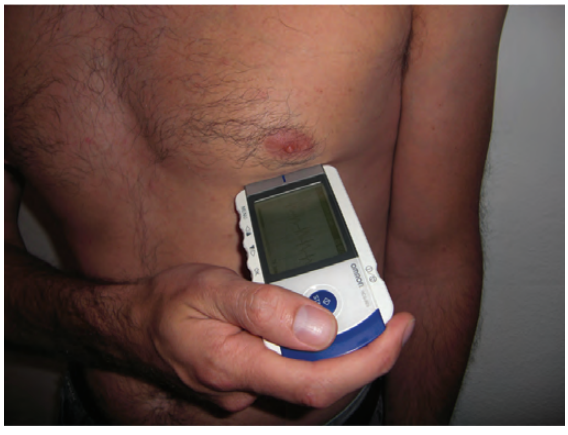

Figure 1 Photograph of a recording procedure using the patient-operated electrocardiography system.

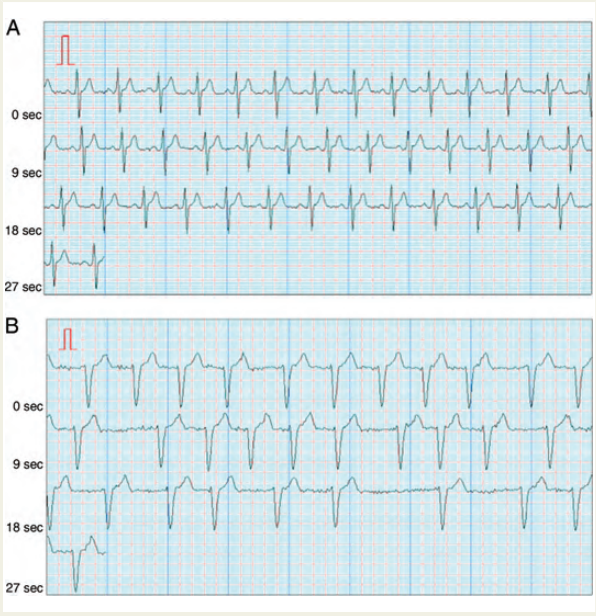

Figure 2 (*A*) Single-lead electrocardiography recording from a patient with sinus rhythm. Electrocardiography is recorded at a paper speed of 25 mm/s. (*B*) Single-lead electrocardiography recording from a patient with atrial fibrillation. Electrocardiography is recorded at a paper speed of 25 mm/s.

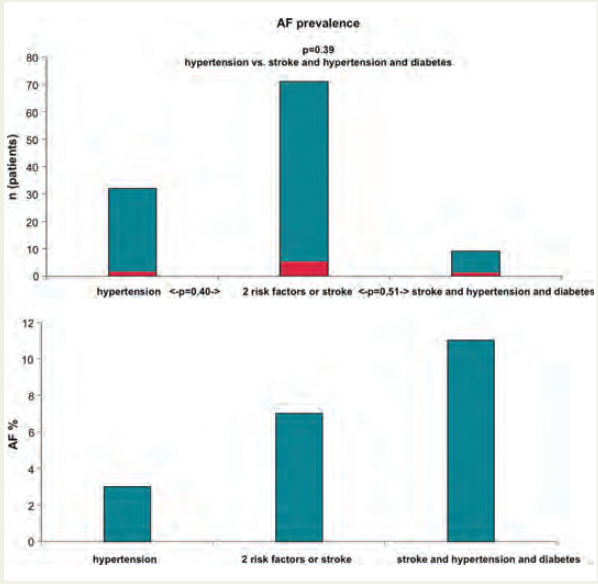

Figure 3 Prevalence of atrial fibrillation in the subgroups; red bars: number of patients with atrial fibrillation; green bars: number of patients without AF; green bars: percentage of patients with atrial fibrillation in the subgroups.

measurement. All patients were able to hold the ECG recorder between the index finger and the left acromastium in the area of standard chest lead C4. Some patients needed help to start ECG measurement; in these patients ($n = 12$) the start button was pressed by clinical staff. Silent AF was found in 7/132 patients (5.3%); four of these patients had been screened after a stroke ($n = 2$) or TIA ($n = 2$), two in a diabetes clinic, and one patient at the hypertension clinic. The prevalence of AF was higher in patients with multiple risk factors for stroke and AF: AF was found in 3% (1/32) patient with hypertension and no other risk factors for AF, but in 7% (5/71) patients with two risk factors including stroke patients (diabetes and hypertension, stroke, or stroke and hypertension), and in 11% (1/9 patients) with stroke, hypertension and diabetes, nevertheless this observable trend was not statistically significant (*Figure 3*). Study nurses performed ECG recordings. If the screening ECG assumed the diagnosis of AF, a standard 12-channel ECG was performed a few minutes later. Two experienced cardiologists who were blind to the 12-lead ECG independently analysed all ECG recordings. Both physicians diagnosed the seven AF episodes from single lead recordings; they suspected no other recordings to represent AF, thus the previously reported high diagnostic accuracy could be confirmed in our study.[13] Standard ECG measurements verified all detected AF episodes. Holter ECG recordings in patients after stroke or TIA revealed chronic AF during the whole registration time in three patients (75%, stroke: $n = 2$, TIA: $n = 1$) and paroxysmal AF in one patient (25%, TIA). Repetitive ECG measurements in the three outpatients 24 h after the first diagnosis of AF revealed sinus rhythm in two patients and persistent AF in one patient. During their treatment on the neurological ward, all patients with stroke or TIA received a standard 12-channel ECG and continuous ECG monitoring during their stay on stroke unit.

Table 1 Patient characteristics, age values are listed as mean ± SD

		All	AF	No AF	*P*
Age (years)	Mean ± SD	64 ± 14	74 ± 6	63 ± 14	0.05
Hypertension	*n* (%)	88 (67%)	5 (71%)	83 (66%)	0.57
Heart failure	*n* (%)	4 (3%)	0 (0%)	4 (3%)	0.80
Diabetes	*n* (%)	36 (27%)	3 (43%)	33 (26%)	0.29
Stroke/TIA	*n* (%)	65 (49%)	4 (57%)	61 (49%)	0.48
Renal failure	*n* (%)	5 (4%)	1 (14%)	4 (3%)	0.24
Sex	Male/female	76/56	7/0	69/56	0.02

Standard ECG or monitoring did not detect further patients with AF in this group ($n = 56$).

Patients with AF were more often males ($P = 0.02$, no females with AF detected in this survey) and significantly older than patients without AF [74 ± 6 years vs. 63 ± 14 (mean ± SD); $P = 0.05$], reflecting two of the main risk factors for AF. There were no further significant differences in age or in the number of screened patients at the different sites of screening between male and female.

Discussion

Main findings

Our data suggest that a simple, patient-operated ECG monitoring system can detect a moderate but relevant number of patients with 'silent', hitherto undiagnosed AF. Such a screening system appears to allow timely, early diagnosis of AF and may be sufficiently simple to be used in a primary care setting. Larger studies are warranted to further evaluate the clinical usefulness of such a simple ECG screening for silent AF.

Silent AF: the scope of the problem

Although many manifestations of AF occur with typical symptoms like tachycardia, palpitations, dyspnoea, or chest pain,[19] 10–40% of all AF patients are asymptomatic.[20] Patients with AF are more likely to die than their peers without AF,[21,22] including patients with 'silent AF',[23] and AF causes many and severe strokes.[3–6] In patients with 'silent', undiagnosed AF, appropriate screening tools would allow to institute therapy before these complications occur. The initial manifestation of AF is indeed an ischaemic stroke in ~5% of stroke patients.[7,9,24,25] Timely detection of AF could help to prevent these strokes.[26] The simple screening employed here was able to detect a relevant number of patients with silent, hitherto undiagnosed AF. Continuous surveillance of the atrial rhythm in the ASSERT trial revealed a subclinical AF prevalence of 10%.[21] Compared with these patients with implanted pacemakers or defibrillators, we were able to detect ~5% AF in our small population by one short ECG recording obtained through a simple, patient-activated, non-invasive device.

A large number of factors associated with the occurrence of AF have been identified[16] such as age, male sex, left ventricular hypertrophy, hypertension, diabetes mellitus, thyroid disease, valvular diseases, and others.[15] Despite the small sample size, two of those factors (age, male sex) were more prevalent in patients with AF in our survey. This may suggest that patients suffering from such conditions may be a good starting point to further evaluate a simple screening tool for AF.

Analyses of implanted device, daily telemetric ECG screening, or long-term Holter monitors have shown that adequate detection of paroxysmal AF requires prolonged and/or repetitive ECG monitoring,[7,9,11–13,27] including detection of AF in survivors of a stroke.[9,10] These technologies are more resource- and time intensive than the simple screening ECG applied here, which would be more suitable for screening larger populations at risk for AF. Although there is less experience with the detection of 'silent' AF in patients who are at risk for stroke and it is likely that extensive ECG screening would detect more patients with AF than the simple screening used in this study. When a higher diagnostic yield is required, patients could use the device employed here for repetitive ECG recordings. The simple screening tool used in this study is sufficient to detect chronic forms of AF.[12] In our study, three patients with diagnosed silent AF showed AF episodes <24 h, whereas four patients showed chronic forms AF. Three of our patients with chronic AF were screened on stroke unit; in these cases a single ECG screening is less than the current recommended form of continuous ECG monitoring. Recent data suggest that these monitor data could be used to detect 'silent' AF.[10] Hence, these patients would most likely have been detected by analysis of the ECG monitoring on stroke unit. Nevertheless, two of them had minimal one more additional risk factor for AF and a broad screening of patients with risk factors may have identified silent AF before occurrence of stroke or TIA and may have allowed the initiation of an adequate anticoagulant treatment to prevent the complications.

Usefulness of simple electrocardiography recorders in patients at risk for atrial fibrillation

The aim of a simple ECG screening tool is not to replace standard ECG as a diagnostic method in clinical practice. Rather, such recorders could provide additional tool whenever standard ECG is not part of the routine diagnostic workup, or may even not be available, but where patients at risk for AF are seen. The screening for atrial fibrillation in the elderly trial showed a relevant number of misinterpreted AF episodes by general practitioners and also a combination of primary care professional and software failed to be sufficiently accurate.[28,29] In contrast to these findings, the device used in our trial has a good sensitivity and specificity in detecting AF episodes even when relying on the automated algorithm.[14] Another potential application could be a daily ECG registration in hospitalized patients by nurses, e.g. concomitant with temperature or blood pressure measurement. In patients requiring ECG monitoring, e.g. stroke survivors, technological advances may allow to use the ECG monitor for AF screening, thereby rendering a device as tested here less helpful.[10]

In an outpatient setting, most patients at risk for AF should be able to use this system after a short instruction. Furthermore, the device allows an independent operation by the patient at home without any need for professional support. In case of any abnormalities, the device will alert the patient who could then contact his or her physician.

Study limitations

We only surveyed 132 patients in specialized outpatient clinics run in a single tertiary care centre. While the approach tested here seems feasible to screen for silent AF using a simple, patient-operated device, this sample size is too small for definitive conclusions, and larger studies are clearly warranted.

The design of our study and the screening ECG device used here only provides a snapshot of 30 s of heart rhythm analysis without any follow-up. While this is sufficient to detect chronic forms of AF,[16] it will miss a sizeable portion of paroxysmal AF.[12] Therefore

the number of affected people is underestimated in our trial with only one single ECG registration. Nevertheless, there are data to suggest that chronic (i.e. permanent or persistent) AF is more often asymptomatic than paroxysmal AF;[30] a fact that may increase probability to detect these episodes and that could be a possible explanation why nearly 50% of AF episodes were detected by a single ECG recording compared with continuous surveillance.[21] Three of seven AF episodes were chronic forms that were detected in patients after stroke. These would have also been detected by standard monitoring during their stay at the stroke unit, albeit with a higher use of technical and human resource.

There might be limitations in the use of the system in patients with palsies of the right arm. It is also conceivable that artefacts occur in patients with different forms of tremor during the measurement that can lead to misinterpretation of the recorded ECG. We did not collect weight and body size of our screened patients to calculate body mass index (BMI), mean BMI in the study of Kaleschke *et al.*[14] was 26 kg/m^2. Extreme obesity might be a limiting factor of signal quality, but in our setting obesity did not influence signal quality. The recording position in the region of standard chest lead C4 represents an area where also in patients with obesity the distance from the body surface to the surface of the heart is mostly only moderate enlarged. Furthermore, the immediately after the recording given feedback of the device helps to obtain recordings with good signal quality.

Despite the relative well-balanced distribution between the sexes in our study, only male patients were found with asymptomatic unknown AF, Possibly reflecting the fact that male sex is a well-known risk factor for AF.[15] Nevertheless, data from the Canada register of AF suggest that patients with symptomatic AF are more often female.[31] Further data sets are needed to investigate this.

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Diagnosis of coronary spastic angina by implantable loop recorder

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The implantable loop recorder (ILR) is a useful tool for evaluation of unexplained syncope. We describe an instructive case of coronary spastic angina (CSA) diagnosed by ST elevation on the ILR electrocardiogram. A 66-year-old woman was referred to us for evaluation of recurrent unexplained syncope. Because the results of conventional examinations were unremarkable, we placed an ILR into subcutaneous tissue of the left pectoral region in the area of V3–V4 leads. Upon follow-up, the patient complained of nighttime chest discomfort, and the ILR electrocardiogram showed corresponding ST elevation. (*Figure 1*, Note the difference between the baseline ILR electrocardiogram and the ILR electrocardiogram obtained during an episode of nighttime chest discomfort.) Transient atrioventricular block was also documented, but there were no symptoms. Ischaemic heart disease, especially CSA, was strongly suspected, and coronary angiography with provocation was performed. Diffuse coronary spasm was observed in the three major coronary arteries by intracoronary injection of acetylcholine. The patient has been free of symptoms on establishment of calcium antagonist therapy and pacemaker implantation. Our case demonstrates alternative use of an ILR—that is, for diagnosis of ischaemic heart disease, although its usefulness depends on placement at the critical site where ST changes can be recorded.

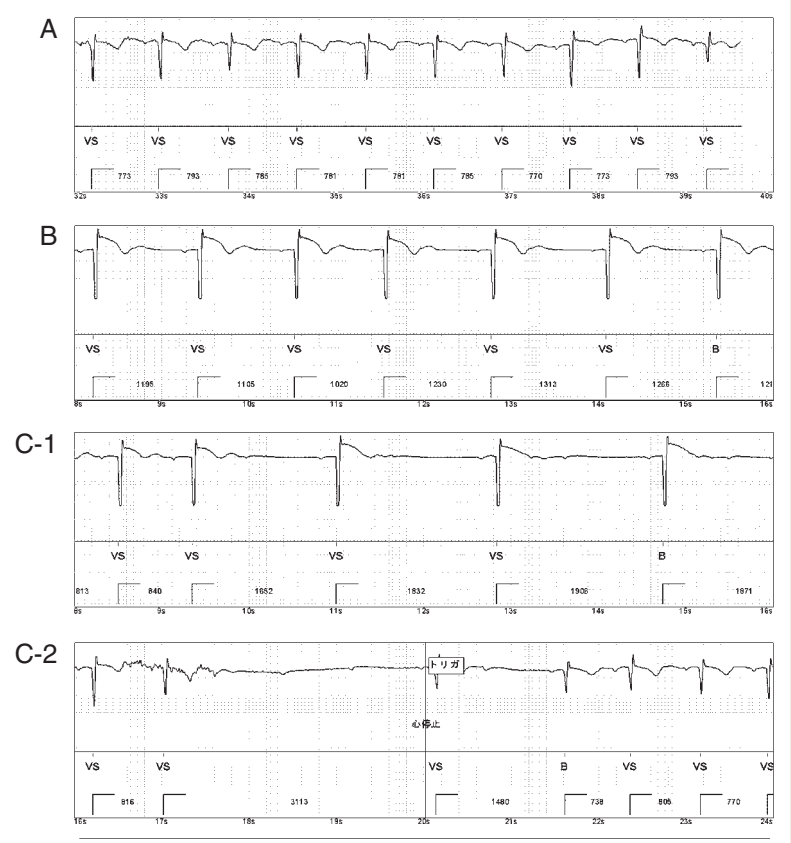

Figure 1

The full-length version of this report can be viewed at: http://www.escardio.org/communities/EHRA/publications/ep-case-reports/Documents/coronary-spastic-angina-loop-recorder.pdf