



Opportunistic screening for atrial fibrillation with a single lead device in geriatric patients

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Abstract

Objective To determine the diagnostic yield of repeated screening for atrial fibrillation (AF) among geriatric patients. **Methods** A pragmatic prospective cohort study into applying opportunistic screening for AF with a handheld single lead ECG device (SLD) in a geriatric cohort. Consecutive patients of 65 years old and older visiting the geriatric outpatient clinic were eligible for inclusion. A 12 lead ECG was performed, followed by measurements with the SLD during every visit to the geriatric outpatient clinic. A frailty index was based on the accumulation of deficits model. **Results** 478 patients were eligible. Patients were excluded if they did not give informed consent (17 patients), had a pacemaker or implantable cardioverter defibrillator (20 patients), or had incomplete medical files (two patients). After exclusion, 439 patients participated in this study. The mean age was 78 years (range 65 to 100 years), 54% were female. AF was known in 89 patients (20%), first detected on the baseline ECG in four patients (1%) and first detected with the SLD in 20 patients (5%) during follow up visits. Sensitivity of the SLD was 90.0%, specificity 99.0%, negative predictive value 99.7%, and positive predictive value 73.5%. Most patients (82%) with AF were frail and 53% were severely frail. **Conclusion** Repeated screening in geriatric patients has a five times higher diagnostic yield than usual care. It was easily combined with usual care. Because of the positive predictive value of 73.5%, it remains necessary to confirm AF with a 12 lead ECG or 24-h Holter monitoring.

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1 Introduction

Atrial fibrillation (AF) increases the risk of stroke, dementia, heart failure and death.^[1–5] The incidence of AF is > 18% in people aged 85 years and older.^[6] Furthermore, AF is associated with loss of independence and frailty,^[2–5] and frail patients are less likely to receive oral anticoagulation (OAC), despite their high-risk profile.^[7–9]

Geriatric patients are frail and have a high prevalence of cardiovascular disease, polypharmacy, impaired daily functioning, falls, and cognitive disorders. The prevalence of AF

in geriatric patients is approximately 25% with about 50% cases being paroxysmal; moreover, the prevalence in these patients is higher than that in the corresponding age-matched elderly population.^[10] AF can easily remain undetected and, consequently, remain untreated. The European Society of Cardiology (ESC) recommends opportunistic screening for AF in patients aged ≥ 65 years, and systematic screening to be considered for high-risk patients.^[11] Because geriatric patients form the majority of the high-risk population, such recommendation is especially relevant to them.

Multiple screening studies using different screening methods have recently been conducted within different populations, and detection rates of new AF ranged from 1.1% to 7.4%.^[11–16] A recent meta-analysis showed that the average detection rate of new AF using single-lead ECG devices was 1.7% (95% CI: 1.4%–2.1%).^[17] However, when multiple recordings were performed, the detection rate was higher,

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namely 4.8%, which is comparable to the 24-hour Holter monitoring.^[17] A major advantage of single-lead ECG devices is that patients can remain seated, they do not need to undress, and measurements are brief. This makes it feasible to screen even the frailest among the elderly, allowing the physician to select for patients who need a confirmatory 12-lead ECG.

A major concern to implement screening is in reaching the frailest patients within the elderly population. The increasing use of smartphones among people aged 65 and older supports the idea of encouraging patient-initiated screening through their smartphones. However, this is challenged by the fact that only 30% of people aged 75 years owned a smartphone in the Netherlands in 2016 (Dutch Central Office of Statistics). Furthermore, geriatric patients often depend on others as they can have cognitive disorders or apathy. This issue is further exacerbated as AF is often asymptomatic causing them to lose the motivation for self-screening. Thus, a better way to reach the very frail might be through physician-initiated screening.

The objective of this study was to determine the rate of newly detected AF when adding a repeated screening step using a handheld single-lead ECG device to the usual follow-up visits of geriatric care. The secondary outcome was to assess the association between AF and frailty. Previous studies screened for AF either at a single timepoint during a routine general practice visit, or incidentally after the presence of palpitations. As a result of repeated screening regardless of symptoms, a higher rate of newly detected AF is expected.

2 Methods

A pragmatic prospective cohort study was conducted on the opportunistic screening for AF among geriatric patients using a single-lead ECG device (SLD), MyDiagnostick[®].^[15,18] Eligible participants included all consecutive patients aged ≥ 65 years at the outpatient geriatric clinic, memory clinic, or Fall and Syncope day clinic (FSC), from June 2017 until June 2018. The patients received printed material explaining the study and were asked to give written informed consent. Patients with pacemakers or implantable cardioverter defibrillators (ICD) or patients unable or unwilling to provide informed consent were excluded.

The baseline characteristics were based on the findings of the comprehensive geriatric assessment (CGA), including the results of the full cognitive assessment, if performed. A frailty index (FI) based on the accumulation-of-deficit model was calculated using the method proposed by Searle, *et al.*^[19] and Rockwood, *et al.*^[20] Forty-four deficits were

selected, comprising of 28 somatic and 6 cognitive functions, and 10 activities of basic daily functioning. The index ranges from 0 (if none of the deficits are present) to 1 (if all deficits are present). Patients were considered to be frail with an index of 0.18 to 0.24, and severely frail with an index of 0.25 or higher.

Upon study entry a 12-lead electrocardiogram (ECG) was performed. As the study commenced, patients without known AF were screened with the SLD in each of their visits at the outpatient clinic. Patients were instructed to sit down on a chair, rest their hands on the physician's desk while gently holding the SLD. They were also asked not to speak during the measurement, which would take 1 min. The inbuilt algorithms of MyDiagnostick allow for automatic detection of any irregular heart rate,^[15] and allow for storage up to 500 SLD results. If an irregular heart rate is detected, the SLD would flash a red cross. AF is defined as an absolutely irregular R-R interval with no discernible P waves. All SLD and baseline ECGs were assessed by two independent cardiologists (JR and MH). The quality of the SLD ECGs was visually rated as too bad, poor, acceptable, or good. If one or both cardiologists rated a SLD ECG as 'too bad', the measurement would be discarded. In case of disagreement, consensus would be reached through discussion between the cardiologists. Because the SLD was not accepted as the only means of diagnosing AF,^[1] a confirmatory 12-lead ECG was performed following positive SLD results.

Patients were screened with the SLD at every visit to the outpatient, FSC or memory clinic, at the beginning and at the end of the consultation. This study focused on the value of adding opportunistic screening to usual care, therefore all scheduled follow-up visits were deemed necessary by the treating geriatrician, and no independent research study visits were carried out. Neither the number of visits nor the intervals between visits were standardised.

Statistical analyses were performed using SPSS for Windows version 20. Baseline characteristics were presented as n (%) or mean \pm SD. Normality of continuous variables was checked before further analysis. For comparisons between continuous variables, the Student's t -test was used and the Chi-squared test for categorical was used. P -values of 0.05 or less were considered significant. Significant differences found in univariate analyses were further tested using the binary logistic regression analysis. Correlations between frailty, age and history of AF in years were assessed using linear regression, while the correlation between frailty and the use of OAC was assessed using binary logistic regression.

3 Results

A total of 561 patients visited the outpatient clinics and FSC. Of them, 478 patients aged ≥ 65 years were eligible for this study. Thirty-nine patients were excluded: 20 had a pacemaker or ICD, 17 did not want to participate, and 2 had incomplete medical records. After exclusion, 439 patients were included.

The baseline characteristics are shown in Table 1. The mean age was 78 ± 7 (range 65 – 100) years and 239 patients (54%) were women. The average number of visits per patient was 2 (range 1–6). Patients on average carried 5 ± 3 comorbidities and were on 6 ± 4 different drugs. A total of 254 (58%) patients were on polypharmacy, which is defined as taking five or more drugs. The five most prevalent diseases were hypertension (63%), hypercholesterolemia (43%), AF (26%), diabetes mellitus (22%), and ischemic heart disease (22%). Patients with AF were older than patients with sinus rhythm (SR) (80.5 vs. 77.6 years, $P < 0.001$). After correcting for age, patients with AF had a significantly higher CHA₂DS₂-VASc score, had more comorbidities, used more drugs, and tended to have a higher prevalence of ischemic heart disease, heart failure, and chronic kidney disease. Patients with AF, more often than patients with SR, experienced

orthostatic hypotension, probably due to more frequent use of diuretics, dihydropyridines, and beta-blockers, as well as had a higher prevalence of heart failure, as shown in Tables 1 and 2. Patients with AF had significantly higher prevalence of hyperthyroidism when compared to those in SR (8% vs. 1%, $P < 0.001$). Among patients with AF, those who were newly diagnosed AF did not have a higher prevalence of hyperthyroidism than patients with known AF (4% vs. 9%, $P = 0.44$).

In total, 1344 SLD ECGs were performed, averagely 3.5 ± 2.2 (range 1 to 13) measurements per patient. There were 64 (4.8%) measurements classified as AF (positive measurements), belonging to 43 (9.8%) patients. A total of 50 (3.7%) SLD ECGs were discarded, 14 (1.0%) due to artifacts, and 36 (2.7%) due to unreliable assessment of atrial activity. The remaining 1294 SLD ECGs were used in this analysis. The quality of the single lead ECGs was good in 1111 (85.9%) measurements, acceptable in 160 (12.4%), and poor in 23 (1.8%). Of the analyzed SLD ECGs, 49 (3.8%) were classified by the device as AF. Of the discarded SLD ECGs, 15 (30.0%) were classified by the device as AF.

The cardiologists agreed on the rhythms of 1284 (99.2%) SLD ECGs. Disagreements about the rhythms on 10 SLD

Table 1. Baseline characteristics.

	Total <i>n</i> = 439	SR <i>n</i> = 326 (74.3%)	AF <i>n</i> = 113 (25.7%)	<i>P</i>	<i>P</i> adjusted for age
Female	239 \pm 54.4	189 \pm 79.1	50 \pm 20.1	0.012	
Age, yrs	78.4 (6.7%)	77.6 (6.8%)	80.5 (6.0%)	< 0.001	
Died within study period	10 (2.3%)	7 (2.1%)	3 (2.7%)	0.755	
Number of morbidities	5 \pm 2.6	5 \pm 2.3	7 \pm 2.7	< 0.001	< 0.001
Number of drugs	6 \pm 3.9	6 \pm 3.9	7 \pm 3.6	0.001	0.017
Polypharmacy (≥ 5 drugs)	254 (57.9%)	168 (51.5%)	86 (76.1%)	< 0.001	< 0.001
Hypertension	278 (63.3%)	194 (59.5%)	84 (74.3%)	0.005	0.018
Hypercholesterolemia	187 (42.6%)	133 (40.8%)	54 (47.8%)	0.195	
Diabetes mellitus	98 (22.3%)	69 (21.2%)	29 (25.7%)	0.322	
CHA ₂ DS ₂ -VASc	3.8 \pm 1.5	3.6 \pm 1.4	4.3 \pm 1.4	< 0.001	< 0.001
HAS-BLED	1.5 \pm 0.7	1.5 \pm 0.7	1.6 \pm 1.4	0.195	
All strokes, (stroke and/or TIA)	68 (15.5%)	42 (12.9%)	26 (23.0%)	0.010	0.015
Heart failure	49 (11.2%)	19 (5.8%)	30 (26.5%)	< 0.001	< 0.001
*Ischemic heart disease	95 (21.6%)	62 (19.0%)	33 (29.2%)	0.023	0.025
Peripheral artery disease	38 (8.7%)	24 (7.4%)	14 (12.4%)	0.101	
Hypothyroidism	31 (7.1%)	17 (5.2%)	14 (12.4%)	0.010	0.047
Hyperthyroidism	12 (2.7%)	3 (0.9%)	9 (8.0%)	< 0.001	< 0.001
COPD	65 (14.8%)	49 (15.0%)	16 (14.2%)	0.822	
Chronic kidney disease, \geq stage 3	60 (13.7%)	35 (10.7%)	25 (22.1%)	0.002	0.011
Syncope	74 (16.9%)	46 (14.1%)	28 (24.8%)	0.009	0.009
Orthostatic hypotension	95 (21.6%)	57 (17.5%)	38 (33.6%)	< 0.001	0.002

Data are presented as *n* (%) or mean \pm SD. *Angina pectoris, myocardial infarction, cardiac artery bypass or percutaneous coronary intervention. AF: atrial fibrillation; BMI: body mass index; COPD: chronic obstructive lung disease; SR: sinus rhythm; TIA: transient ischemic attack.

ECGs were resolved through discussion. After achieving consensus, 36 SLD ECGs (2.7% of total and 73.5% of positives) were classified as AF, 13 as false-positive (1.0% of total and 26.5% of positives), and 4 (0.3%) as false-negatives (atrial flutter). The sensitivity of the device for detecting AF was 90.0%, specificity was 99.0%, negative predictive value was 99.7%, and positive predictive value was 73.5%. At baseline, 89 (20.3%) patients were known with AF and AF was newly diagnosed in 24 (5.5%) patients, constituting to an overall prevalence of 25.7%. Of these 24 patients, four patients (0.9%) showed AF at baseline and in 20 patients, AF was newly detected with the device.

The use of medication is summarized in Table 2, and a detailed list of medications can be found in the Supplementary Table 1S. The five most commonly used types of drugs were vitamin supplements (51%), proton pump inhibitors (43%), lipid-lowering drugs (41%), angiotensin converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor

blockers (ARBs) (40%), and beta blockers (36%). Of the 89 patients who were known to have AF, 77 (87%) used oral anticoagulation (OAC), 56 (73%) used a vitamin K antagonist, and 21 (27%) had NOAC. Three patients with newly diagnosed AF were already on OAC before the diagnosis. Two of these patients were treated under the suspicion of AF even though this had never been proven on an ECG or a Holter monitor. The third patient was known to have an aneurysm cordis due to ischemic heart disease. Of patients with AF, there were 4 (4%) who were on both antiplatelet agents (APA) and OAC, 4 (4%) were only on APA and 8 (9%) who were not on any kind of antithrombotic medication.

Table 3 shows the functional, mental and cognitive states of patients. Patients with AF were significantly frailer than those without AF (FI: 0.25 vs. 0.17, $P < 0.001$). Only 20 (17.7%) patients with AF were not considered frail. Of the patients in SR, 65 (20%) were severely frail and of patients

Table 2. Medication use in the patients.

	Total, <i>n</i> = 439	SR, <i>n</i> = 326	AF, <i>n</i> = 113	<i>P</i>
Oral anticoagulants	88 (20.0%)	8 (2.5%)	80 (70.8%)	< 0.001
Vitamin K antagonist	65 (14.8%)	7 (2.1%)	58 (51.3%)	< 0.001
NOAC	23 (19.5%)	1 (0.3%)	22 (19.5%)	< 0.001
Anti platelet agent	115 (26.2%)	100 (30.7%)	15 (13.3%)	< 0.001
ACEI or ARB	174 (39.6%)	121 (37.1%)	53 (46.9%)	0.067
Beta blocker	157 (35.8%)	91 (27.9%)	66 (58.4%)	< 0.001
Loop diuretics	39 (8.9%)	15 (4.6%)	24 (21.2%)	< 0.001
Thiazide diuretics	57 (13.0%)	48 (14.7%)	9 (8.0%)	0.065
Potassium retaining diuretics	20 (4.6%)	9 (2.8%)	11 (9.7%)	0.002
Lipid lowering drugs	181 (41.2%)	129 (39.6%)	52 (46.0%)	0.230
Dihydropyridines	86 (19.6%)	56 (17.2%)	30 (26.5%)	0.031
Anti arrhythmic, not β -blocker	20 (4.6%)	2 (0.6%)	18 (15.9%)	< 0.001
Proton pump inhibitor	189 (43.1%)	136 (41.7%)	53 (46.9%)	0.337
Vitamin supplements	222 (50.6%)	166 (50.9%)	56 (49.6%)	0.803

Data are presented as *n* (%). ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; NOAC: non-vitamin K antagonist.

Table 3. Functional, mental, and cognitive states of the patients.

	Total <i>n</i> = 439	SR <i>n</i> = 326 (74.3%)	AF <i>n</i> = 113 (25.7%)	<i>P</i>	<i>P</i> adjusted for age
Frailty index	0.19 ± 0.1	0.17 ± 0.1	0.25 ± 0.1	< 0.001	< 0.001
Parkinsonism	35 (8.0%)	20 (6.1%)	15 (13.3%)	0.016	0.014
Falls	146 (33.3%)	97 (29.8%)	49 (43.4%)	0.008	0.056
Dependence in ADL	76 (17.3%)	48 (14.7%)	28 (24.8%)	0.015	0.120
Dependence in IADL	176 (40.1%)	120 (36.8%)	56 (49.6%)	0.017	0.107
Visual impairment*	183 (41.7%)	130 (39.9%)	53 (46.9%)	0.192	
Hearing impairment	88 (20.0%)	64 (19.6%)	24 (21.2%)	0.713	
Mild cognitive impairment	152 (34.6%)	112 (34.4%)	40 (35.4%)	0.841	
Dementia, all forms	102 (23.2%)	76 (23.3%)	26 (23.0%)	0.947	

Data are presented as mean ± SD or *n* (%). *Treated cataract included. ADL: activities of daily living; AF: atrial fibrillation; IADL: instrumental activities of daily living; SR: sinus rhythm.

with AF, 60 (53%) were severely frail. A higher FI did not lower the likelihood of using OAC for patients with AF (OR = 0.187, 95% CI: 0.001–26.661). A weak correlation of 0.004 per year (adjusted $R^2 = 0.092$, $P < 0.001$) was found between increasing age and increasing FI. For both known and newly diagnosed AF, neither age (adjusted $R^2 = 0.007$, $P = 0.19$) nor the history of AF in years (adjusted $R^2 = 0.001$, $P = 0.30$) correlated with FI. The prevalence of mild cognitive impairment (MCI) and dementia was not significantly different between those with and those without AF (23.3 vs. 23.0%, $P = 0.95$).

4 Discussion

Our study showed that with a simple approach using a SLD, a very high rate of newly diagnosed AF can be found in geriatric patients during follow-up visits. Opportunistic screening with this device was applied at outpatient clinics in a pragmatic fashion, without delaying or complicating the usual care. By screening during the follow-up visits, AF was detected in 4.6% of patients, in addition to the 0.9% cases that were found through baseline ECGs. Patients were screened 3.5 times on average, which was equal to 3.5 min of screening. This is clearly less than the average of 19 min of intermittent recording that was reported in a recent meta-analysis, but with a comparable rate of newly detected cases of AF.^[17] Adding repeated measurements onto follow-up visits detected more new cases than screening at a single time point with the same device did, as was done by Tieleman, *et al.*^[15] and Kaasenbrood, *et al.*^[16] who reported the rates of newly detected cases of AF of only 1.6% and 1.1%, respectively. The SLD delivered measurements of adequate to good quality in 95% (1271 out of 1344 single lead ECGs) of the attempts. However, because of the positive predictive value of 73.5%, it remains necessary to confirm AF by means of a 12-lead ECG or a 24-h Holter monitoring. Considering the negative predictive value of 99%, this SLD is suitable to aid the physician in selecting patients who will or will not need a confirmatory ECG or Holter monitoring.

Our results showed that there is a very high risk that AF will remain undetected if geriatric patients are not repeatedly screened for presence of AF. Repeated screening has been proven to be an efficient strategy and can be easily combined with usual care. We expect if the addition of opportunistic screening onto follow-up visits would be implemented in other outpatient clinics with high-risk populations as well, this will lead to detection of new cases, independent of the SLD used. We encourage other researchers to investigate the efficacy of repeated screening for AF in different settings and with different devices.

The average FI of 0.19 in this cohort and its weak correlation with age is in line with what was previously reported.^[21] The FI of 0.26 in patients with known AF and 0.24 in patients with newly diagnosed AF indicates that they are severely frail and form a group of patients who are especially vulnerable to adverse events. Of the patients with AF, 82% were frail and 53% severely frail. No correlation was found between the history of AF in years and the FI, which is possibly due to the wide range (1 to 33 years) in the history of AF in years and the relatively small group of patients with AF ($n = 89$). The substantial difference in FI between those with SR and those with known AF raised the question of whether AF is a contributing factor to becoming frail. We strongly advise that this is further investigated, preferably using a CGA-based FI to identify frail patients.

In this study, 87% of patients with known AF were on OAC, which is considerably higher than 58% reported by Tulner, *et al.* for a 2004 cohort.^[22] In our cohort, a higher FI did not lead to a lower likelihood of OAC use (OR = 0.18, 95% CI: 0.001–26.7), which is in contrast with the FRAIL AF study.^[9] A possible explanation is that nowadays, the risk of stroke is considered greater than the risk of anticoagulant-related bleeding even in the severely frail. To what extent severe frailty leads to anticoagulant-related major bleeding episodes remains a question yet to be answered.

A limitation of this study was the small sample size of patients with known or newly diagnosed AF, which limited the possibility of studying the correlations between the characteristics of AF and the incidence of outcomes such as cognitive disorders and frailty. Concerning cognitive disorders, another probable limitation lies in selection bias. Contrary to the literature, our cohort study found no correlation between AF and cognitive disorders. We postulated that a selection bias probably occurred during the referral of patients presenting with cognitive complaints to our memory clinic, which led to a high proportion of cognitive disorders among both patients with SR and with AF. A further explanation could be that the association between AF and cognitive decline and dementia is stronger in people aged < 70 years than in the very elderly, as was shown by Bunch, *et al.*^[5]

In conclusion, more than 25% of patients in the present geriatric cohort experienced AF. Newly diagnosed AF was found in 5.5% of the patients. Complementing usual outpatient care with repeated screening is easy to implement and is effective because it can lead to a five times higher diagnostic yield compared to a single 12-lead ECG during the first patient contact. Our findings strongly support the 2016 ESC recommendation to screen patients at high risk for AF in an opportunistic manner and we advise to integrate such practice of opportunistic screening for AF into the customary care of ambulatory geriatric patients.

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