SCIENTIFIC LETTER

Frequent atrial premature contractions as a surrogate marker for paroxysmal atrial fibrillation in patients with acute ischaemic stroke

D Wallmann, D Tüller, N Kucher, J Fuhrer, M Arnold, E Delacretaz

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The association between atrial fibrillation (AF) and stroke is well documented.¹ Oral anticoagulation may reduce the risk of stroke in relation to AF by about two thirds.¹ Thus, patients with ischaemic stroke commonly undergo ambulatory ECG to detect asymptomatic paroxysmal AF. However, 24 hour ECG recordings have a low yield to detect AF in this population.² Electrophysiological studies in patients with paroxysmal AF have identified frequent premature beats originating predominantly from the pulmonary veins as a main source of triggers that initiate AF.^{3,4} These frequent premature beats can be identified by 24 hour ECG recordings.⁵

The present study investigated whether the presence of frequent atrial premature contractions (APCs) in 24 hour ECG recordings is associated with a greater incidence of AF in patients with ischaemic stroke.

METHODS

Consecutive patients who suffered an acute ischaemic stroke and without known AF were identified. Patients with persistent severe cognitive disturbances and severe aphasia, as well as those with a life expectancy shorter than six months, were excluded. Furthermore, documented AF in the initial 24 hour ECG was an exclusion criteria. The patients underwent an echocardiography and a 24 hour ECG recording within 2–6 days after admission. Nine patients were excluded after initial enrolment because of death (n = 6), retrospectively known paroxysmal AF before ischaemic stroke (n = 1), or unconfirmed diagnosis of ischaemic stroke (n = 2). All 99 remaining patients were prospectively followed up by their primary care physicians. Ambulatory 24 hour and seven day ECG recordings were used at the discretion of the primary care physicians to document AF in patients who developed symptoms suggesting arrhythmias. Episodes of AF were correlated with the presence of frequent APCs in the initial ambulatory ECG. Patient allocation into two groups was based on frequency of APCs. High frequency (frequent APCs) was defined as the fourth quartile and low frequency was defined as quartiles 1–3.

Continuous values are presented as mean (SD). Student's *t* test and χ^2 test were used to compare groups when appropriate. Multiple logistic regression analysis was performed for variables univariately associated with frequent APCs. A probability value of $p < 0.05$ was considered significant. All statistical analyses were done with Statview 4.5 (Abacus Concepts Inc) and SPSS 10.0 for Windows (SPSS Inc, Chicago, Illinois, USA).

RESULTS

A subgroup of patients with frequent APCs was identified. Twenty four patients had frequent APCs (fourth quartile, 70 APCs or more in 24 hours) and 75 patients had infrequent APCs (quartiles 1–3, < 69 APCs in 24 hours). Table 1 lists the clinical characteristics of patients with and without frequent

APCs. There was no significant difference between these two groups with respect to left ventricular mass index, left ventricular ejection fraction, and prevalence of cardiovascular risk factors and of coronary or valvar heart disease. Patients with frequent APCs were older and had larger left atria than did patients without frequent APCs. AF was documented in 12 of 99 patients during a mean follow up of 22.4 (17.8) months. AF occurred in eight patients with frequent APCs and in four patients without frequent APCs (33% *v* 5%, respectively, $p = 0.001$). The increased incidence of AF among patients with frequent APCs was significant with an odds ratio of 9.3 (95% confidence interval 1.7 to 49.6, $p = 0.01$) after adjustments for age and left atrial diameter in a multiple logistic regression model.

When patients who developed AF (n = 12) were compared with patients without AF (n = 87), there was no difference in age, sex, prevalence of cardiovascular risk factors, presence of coronary or valvar heart disease, left ventricular mass index, and left ventricular ejection fraction. Left atrial size was larger in patients who developed AF than in patients without AF (50 (10) mm *v* 39 (7) mm, respectively, $p < 0.001$). The number of APCs in 24 hours was 2237 (3866) in patients who developed AF versus 143 (480) in patients without AF ($p < 0.001$). Frequent APCs were present in 67% (n=8) of patients who developed AF and in only 18% (n=16) of patients without AF ($p < 0.001$).

DISCUSSION

Increasing evidence suggests that AF episodes are often triggered by focal extrasystolic activity.^{3,4} Conversely, ablation of the arrhythmogenic foci abolishes paroxysmal AF in selected patients, showing the pathophysiological importance of frequent APCs.^{3,4} These recent findings motivated the present attempt to correlate the presence of arrhythmogenic triggers with an increased incidence of AF.

Patients with ischaemic stroke were selected as a study group because improvement in detection of AF as a cause of stroke is desirable. Indeed, current diagnostic strategies often fail to detect AF as a potential cause of embolic events, and unrecognised intermittent AF is a major risk factor for recurrent stroke, which is potentially preventable.¹

The present study showed, firstly, that frequent APCs can be recorded in a subgroup of patients with acute ischaemic stroke. Furthermore, frequent APCs are associated with a greatly increased incidence of AF. AF occurred in 33% of patients with frequent APCs, whereas only 5% of patients without frequent APCs developed AF. Thus, patients with frequent APCs constitute a subgroup at high risk of recurrent stroke. A search for paroxysmal AF in patients with frequent

Abbreviations: AF, atrial fibrillation, APC, atrial premature contraction

Table 1 Clinical characteristics of 99 patients with ischaemic stroke in relation to frequency of atrial premature contractions

	Quartiles 1–3 (0–69 APCs) (n=75)	Quartile 4 (≥70 APCs) (n=24)	Odds ratio (95% CI)	p Value
Age (years)	61 (14)	70 (12)	1.1 (1.01 to 1.09)	0.01
Male sex	42 (56%)	15 (63%)	1.3 (0.5 to 3.4)	0.58
Coronary artery disease	12 (16%)	5 (21%)	1.9 (0.6 to 6.0)	0.25
Diabetes	15 (20%)	6 (25%)	1.3 (0.5 to 3.9)	0.6
Current or former cigarette smoker	25 (33%)	5 (21%)	0.5 (0.2 to 1.6)	0.25
Dyslipidaemia	31 (41%)	13 (54%)	1.7 (0.7 to 4.2)	0.27
Hypertension	50 (67%)	13 (54%)	0.6 (0.2 to 1.5)	0.27
Two or more cardiovascular risk factors	35 (47%)	12 (50%)	1.1 (0.5 to 2.9)	0.78
Echocardiographic findings				
Left atrial size (mm)	39 (7)	43 (9)	1.1 (1.0 to 1.1)	0.04
LV mass index (g/m ²)	108 (36)	122 (40)	1.0 (0.996 to 1.0)	0.17
LV ejection fraction (%)	0.66 (0.07)	0.69 (0.08)	1.1 (0.995 to 1.2)	0.07
Mitral regurgitation	4 (5%)	1 (4%)	0.8 (0.1 to 7.2)	0.74
Paroxysmal AF	4 (5%)	8 (33%)	8.9 (2.4 to 33.1)	0.001

Values are mean (SD). APC, atrial premature contraction; AF, atrial fibrillation; LV, left ventricle.

APCs by repeated 24 hour ECGs or event recordings may allow the detection of paroxysmal AF earlier and may prevent complications.

APCs may be a marker of other risk factors for stroke—that is, they may be related to left atrial enlargement, which in turn may cause increased thrombus formation and stroke. Indeed, left atrial enlargement was associated with an increased incidence of AF in the present study, as in earlier reports. However, multivariate analysis showed that the presence of frequent APCs was an independent risk factor for the occurrence of AF.

Some patients may have developed episodes of asymptomatic AF that were not detected in the follow up. Furthermore, detection of paroxysmal AF does not establish AF as the cause of stroke.

This study showed an association between the presence of frequent APCs in 24 hour ECG recordings and a greatly increased incidence of AF in patients with ischaemic stroke. Further studies are needed to delineate the optimal management of patients with frequent APCs.

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Authors' affiliations

D Wallmann, D Tüller, N Kucher, J Fuhrer, E Delacretaz, Swiss Cardiovascular Centre Bern, University Hospital, Bern, Switzerland
M Arnold, Neurology, University Hospital, Bern

Correspondence to: Professor Etienne Delacretaz, Swiss Cardiovascular Centre Bern, University Hospital, CH-3010 Bern, Switzerland; etienne.delacretaz@insel.ch

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