Research Article

High Prevalence of Paroxysmal Atrial Fibrillation in A Selected Population of Patients with Stroke and Transient Ischemic Attack

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Abstract

Background: Paroxysmal atrial fibrillation (PAF) is a common cause of ischemic stroke, but difficult to disclose in the post-stroke workup. Current practice guidelines recommend at least 24 hour cardiac rhythm monitoring to patients with stroke or transient ischemic attack (TIA). The diagnostic yield of this strategy is, however, limited. We aimed to demonstrate that simple selection of patients for 7 day Holter Monitoring (HM) could increase the detection rate of PAF in stroke and TIA patients.

Methods: In this single centre observational study, 58 patients with acute ischemic stroke or transient ischemic attack were enrolled prospectively. Only patients ≥62 years with absence of obvious vascular aetiology, valve disease or previous history of atrial fibrillation were included in the study. All patients had a 7 day Holter monitoring (HM), with subsequent analysis by specially trained study nurses. PAF was divided by duration >30s and ≤30s. An independent cardiologist confirmed all documented PAF episodes.

Results: Overall PAF occurred in 21 (36%) patients. 16 (27%) had PAF >30s duration and 5 (9%) experienced brief burst of PAF <30s duration. One patient experienced both types of PAF episodes. PAF occurred in 13 (59%) of TIA patients (n=22) and in 8 (22%) patients with ischemic stroke (n=36). None of the patients reported symptomatic PAF.

Conclusion: In this small study population we demonstrated, that simple selection on basis of age and absence of obvious vascular aetiology could improve the diagnostic yield of a 7 day Holter monitoring.

INTRODUCTION

Atrial fibrillation (AF) is a strong independent risk factor of stroke, estimated to cause 18-25% of all ischemic strokes [1]. With an age dependent prevalence and increasing life expectancies, AF is a growing public health concern [2]. Detection of AF in the post stroke cardiac work-up is arguably the most important finding, because a change from antiplatelet to oral anticoagulant therapy will be needed to adequately lower the high risk of re-stroke [3]. AF presentation is, however, often paroxysmal and asymptomatic, making diagnosis difficult in the post-stroke work-up [4].

To detect paroxysmal atrial fibrillation (PAF), current clinical guidelines recommend at least 24-hour cardiac rhythm monitoring in stroke patients [5,6]. This screening approach will, based on previous studies, detect PAF in approximately 5% of unselected stroke and transient ischemic attack (TIA) patients and presumably leave a number of patients undiagnosed and insufficiently treated [7,8]. Detections rates can be increased with prolongation of monitoring, but the optimal method and duration of monitoring has yet to be established.

Strategic selection of patients for extended monitoring should be considered in stroke patients at a particularly high risk of AF. This could optimize the diagnostic yield. The aim of this study is to determine the prevalence of PAF in a selected group of stroke and TIA patients who, due to older age and no obvious vascular aetiology, has presumed higher pre-test probability of PAF [9].

MATERIALS AND METHODS

We conducted a prospective observational single-center study at the department of Neurology; Roskilde Hospital. It was a non-intervention study aiming to validate a new procedure regarding workup of stroke and TIA patients. The study did not
need approval by the local ethics committee, but the committee was made aware of the study and had no objections.

Over a period of 15 months we enrolled 58 patients into the study meeting the following criteria:

- Age ≥62 years
- Symptoms of stroke or TIA
- No sign of vascular aetiology (defined as carotid stenosis >50% or symptomatic arterial dissection)
- No current treatment with oral anticoagulants, prior history of AF or valve disease.

All patients had baseline ECG and prior medical history screened for AF.

Demographic variables including age, date of event, risk factors for stroke, past cardio/cerebrovascular history, stroke severity and test results (CT, carotid-doppler ultrasound) were documented in a standardized case-report form. Patients were subdivided by severity into TIA, minor stroke, non-disabling stroke, disabling stroke and fatal stroke, see table 1.

All patients underwent seven day two lead holter monitoring (HM) (Lifecard CF, Spacelabs Healthcare, Issaquah, WA). Recordings were analysed by 3 trained study nurses assisted by the Life-screen software also provided by Spacelabs Healthcare. This was done in two steps: First, the ECG recordings were visually analyzed minute-by-minute and all suspected AF episodes highlighted in the Life-screen software. The heart rate and R-R intervals were afterwards viewed with lifescreen tools "RR-histogram" and "Heart Rate", to identify periods with high heart rate variability as seen in atrial fibrillation. AF was defined as irregular ventricular response in the absence of p-waves or with fibrillatory waves [10]. Recordings were also considered positive if atrial flutter was detected, seeing as these arrhythmias often coincide and carries similar risk of stroke [11].

An independent cardiologist confirmed all documented episodes of PAF and was consulted in any case of uncertainty. Primary endpoint was detection of PAF and our secondary endpoint to identify number of PAF episodes >30s and ≤30s [10].

### DISCUSSION

In a selected group of stroke and TIA patients, who, due to older age and absence of obvious vascular aetiology had a higher pre-test probability of PAF, we identified PAF in 36% of patients. This is high compared with previous studies examining unselected as well as selected stroke patients [7,12]. Even excluding patients with episodes <30s duration, traditionally required for diagnosis, leaves us with a high 27% detection rate.

Previous studies on PAF detection in stroke patient have shown widely varying detection rates ranging from 0-42%. This can be explained by differences in study population, length and method of monitoring, time from stroke to initiation of monitoring and definition of PAF as illustrated in two recent meta-analysis [8,13]. In the meta-analysis by Kishore et al. PAF was reported in 6,2% of unselected patients and 13,4% of selected stroke patients [13]. Only a few studies have reported the prevalence of PAF in cryptogenic stroke patients using a 7 day non-invasive monitoring technique, and detection rates in these studies range from 1,7-14,2%. There is overall, in line with our result, a tendency towards higher detection rates with extended monitoring on selected patients [13-15].

The term cryptogenic, implies that no obvious large vessel-, small vessel disease or cardio-embolism could be detected in the primary evaluation. In our study we did not exclude patients with lacunar infarctions as seen in small vessel disease, making the population studied different from the above-mentioned studies. However, 3(25%) of patients with evidence of small vessel disease on CT had a PAF. Even though the number of patients with lacunar infarcts, is too few to show any significance, it indicates that these patients could also benefit from extended cardiac monitoring.

Various non-invasive and invasive methods of monitoring have been studied in stroke patients, and each technique has its own pros and cons. The invasive techniques as the implantable loop recorders (ILR) allow for lengthier monitoring periods, but are costly and associated with the general risks of invasive procedures [16]. Non-invasive methods include the external-loop recorders, continuous in-patient telemetry, holter monitoring and mobile out-patient telemetry [17, 18]. The external loop recorders allows longer monitoring periods compared to HM and in-patient telemetry, but are dependent on patient compliance, which, in many stroke patients, can be difficult [19]. Holter monitoring and in-patient telemetry ensures continuous monitoring, but given the need for time-consuming manual assessment, the duration...
of monitoring can be limited. Furthermore comparative studies on HM and in-patient telemetry show contradictory result. One study finds HM superior to in-patient telemetry, while another the opposite [20,21]. This divergence may reflect varying competencies of staff and interpretive software to identify paroxysmal atrial arrhythmias. We chose HM since it does not confine patients to the bed, thereby having the advantage of early patient mobilisation, which is important in post-stroke rehabilitation [22,23] and furthermore makes monitoring possible after discharge from hospital. In addition a 7 days HM is previously proven cost-effective [24].

We evaluated a simple selection strategy based on two known predictors of PAF, but other predictors such as imaging results (infarct pattern, echocardiography), premature supraventricular beats and biomarkers, have been identified and could potentially contribute to optimize detection outcomes even further [25-28]. Based on PAF predictors different strategies for selection of patients for extended monitoring have been developed, but there is to our knowledge no data favouring one method over the other [29,30].

In our study patients were selected based on age and absence of symptomatic carotid stenosis, seeing as the two parameters have been identified as predictors of PAF in stroke patients and are part of the Score fore Targeting of Atrial Fibrillation (STAF) score suggested by Suissa et al [29,31]. We were, however, not able to fully utilise the STAF score, because echocardiography, needed for measurement of the left atrium, is not available for all stroke patients in our clinic. It is our impression, that most stroke centres do not use echo-cardiography as part of a standard work-up after stroke, making our selection strategy relevant for centres with similar resources.

In the present study patients with PAF had a significantly higher CHA 2DS2VASc scores emphasising the importance of recognising, that several risk factors can co-exist, and that carotid stenosis does not exclude AF as the possible cause of stroke. Furthermore, in patients with AF and ischemic stroke, the aetiology is not necessarily cardioembolic [32]. This can potentially be addressed by the implementation of novel biomarkers as N-terminal pro brain natriuretic peptide, which has shown good accuracy in predicting PAF in cryptogenic stroke patients [33-37]. Ideally a validated, cost-effective scoring system based on known predictors of PAF in stroke patients should be developed and implemented in clinical practice guidelines.

Five of our patients presented with solely brief episodes of PAF (<30s), which is shorter than the traditional threshold for diagnosis and treatment. There are no guidelines addressing how to treat these patients, even though the episodes are likely to be clinically relevant. Khan et al demonstrates indecision in the clinical practice of anticoagulation for brief atrial arrhythmias [38]. Based on careful evaluation, all patients with brief episodes of PAF in our study were treated with oral anticoagulants, but further study is needed to determine the risks and benefits associated with anticoagulation of brief PAF episodes in stroke and TIA patients.

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Table 1: Severity of stroke.

<table>
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<tr>
<th>Symptoms &lt; 24 hours</th>
<th>Symptoms &gt; 24 hours</th>
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<tbody>
<tr>
<td>Transient Ischemic Attack (TIA)</td>
<td>None to mild residual symptoms of no functional relevance</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>Moderate residual symptoms not preventing everyday life</td>
</tr>
<tr>
<td>Non-disabling stroke</td>
<td>Severedebilitating residual symptoms</td>
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<tr>
<td>Fatal stroke</td>
<td>Death within 4 weeks of the cerebral infarction</td>
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Limitations: In the study period, there were an unknown number of patients meeting the inclusion criteria, who failed to be included in the study. This was partly because of a limited number of available Holter Monitors, but also because of irregular selection of patients for monitoring. The possibility of selection bias in our small population is therefore present and our high detection rate should be interpreted in light of these limitations.

CONCLUSION

In this small selected population of stroke and TIA patients we found a relatively high prevalence of PAF by 7 day HM, stressing the importance of careful cardiac evaluation of stroke patients at higher risk of PAF. Until firm data from large randomized controlled trials is available to guide us choosing the most cost-effective monitoring strategy, we recommend that prolonged cardiac rhythm monitoring should be offered to stroke and TIA patients with no obvious vascular aetiology.

ACKNOWLEDGEMENTS

Special thanks to study nurses Rie Ulrikke Nielsen, Janne Lise Vadgaard and Inge Quistgaard Nielsen for thorough manual assessment of the Holter recordings.

REFERENCES


