Clinically important atrial arrhythmia and stroke risk: a UK-wide online survey among stroke physicians and cardiologists

A.J. RANKIN1*, R.T. TRAN1*, A.H. ABDUL-RAHIM2, A.C. RANKIN3 and K.R. LEES2

From the 1Acute Stroke Unit, Western Infirmary Glasgow, G11 6NT, UK 2Institute of Cardiovascular and Medical Sciences, University of Glasgow, G12 8QQ, UK and 3School of Medicine, University of Glasgow, G12 8QQ, UK

*Joint first coauthors.
Address correspondence to A.J. Rankin Acute Stroke Unit, Western Infirmary Glasgow, Dumbarton Road, Glasgow, UK. email: alastair.rankin@nhs.net

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Summary

Background: A recording of ≥30 s is required for diagnosis of paroxysmal atrial fibrillation (AF) when using ambulatory electrocardiography (ECG) monitoring. It is unclear if shorter runs of atrial arrhythmia are relevant with regard to stroke risk.

Aim: To assess current management of patients with atrial arrhythmia of <30 s duration detected on ambulatory ECG.

Design: Online survey.

Methods: An online survey was sent to cardiologists and stroke physicians in the UK, via their national societies.

Results: A total of 205 clinicians responded to the survey (130 stroke physicians, 64 cardiologists, 11 other). Regarding diagnosis of AF, 87% of responders would accept a single 12-lead ECG. In contrast, only 45% would accept a single episode lasting <30 s detected on ambulatory monitoring. There was more agreement with regard to the decision to anticoagulate. When asked whether they would anticoagulate eight hypothetical patients with non-diagnostic paroxysms of AF, there was a mean agreement of responses of 78.6%, with up to 94.1% agreement for high-risk patients. There was a trend suggesting that stroke physicians were more likely to accept an atrial arrhythmia of <30 s as ‘AF’ than cardiology specialists [OR 1.63 (95% CI 0.88–3.01), P = 0.12].

Conclusions: There is a lack of consensus on the diagnosis and management of patients with brief runs of atrial arrhythmia detected on ambulatory ECG. Further research is needed to clarify the risk of stroke in this unique population of patients.

Introduction

Atrial fibrillation (AF) is a common and treatable independent risk factor for ischaemic stroke.1,2 With appropriate identification and treatment, the annual risk of recurrent stroke in patients with AF can be reduced by two-thirds.3 AF can be paroxysmal, persistent or permanent, and the natural history may progress through these stages. With regard to paroxysmal AF, the current European Society of Cardiology (ESC) guidelines advise that, when using ambulatory electrocardiography (ECG) monitoring for diagnosis, a recording showing the typical features of AF (i.e. ‘atrial arrhythmia with irregular ventricular response and absence of P waves’) lasting ≥30 s is required.4 However, it remains unclear if shorter runs of atrial arrhythmia detected on ambulatory ECG monitoring could also be relevant with regard to stroke risk. The risk of stroke from paroxysmal AF is the same as that seen in persistent disease.5 Accordingly, all patients
with AF (regardless of whether this is paroxysmal or persistent) should be considered for anticoagulation. Common risk predictor tools to aid this decision (e.g. CHA2DS2-VASc) do not include the duration or nature of AF in the calculation.6

The number of patients undergoing ambulatory ECG monitoring is increasing. Ambulatory 24–72 h ECG monitoring is now a routine investigation offered to patients discharged following ischaemic stroke.7 The detection rate of AF in ‘cryptogenic’ stroke is between 12 and 25%.8,9 The diagnostic yield of AF in this population increases further with increasing duration of ambulatory monitoring.10–15 A new diagnosis of AF is reached in an additional 2–4% of post-stroke patients for each additional 24-h period of ambulatory ECG monitoring.10,12 However, there is a subgroup of patients who are detected as having short runs of arrhythmia, which are electrocardiographically consistent with AF, but which do not fit the current diagnostic criteria for duration. Consequently these patients are diagnostically orphaned. There are insufficient data from existing studies to assess the risk of stroke in this situation. This gives rise to a clinical dilemma, should we anticoagulate these patients?

In the absence of trial evidence, the authors chose to survey specialist opinion in order to gauge current practice and to assess whether there is divergence of opinion among cardiologists and stroke specialists. ‘How are we currently managing patients who show features of AF on ambulatory monitoring but the duration of the paroxysm does not meet current diagnostic criteria?’

Methods

A questionnaire was created using the internet site ‘www.surveymonkey.com’. An online format was adopted in order to maximize response rate. There were nine questions in total (Table 1): two questions sought basic demographic data of the respondents; four were aimed at determining exactly what would satisfy each individual physician’s requirements for a diagnosis of AF; and three dealt with specific factors which would affect a physician’s decision to anticoagulate. All clinical questions were aimed at eliciting what clinicians do in practice, rather than questioning their knowledge of guidelines. As an evaluation of current practice among professional colleagues, ethical approval was not required and this was confirmed by the West of Scotland Research Ethics Committee.

The survey was distributed to members of the British Association of Stroke Physicians (BASP), the British Cardiovascular Society (BCS) and the Scottish Cardiac Society (SCS) along with a cover letter detailing the background of the project. BASP sent out an email to their mailing list with details of the survey, while BCS and SCS included a link to the survey in their respective newsletters during March 2014. Prospectively a target of 200 responses was set. After 4 weeks, the societies (BASP, BCS and SCS) were contacted again and asked to send out a reminder email. BASP and BCS both sent out reminder emails and the survey was closed 4 weeks later.

Descriptive statistics were produced for each question with calculation of odds ratios (OR) to assess interspecialty differences where appropriate. Reported ORs and the associated 95% confidence intervals (95% CIs) express the odds of respondents giving a specified answer based on their specialty. The ORs were calculated using binary logistic regression. Reported analyses were undertaken using SAS version 9.3 (SAS Institute, Inc., Cary, NC). Figures were created using Microsoft Excel 2007 Software (Microsoft).

Results

Demographics

A total of 205 responded to the survey invitation, with complete information available for 184. There were 120 (58.5%) responders who selected a stroke-related job description (99 consultant stroke physicians, 21 stroke trainees) and 64 (31.2%) with a cardiology-related job (44 consultant cardiologists and 20 cardiology trainees) (Figure 1). An additional 21 responders selected ‘other’, 10 of whom stated a special interest in stroke-medicine (8 neurologists, 1 stroke-rehabilitation specialist and 1 geriatrician) and were classified as stroke specialists for further analyses. Responders were distributed throughout the UK, with 136 selecting a city in England, 34 from Scotland and 35 other. Complete survey data were missing for 18 people who stopped the survey after the first page despite programming to try to ensure participants could not skip questions.

Electrocardiographic diagnosis of AF

A total of 179 (87.3%) of all responders stated that they would deem a 12-lead electrocardiogram showing features consistent with AF as sufficient evidence to support a diagnosis. When using ambulatory ECG monitoring, 92 (44.8%) participants reported that they would accept a single episode lasting <30 s (Figure 2), with 48 classifying even 0–10 s as sufficient (Table 2). The proportion of all responders accepting a diagnosis increased to 54.4% if the recording showed multiple episodes
Table 1  Survey questionnaire

1) Please select your job description?
   - Consultant stroke physician
   - Consultant cardiologist
   - Stroke trainee
   - Cardiology trainee
   - Other (please specify)

2) Regarding the diagnosis of AF, which of the following would you consider sufficient evidence to support a diagnosis of ‘paroxysmal AF’:
   (a) A single 12-lead ECG showing typical features of AF (‘atrial arrhythmia without P waves and with irregular ventricular response’) in a patient with no previous history of AF and who is now in sinus rhythm:
      - Yes
      - No
   (b) A 24-h ECG monitor showing a single episode of ‘atrial arrhythmia without P waves and with irregular ventricular response’ lasting:
      - 0–10 s
      - ≥11 s
      - ≥21 s
      - ≥30 s
   (c) A 24-h ECG monitor showing multiple episodes of ‘atrial arrhythmia without P waves and with irregular ventricular response’ which ‘cumulatively’ last:
      - <30 s (Yes/No)
      - ≥30 s (Yes/No)

3) If a 24-h ECG monitor shows episode an of ‘atrial arrhythmia without P waves and with irregular ventricular response’, but the duration is too short to meet your criteria, would you: (pick one)
   - Arrange repeat 24-h ECG monitoring
   - Arrange longer ambulatory ECG monitoring (e.g. 72 h Holter)
   - Take no further action
   - Depends on the patient
   - N/A (diagnosis already made)

4) All other factors being equal (e.g. CHA2DS2-VASc, HAS-BLED), does the duration of paroxysms of ‘atrial arrhythmia without P waves and with irregular ventricular response’ on an ambulatory ECG affect your decision to anticoagulate?
   - Yes
   - No

5) By current ESC guidelines, a paroxysm of atrial arrhythmia without P waves and with irregular ventricular response lasting <30 s is insufficient to be diagnostic of paroxysmal AF. In your clinical practice, would you consider anticoagulation treatment (assuming no contraindication) in a patient with a single run of ‘atrial arrhythmia without P waves and with irregular ventricular response’ of <30 s duration on ambulatory ECG if:
   - The patient is male and has a CHA2DS2-VASc score = 1. (Yes/No)
   - The patient has CHA2DS2-VASc score ≥ 2 but no previous stroke/TIA. (Yes/No)
   - The patient has had a recent ischaemic stroke for which no potential cause had been identified. (Yes/No)
   - The patient has had a recent TIA for which no potential cause had been identified. (Yes/No)

6) In your clinical practice, would you consider anticoagulation treatment (assuming no contraindication) in a patient with multiple runs of ‘atrial arrhythmia without P waves and with irregular ventricular response’ each of <30 s duration on ambulatory ECG if:
   - The patient is male and has a CHA2DS2-VASc score = 1. (Yes/No)
   - The patient has CHA2DS2-VASc score ≥ 2 but no previous stroke/TIA. (Yes/No)
   - The patient has had a recent ischaemic stroke for which no potential cause had been identified. (Yes/No)
   - The patient has had a recent TIA for which no potential cause had been identified. (Yes/No)

7) Please tell us the city in which you work.

8) Do you have any comments?
   The investigators welcome any comments or observations which you would like to highlight at this time. Please feel free to tell us why you selected any of the answers if you wish.
of arrhythmia (cumulatively lasting <30 s). There was no significant difference between cardiologists and stroke specialists with regard to the acceptance of a diagnosis of AF following a single episode of atrial arrhythmia lasting <30 s [OR 1.63 (95% CI 0.88–3.01), P=0.12]. Similarly, there was no difference in responses between trainees and consultants [OR 1.15 (95% CI 0.58–2.27); P=0.69].

When asked if 24-h ECG recording revealed an atrial arrhythmia of which the duration was too short to meet the responder’s diagnostic criteria, 88 (42.9%) responders would arrange a longer duration of ECG monitoring, whereas 74 (36.1%) stated that it would depend on the individual patient. The question was felt not applicable to 26 (12.7%) participants whose diagnostic criteria had already been met. The remaining participants would either arrange repeat 24-h monitoring (5.4%) or take no further action (2.9%) (Table 3).

**Decision to anticoagulate**

With regard to the decision to anticoagulate, 90 out of 187 (48.1%) stated that the duration of atrial

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**Table 2** Minimum duration of paroxysm required to satisfy diagnosis for a single episode detected on ambulatory monitoring

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Response count</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–10 s</td>
<td>23.4</td>
</tr>
<tr>
<td>≥11 s</td>
<td>16.6</td>
</tr>
<tr>
<td>≥21 s</td>
<td>4.9</td>
</tr>
<tr>
<td>≥30 s</td>
<td>55.1</td>
</tr>
</tbody>
</table>

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**Figure 1.** Proportion of responders by specialty.

**Figure 2.** Response analysis for diagnosis of ‘AF’.
arrhythmia captured on ambulatory monitoring affected their decision. There was no significant difference between stroke and cardiology specialists in this regard [OR 0.66 (95% CI 0.36–1.25), P = 0.21]. Figure 3 shows the response rates with regard to the decision to anticoagulate in eight different clinical settings. A total of 27 of 184 (14.7%) responders would anticoagulate a patient who was male with a CHA2DS2-VASc score of 1 if he had a single episode of atrial arrhythmia lasting <30 s detected by ambulatory monitoring. This increased to 74 (40.2%) responders if the ambulatory monitoring revealed multiple episodes (each lasting <30 s).

If the ambulatory recording showed a single episode of atrial arrhythmia, 81 (44.0%) responders would anticoagulate a patient with a CHA2DS2-VASc of 2 without previous cerebrovascular disease, 165 (88.2%) if the patient had suffered a recent cryptogenic ischemic stroke, dropping to 154 (82.4%) if symptoms had been only transient, i.e. transient ischaemic attack (TIA) rather than stroke. These figures increased to 132 (71%), 176 (94.1%), 170 (92.4%), respectively if the same hypothetical patients had multiple, rather than single, paroxysms of atrial arrhythmia captured. Overall, with respect to anticoagulation, there was a mean agreement of responses across the eight hypothetical situations of 78.6%. There was no difference between specialties in terms of the likelihood of anticoagulating a low-risk patient (CHA2DS2-VASc = 1) with a single episode of atrial arrhythmia detected [OR 2.00 (95% CI 0.70–5.70), P = 0.19].

Table 3 Percentage of responses for further investigation of non-diagnostic runs of atrial arrhythmia

<table>
<thead>
<tr>
<th>If a 24-h ECG monitor shows an episode of atrial arrhythmia without p waves and with irregular ventricular response, but the duration is too short to meet your criteria, would you:</th>
<th>Percentage</th>
<th>Response count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrange repeat 24-h ECG monitoring</td>
<td>5.4</td>
<td>11</td>
</tr>
<tr>
<td>Arrange longer ambulatory ECG monitoring (e.g. 72-h Holter)</td>
<td>42.9</td>
<td>88</td>
</tr>
<tr>
<td>Take no further action</td>
<td>2.9</td>
<td>6</td>
</tr>
<tr>
<td>Depends on the patient</td>
<td>36.1</td>
<td>74</td>
</tr>
<tr>
<td>N/A (diagnosis already made)</td>
<td>12.7</td>
<td>26</td>
</tr>
</tbody>
</table>

Figure 3. Response analysis of the attitudes towards anticoagulation depending on risk and ambulatory ECG profile.

Discussion
The results of this UK-wide online survey amongst stroke physicians and cardiologists indicate that
there is a lack of consensus with regard to how specialists manage patients who have short runs of atrial arrhythmia detected on ambulatory ECG monitoring. When an atrial arrhythmia that is electrocardiographically consistent with AF is detected on ambulatory monitoring, 45% of responders would accept a single episode lasting <30 s as being sufficient evidence to support a diagnosis. Similar division of opinion was reported with only 42.9% of the cohort in agreement with regard to the further investigation of these patients. There was no significant difference in responses between cardiologists and stroke physicians.

In keeping with current European guidelines, the majority of responders (87%) would accept a single 12-lead ECG as sufficient evidence to support a diagnosis of AF. A 12-lead ECG is 10 s long. It is unlikely that a 10 s paroxysm of arrhythmia is, in itself, sufficient to be thrombogenic. The critical duration of atrial arrhythmia that is required to increase stroke risk is not known. However, it is reasonable to assume that any atrial arrhythmia on a 12-lead ECG has been present for longer than 10 s in order for it to be captured on the recording. A similar assumption can be applied to short runs of atrial arrhythmia detected on ambulatory monitoring. Ambulatory monitoring has been shown to have a detection rate of between 2 and 6% for paroxysmal AF over a 24-h period. It is therefore conceivable that if the monitor detects a paroxysm of <30 s, then the same patient may have longer paroxysms outwith the monitored time period. This rationale is evident in the survey results, with an increase in the proportion of responders accepting a diagnosis if the patient has multiple, instead of single, short paroxysms detected. A recent trial by Kochhäuser et al. supports this logic, having shown that the presence of numerous short supraventricular premature beats is predictive of future AF in patients with cryptogenic stroke. However, extrapolating this reasoning to treatment is hypothetical rather than evidence based. No single study has looked at the stroke-risk associated with very short paroxysms of AF. Although paroxysmal and persistent AF have been shown to carry the same increased risk of stroke, the duration of paroxysmal episodes in the literature is much longer than those discussed here. In the study by Friberg et al., patients in the paroxysmal group could have episodes of atrial arrhythmia lasting up to 7 days. Healey et al. found patients with subclinical paroxysmal AF were 2.5 times more likely to have a stroke but had to have a minimum duration of 6 min of atrial tachycardia to be included. Interestingly, further work from the same group has shown a poor temporal relationship between paroxysms of AF and stroke; with only 35% of their cohort showing AF within 30 days prior to stroke. This study only recorded paroxysms of AF lasting >6 min and so raises the question if there might be a closer temporal relationship with shorter paroxysms.

Despite the disparity in clinicians’ individual diagnostic standards, there does appear to be more agreement in terms of clinical practice. When asked whether they would advise anticoagulation for eight hypothetical patients who have non-diagnostic paroxysms of AF detected on ambulatory monitoring there was a mean agreement of responses of 78.6%, with 94.1% agreeing that they would recommend anticoagulation for a patient who has had a recent ischaemic stroke for which no cause has been identified and is found to have multiple episodes <30 s on ambulatory monitoring. Likewise, 85.3% would not recommend anticoagulation if the patient was male with low risk (CHA2DS2-VASC = 1) and had only a single paroxysm detected on monitoring. This suggests that while the duration of paroxysmal episodes does influence a clinician’s decision to anticoagulate it is only one of many factors that they balance.

The results of this survey highlight a dilemma that commonly occurs in clinical practice and for which there is no existing evidence to guide management. The results reveal that even expert opinion is divided and so across the country patients are receiving inconsistent management for a condition in which both treatment (anticoagulation) and the omission of treatment carry the potential for serious morbidity and mortality. Further research in this area will however be challenging. The imprecision of ambulatory monitoring at detecting paroxysmal AF means that a large number of participants would be required to provide definite answers. Implantable cardiac monitoring devices, for example, implantable loop recorders, may be the way forward to detect paroxysmal AF in the long term but they require an invasive procedure with associated risk of complications such as infection, bleeding, discomfort etc. They also cost more than other non-invasive ambulatory methods.

An international effort to pool data from several completed international AF-detection trials in post-stroke/TIA setting is currently underway using the Virtual International Cardiovascular and Cognitive Trials Archive-AF, as a collaborative platform. The collaboration aims to combine available data to facilitate exploratory and epidemiological analyses of stroke recurrence risk and predictors associated with short atrial arrhythmias post-stroke.

The design of the survey has several limitations. Inherent to voluntary surveys there is the risk of self-selection bias—were clinicians with active interest
or agenda more likely to answer?—and social-desirability bias—did responders answer in a way that they feel they should answer rather than what they actually do? The survey was anonymized to try to minimize this bias. The multiple choice options for the clinical questions were not exhaustive and may have forced a participant to reply in an unrepresentative or over-simplified manner. For instance, in the comments section, several clinicians alluded to the distribution of ischaemic stroke influencing their decision to anticoagulate in borderline patients, with factors such as bi-hemispheric distribution, large vessel vs. small vessel disease and the presence of carotid disease being taken into account. For the purpose of the survey, all clinical questions assumed no contraindication to anticoagulation; however, we realize this is an oversimplification and in clinical practice there are many relative contraindications that make this decision more complex.

The cohort of responders was small and therefore may not be representative of the wider population of specialists. There may have been crossover in membership between SCS and BCS members; however, we think the risk of duplicate submissions is negligible. There was a far greater response rate amongst stroke specialists than cardiologists, with 130 stroke specialists and 64 cardiologists completing the survey from potential pools of 597 BASP members and 2500 BCS members. This may imply a more active interest in this topic amongst stroke physicans, but there are many confounding variables including the different methods by which the survey was distributed to the two groups (BASP sent a specific email to its membership whereas BCS and SCS included a link in their weekly newsletters). There was no significant difference in responses between the cardiologists and stroke physicians. However, there was a trend that stroke physicians were more likely to accept a diagnosis of <30 s of arrhythmia and were more likely to advise anticoagulation for lower risk patients. Given the small data set we cannot exclude the possibility of a type I error. By definition, stroke physicians are more likely to treat patients with AF for secondary prevention of stroke, rather than primary prevention. The absolute risk reduction achieved from anticoagulation in patients with AF is greater in secondary prevention, while the risk of harm is similar in both groups.\textsuperscript{3,20} This could account for any trend towards lower thresholds of treatment amongst stroke physicians.

In conclusion, there is a lack of consensus among specialists with regard to the diagnosis and further investigation of patients who are detected as having short runs of atrial arrhythmia on ambulatory ECG monitoring. This is an area of clinical importance in that both treatment and the withholding of it have the potential for significant morbidity and mortality. In spite of the lack of evidence, there does appear to be more agreement in terms of managing patients at the extreme ends of the risk profile, but the management of intermediate risk patients is much more variable. Further research is needed to clarify the risk of stroke and facilitate guideline development for this unique population of patients.

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