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Short runs of atrial arrhythmia and stroke risk: a European-wide online survey among stroke physicians and cardiologists

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ABSTRACT A recording of ≥ 30 seconds is required to diagnose paroxysmal atrial fibrillation when using ambulatory ECG monitoring. It is unclear if shorter runs are relevant with regards to stroke risk.
Methods An online survey of cardiologists and stroke physicians was carried out to assess current management of patients with short runs of atrial arrhythmia within Europe.
Results Respondents included 311 clinicians from 32 countries. To diagnose atrial fibrillation, 80% accepted a single 12-lead ECG and 36% accepted a single run of < 30 seconds on ambulatory monitoring. Stroke physicians were twice as likely to accept < 30 seconds of arrhythmia as being diagnostic of atrial fibrillation (OR 2.43, 95% CI 1.19–4.98). They were also more likely to advocate anticoagulation for hypothetical patients with lower risk; OR 1.9 (95% CI 1.0–3.5) for a patient with CHA_2DS_2-VASc = 2.
Conclusion Short runs of atrial fibrillation create a dilemma for physicians across Europe. Stroke physicians and cardiologists differ in their diagnosis and management of these patients.

KEYWORDS atrial arrhythmia, detection, online survey, stroke

DECLARATION OF INTERESTS KRL is chairman of the independent data monitoring committee for the ESUS-RESPECT trial sponsored by Boehringer Ingelheim, and has received grant support for research into post-stroke AF detection from the Chief Scientist Office for Scotland.

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INTRODUCTION

Atrial fibrillation (AF) is a risk factor for ischaemic stroke, independent of whether the condition is permanent, persistent or paroxysmal.[1] The diagnosis requires consideration of long-term oral anticoagulant use as stroke thromboprophylaxis. For an electrocardiographic diagnosis of AF on ambulatory monitoring, the European Society of Cardiology advises that a recording showing typical features of AF lasts ≥ 30 seconds.[2] The clinical significance of shorter runs of atrial tachyarrhythmia (i.e. those lasting < 30 seconds), which electrocardiographically resemble AF, is unknown.

There is increasing interest in asymptomatic AF and stroke. These 'occult'[3] or 'silent'[4] AF episodes are thought to confer a significant stroke risk, but may have gone undetected by conventional investigation. A recent review concluded that silent AF is found in approximately 30% of patients with cryptogenic stroke.[4] However, in line with guidelines, the majority of studies included required a recording ≥ 30 seconds for a diagnosis of AF. A major factor in the selection of this threshold may be the use of algorithms for automated detection of AF that demand a certain number of R-R intervals to assess variability with sufficient confidence to trigger the diagnosis, rather than on clinical grounds alone.

There is no evidence to suggest that a run of AF lasting > 30 seconds is more important than a shorter episode. Binici et al. found that the risk of death or stroke in previously healthy individuals was significantly higher in those with 'excessive supraventricular ectopic activity'.[5] Furthermore, Kochhäuser et al. demonstrated that numerous runs of supraventricular premature beats are predictive of future AF in patients with cryptogenic stroke.[6] However, no consensus exists as to how such ambulatory ECG findings should be investigated, diagnosed and managed.

This clinical dilemma was highlighted in a recent survey of stroke physicians and cardiologists within the UK, which explored current management of patients with short runs of atrial arrhythmia suggestive of AF on

ambulatory ECG monitoring.[7] However, the findings may be limited and relevant to the standard of practice in the UK only. In this study, we aimed to evaluate and compare clinical practice relating to the short runs of atrial arrhythmias and the perception of stroke risk among stroke physicians and cardiologists across Europe.

METHODS

Survey questionnaire

A survey questionnaire was created using Survey Monkey (www.surveymonkey.com). This comprised 12 questions: three to define basic demographic data for respondents; four to determine each respondent's diagnostic criteria for AF; two to establish their current practice regarding the investigation of possible AF following ischaemic stroke; and three to investigate specific factors that would influence a physician's decision to start oral anticoagulant treatment (Appendix 1, available with the online version of this paper). All questions required an answer to complete the survey, with space for optional additional comments at the end. The aim was not to assess physicians' knowledge of clinical guidelines, but rather to elicit what clinicians do in their daily practice. For the purposes of the survey, electrocardiographic findings suggestive of AF were defined as 'atrial arrhythmia without p waves and with irregular ventricular response'.

The online survey was opened on 3 December 2014 and a link to the survey was emailed to national and European societies for cardiology and stroke medicine, along with a cover letter providing additional information. The survey link was included in the electronic newsletters of the European Society of Cardiology, the European Stroke Organisation and the AF Association. In order to maximise the response rate, national cardiac and stroke societies affiliated with the above European organisations were emailed directly (59 and 31 societies, respectively). A reminder email was sent in March 2015. Positive responses were received from the following national societies confirming the distribution of the survey to clinicians within their organisation: Danish Stroke Society, Italian Stroke Organization, Swedish Society of Cardiology, Israel Working Group on Cardiac Pacing and Electrophysiology of the Israel Heart Society, Belgian Heart Rhythm Association, and Belgian Society of Cardiology. The survey was closed on 1 May 2015. Ethical approval for the survery study was granted from the Ethics Committee of the Medical, Veterinary and Life Sciences College, University of Glasgow, UK.

Data analysis

The results of the completed online survey were downloaded and descriptive statistics were produced for each question. Pearson Chi-Squared analysis was used for categorical data. Odds ratios (OR) were calculated using binary logistic regression. Reported OR and the associated 95% confidence intervals (95% CI) expressed the odds of respondents giving a specified answer based on their specialty, with respondents who expressed a dual interest in 'both stroke medicine and cardiology' being excluded from analyses. The concordance for the decision to start oral anticoagulant treatment (based on eight hypothetical cases) between clinicians in stroke versus cardiology specialties was quantified by Cohen's kappa coefficients.[8] In view of unequal numbers in the two specialties, a sample of individuals from the larger specialty were selected at random to produce comparable pairs to test the agreement, with individual answers from the eight hypothetical scenarios being analysed sequentially. Analyses were undertaken using IBM SPSS (V22.0, New York), SAS version 9.3 (SAS Institute, Inc., Cary, NC, USA) and Microsoft Excel 2011 (Microsoft, USA).

RESULTS

Demographics

A total of 311 clinicians completed the survey, of whom 223 (72%) had a special interest in stroke medicine, 52 (17%) in cardiology and 36 (12%) in both stroke medicine and cardiology. The majority of responders, 265 (85%), had completed specialty training. Responders came from 32 countries across Europe. The three countries that contributed the most responses were Germany 74 (24%), UK 46 (15%) and Turkey 44 (14%).

Electrocardiographic diagnosis of AF

A total of 250 (80%) stated that they would accept a single 12-lead ECG showing features consistent with AF as sufficient evidence to support a diagnosis. When using ambulatory monitoring, 111 (36%) would accept an episode of 'atrial arrhythmia without p waves and with irregular ventricular response' lasting less than 30 seconds to support a diagnosis of AF. This rose to 188 (61%) if multiple episodes of under 30 seconds' duration were detected. The minimum duration of a single episode to support a diagnosis varied widely, with 64 (21%) accepting an episode of 1–10 seconds on ambulatory monitoring, while 17 (6%) demanded greater than 2 minutes to meet their diagnostic threshold. Stroke physicians were twice as likely as cardiologists to accept < 30 seconds of atrial arrhythmia as being sufficient to diagnose AF (OR 2.4, 95% CI 1.2—5.0).

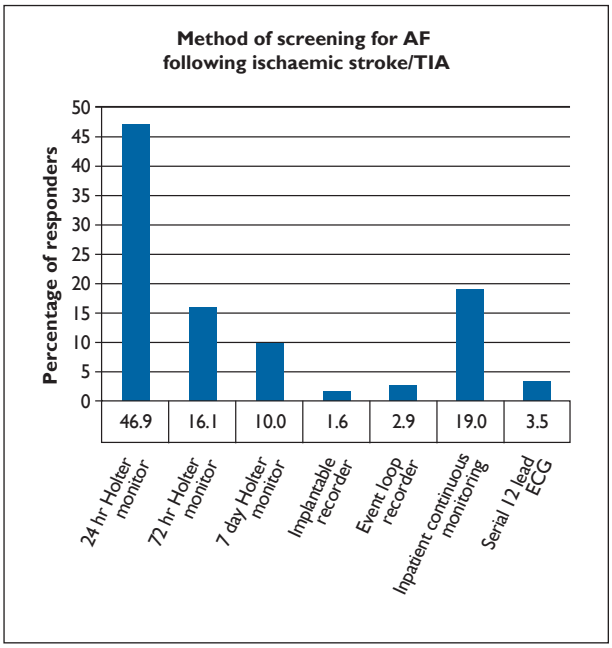

FIGURE 1 Current methods for screening for AF following ischaemic stroke/TIA

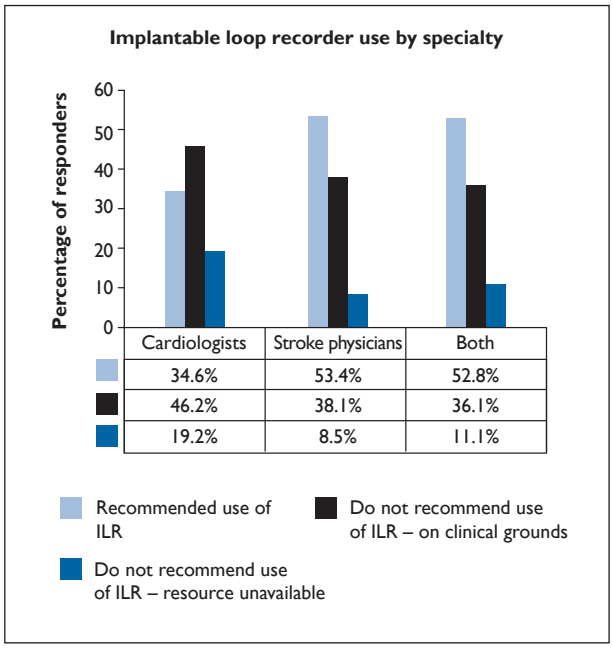

FIGURE 2 Use of implantable loop recorders by specialty

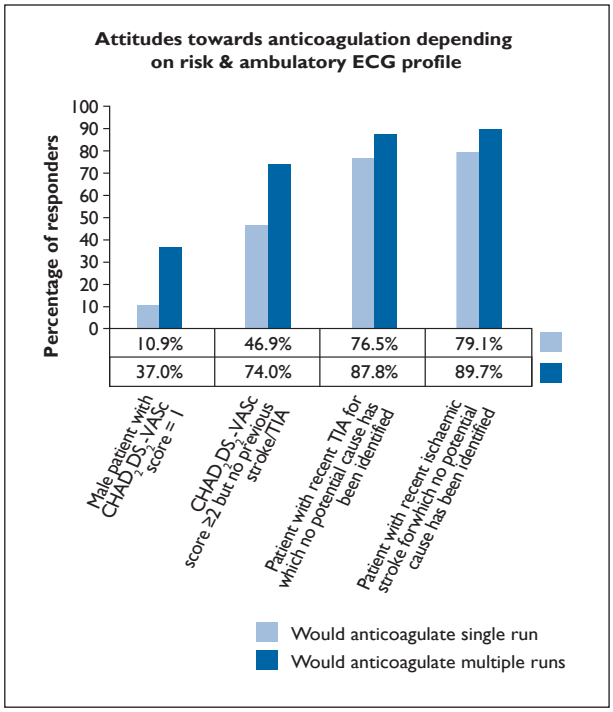

FIGURE 3 Response analysis of the attitudes towards anticoagulation depending on risk and ambulatory ECG profile

In the event that 24 hour ambulatory ECG monitoring revealed an episode of possible AF but the duration was too short to meet the responder's diagnostic threshold, the majority (175; 56%) would arrange longer ambulatory monitoring.

Screening for AF after ischaemic stroke or TIA

The most commonly reported method for screening for AF following ischaemic stroke or transient ischaemic attack (TIA) was ambulatory ECG, as shown in Figure 1. Table 1 shows the most popular method reported by country.

The use of implantable loop recorders for the investigation of suspected AF

A total of 278 (89%) advocated the use of implantable loop recorders (ILR) for investigation of suspected AF in selected patients, but only half of the responders were currently using implantable devices in clinical practice. A third stated that the resource was not available. The remaining responders would not use ILRs in this setting based on clinical grounds (Figure 2). The use of ILRs varied by country (Table 1). In comparison to cardiologists, stroke physicians were 2.6 times more likely to advocate the use of ILRs on clinical grounds for the detection of AF in selected patients (OR 2.6, 95% CI 1.1–5.9).

Decision to start anticoagulant treatment as stroke prevention

With regards to the decision to start anticoagulant treatment, 132 (42%) said the duration of atrial arrhythmia detected on ambulatory monitoring would affect their decision. Figure 3 shows the response rates for the decision to commence anticoagulant treatment in eight hypothetical clinical settings. Overall, there was a mean agreement of responses of 77% across the eight clinical scenarios.

When comparing the decision of starting oral anticoagulant treatment by cardiologists and stroke physicians across the eight clinical scenarios, there was a

TABLE 1 Results by country

Country	n	% stroke physicians	% who accept 12-lead ECG	% who accept < 30 seconds on ambulatory monitoring	Most common method used to screen for AF post-stroke	% who currently use ILR for detection of possible AF post-stroke
Germany	73	85	84	49	24-hr Holter	95
UK	45	58	71	38	24-hr Holter	27
Turkey	44	98	68	46	24-hr Holter	21
Belgium	26	39	85	31	24-hr Holter	62
Denmark	14	50	100	14	Inpatient continuous monitoring/72-hr Holter	57
Italy	12	92	67	25	Inpatient continuous monitoring	67
Hungary	10	10	90	30	24-hr Holter	30
Poland	9	0	100	22	24-hr Holter	11
Switzerland	8	100	75	25	7-day Holter	50
Portugal	7	100	86	29	24-hr Holter	57
Spain	7	71	86	14	Inpatient continuous monitoring	29
Slovenia	6	83	83	33	24-hr Holter	33
Netherlands	5	80	100	60	24-hr Holter	40
Finland	5	80	80	40	24-hr Holter	40
Other (< 5 responses)*	40	78	83	20	24-hr Holter	35

*Other countries include: Albania, Australia, Austria, Belgium, Bulgaria, Costa Rica, Estonia, France, Georgia, Greece, Indonesia, Israel, Latvia, Luxembourg, Norway, Philippines, Republic of Ireland, Romania, Russia, Serbia, Sweden, Ukraine, USA, United Arab Emirates

'fair agreement' in responses (Kappa = 0.38 (95% CI 0.29–0.47); p <0.001). For six of the eight hypothetical patients there was no difference between the two specialties. However, stroke physicians were more likely to advocate long-term anticoagulation for two of the lower risk patient examples. Stroke physicians were almost three times more likely to initiate oral anticoagulants for a male patient with a CHA_2DS_2-VASc score of 1, if they had multiple short episodes of arrhythmia on ambulatory monitoring (OR 2.7, 95% CI 1.3–5.7). Stroke physicians were also twice as likely to start anticoagulant treatment for a patient with a CHA_2DS_2-VASc score of 2 but with no previous stroke, if their ambulatory monitoring showed a single episode of atrial arrhythmia lasting < 30 seconds (OR 1.9, 95% CI 1.0–3.5).

DISCUSSION

The results of this European-wide survey highlight the clinical dilemma faced by stroke physicians and cardiologists with regards to investigation and management of patients with short runs of atrial arrhythmia.

These results mirror those of a recent survey among physicians in the UK, which found a lack of consensus on diagnosis and management of this subgroup of patients.[7] In comparison to the previously reported UK cohort, diagnostic thresholds were similar: 80.4% would accept a single 12-lead ECG as diagnostic of AF whereas only 35.7% would accept a single run of atrial arrhythmia resembling AF lasting < 30 seconds. The corresponding figures from the UK-wide survey were 87.3% and 44.8%, respectively. However, within the European cohort there were significant differences between stroke physicians and cardiologists that were not detected in our previous survey.[7] For instance, stroke physicians were twice as likely to accept a run of arrhythmia lasting < 30 seconds as diagnostic of AF, and were also more likely to advocate a long-term oral anticoagulant for some lower risk patient categories. The current survey also adds information regarding the views and utilisation of ILRs to screen for AF, with the majority (89.4%) of responders supporting their use on clinical grounds, but far fewer (50.2%) using them in current clinical practice due to resource constraints.

The results of this survey are produced at a time when there is much debate surrounding the clinical importance of both the frequency and duration (i.e. burden) of atrial arrhythmia episodes with regards to stroke risk. Some data suggest a positive relationship between increasing AF burden and risk of thromboembolic stroke.[9,10] Conversely, data from recent trials suggest a poor temporal relationship between AF and stroke.[11–13] In a subgroup analysis of data extracted from the TRENDS study, only 27.5% of participants who went on to develop an ischaemic stroke had had an episode of AF within a month prior to suffering a stroke;[11] the corresponding figure from the ASSERT trial was 15.4%.[12] However, both these studies required participants to have an atrial arrhythmia lasting a minimum of 5 minutes to be included in the primary analysis.[10,11] The question remains as to whether there exists a closer temporal relationship of stroke with shorter runs of atrial arrhythmia. Runs of AF lasting < 30 seconds are thought to predispose to AF and contribute to stroke risk.[5,6,14,15] A recent systematic review and meta-analysis has shown that these brief paroxysms are also common in the early days post-stroke.[16] Therefore, it may be that the studies that require longer periods of AF for inclusion do not give an accurate representation of the relationship between AF burden and stroke risk.

The minimum duration of AF used within trials is often based on technical failings of detection algorithms rather than on scientific grounds. Indeed, these failings are a major factor in the choice of the 30 second threshold that the European Society of Cardiology advises for ECG diagnosis of AF. The algorithms used by automated detection mechanisms demand a minimum number of R-R intervals to assess variability with enough confidence to deliver a diagnosis of AF. Thus, the threshold depends on a low sensitivity test; a new, higher sensitivity approach may prompt different guidance.

While use of implantable recording devices to detect AF post-cryptogenic stroke offer the most comprehensive means of detection, they are invasive and, as the results of this survey have shown, prohibitively expensive in some countries. Randomised trials are currently examining the use of non-vitamin K antagonist oral anticoagulants versus antiplatelet therapy as a potential alternative to exhaustive AF screening.[17,18] These studies assume that many cryptogenic strokes are embolic in nature and therefore potentially justify treatment. While the treatment effect of anticoagulants for patients in sinus rhythm is not known, positive outcomes in these trials may reduce the need for expensive and invasive monitoring. However, it may be more cost-effective and ethically justifiable to perform more rigorous screening for AF.

The majority of respondents to this survey accepted a single 12-lead ECG as diagnostic of AF – the assumption being that in order for such a finding to be revealed on a 10 second recording, the abnormal rhythm is likely to be present more permanently. Extrapolating this further, it is not unreasonable to assume that, if a short run of AF is picked up on a 24-hour Holter monitor, longer paroxysms may be present outwith the monitored period. Indeed, a number of recent clinical trials using advanced technology to detect AF have demonstrated that the prevalence of AF post-cryptogenic stroke is significantly higher than previously thought, and in particular that longer periods of monitoring significantly increase the diagnostic yield of AF.[19–21] Current clinical practice seems to be aligned with this evidence, as demonstrated by 56% of responders choosing to arrange longer ambulatory monitoring if initial 24-hour monitoring is suggestive, but not diagnostic of AF. However, with the pick-up rate for 24-hour Holter monitoring being as low as 3.2% at 30 days,[20] the rationale behind guidelines recommending 24-hour monitoring as a first line screening tool, as selected by 47% of respondents to the current survey, is called into question. There is a suggestion that it may be sensible for guidelines to recommend a longer minimum period (e.g. 72-hour or 7-days) of monitoring as the standard approach.

This survey highlights that the clinical dilemma faced by physicians is not unique to the UK. It included a larger number of physicians across a wider geographical area than the previous survey, and reiterates the need for further trial evidence in this area. This study has a number of limitations, some of which are inherent to the online survey approach.[7] Despite the survey being sent to many national and international stroke and cardiology societies, the response rate was low, with small numbers from many countries, and no responses from others. We are not able to provide a definitive number of non-responders, but acknowledge that given the size of the societies contacted, this number is likely to be large. Over half (53%) of the responses came from three countries. The results, therefore, are not necessarily applicable to Europe as a whole, neither are they necessarily representative of the populations of stroke or cardiology doctors in their respective countries. A greater proportion of responders (72%) were stroke physicians, who encounter this problem daily and see the consequences of incorrect decisions. Stroke physicians are also more likely to see patients with AF for secondary prevention of stroke, whereas cardiologists commonly manage patients with AF in the lower risk setting of primary prevention. This difference in risk profile between the two populations of patients could explain the differences in attitudes between the two specialties. The degree of investigation required to satisfy clinicians that 'no cause had been identified' for a recent TIA/ischaemic stroke is likely to vary between centres. We specifically avoided a prescriptive approach on what would be sufficient evidence to call a stroke cryptogenic to allow assessment of the responders'

current clinical practice. The information provided is consistent with the level of detail in guidelines.

In conclusion, short runs of AF create a clinical dilemma for physicians across Europe. There is significant variation between cardiologists and stroke physicians with regards the diagnosis and management of patients with short runs of atrial arrhythmia, meaning that the same patient will be treated differently depending on which specialist that they see. The exact relationship between short runs of AF and stroke risk remains unknown and further research is required to allow guideline development for this clinically important population who are presently deprived of optimal thromboprophylaxis.

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