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Searching for atrial fibrillation post-stroke with prolonged monitoring: Do it early, but should we be looking for something else?

Performing extended monitoring for atrial fibrillation (AF) in a general, untargeted population, is widely contentious, as the cases of subclinical AF identified in this manner generally have low stroke risk, and as such is not recommended in guidelines [1]. Extended monitoring following stroke, particularly cryptogenic (CS) or embolic stroke of unknown source (ESUS), is less contentious as these subclinical AF cases have a much higher stroke recurrence rate so treatment with oral anticoagulants (OAC) would be recommended. The highest yield of AF occurs when monitoring is performed very early after stroke, i.e., during the stroke admission or soon after discharge. Most stroke management guidelines recommend early monitoring for AF and a 24-hour Holter monitor, though more recently Holter monitoring of at least 72-hours has been recommended [1,2].

The timing of monitoring is crucial, as identification that AF was the likely cause of stroke will change treatment from antiplatelets to oral anticoagulants. Early monitoring in the stroke unit is not always possible, but when nurses do monitor for AF systematically, a higher rate of AF detection than usual care is observed [3]. Unfortunately, even in high income countries where telemetry is available, ECG monitoring is not always performed, often due to patients being absent for multiple investigations including imaging. If telemetry is performed, stroke unit nurses and even medical staff may not be experienced in arrhythmia diagnosis. Furthermore, although standard practice is a 24-hour Holter performed after discharge, only ~25% of patients receive this [3,4]. Thus, many cases of paroxysmal AF go unrecognised in this crucial early post-stroke period.

Post-discharge outpatient mobile telemetry is not common practice in many countries, and implanted monitors are expensive and infrequently used after CS and ESUS, and may be implanted relatively late after stroke. In CRYSTAL-AF, monitors were implanted a mean of 3 months post-stroke and found 8.9% of AF over 6 months [5]: if monitoring had begun at month 0, the incidence of AF detected may have be much higher. When comparing studies of incidence of new AF post-stroke by ECG devices, it is crucial to know how long after stroke monitoring commenced, and whether additional monitoring such as inpatient telemetry or Holter-monitoring was also performed earlier. There will be a much higher AF incidence if monitoring was commenced early, and an artificially lower incidence with late commencement, or if extended inpatient ECG monitoring has not occurred.

The meta-analysis by Noubiap et al in this issue of the journal [6] nicely illustrates that the yield of AF identified from implanted monitors (ICM), or outpatient telemetry increases as the duration of monitoring increases. In the meta-analysis, half the AF cases with ICM were found in the first 6-months, but the imprecision of timing from stroke to commencement of monitoring makes this figure unreliable. The authors were therefore unable to determine the true relationship of time to AF detection and the duration of monitoring, due to the lack of information in most of the included studies on when ECG monitoring started after stroke, a limitation of the data. This could cause underestimation of the sharp rise in early incidence if monitoring was started weeks or months after stroke.

People with AF identified in the first 6-months to 1-year after stroke have a high recurrent stroke risk, and higher than the risk of subclinical AF identified in a non-stroke population with implanted devices [7]. AF found on longer monitoring, up to 2–3 years after stroke, may not necessarily be related to the index stroke, but may be relevant to future stroke risk. However, in these cases, atrial myopathy may have caused the stroke without the paroxysmal AF being present at the time. A number of studies which examined the temporal relationship between subclinical AF found on cardiac implanted electronic devices and stroke found that in most cases there is no close relationship [8]. Therefore, AF may be more a marker of the atrial myopathy which underlies cardio-embolism than just a risk factor, which could explain the appearance of the marker some years post-stroke [9]. This may be the reason why a proportion of ESUS and CS could be due to cardio-embolism even without AF. In their review, Noubiap et al showed that higher rates of subclinical AF are identified in ESUS compared to CS (22% vs 14.2% at 6-months) [6]. This was confirmed in the recent study by Kitsiou et al who followed patients with ESUS for 3-years, finding 41% with subclinical AF and a much higher stroke recurrence of 23% [10].

Of course, ESUS can also occur from non-stenosing plaque in the aorta or great vessels, rather than cardio-embolism. While blood stasis in the fibrillating left atrium is the usual explanation for cardio-embolism in AF, we need to recall that a combination of the three factors according to the classical Virchow's can play an important role: these are blood hypercoagulability, stasis of blood flow, and endothelial injury which may result from atrial myopathy or atherosclerosis in the great vessels. Both endothelial injury and blood stasis may occur from atrial myopathy, potentially without AF being present, and if combined with hypercoagulability could lead to stroke. Although the RE-SPECT ESUS and NAVIGATE ESUS trials showed no benefit in giving OAC to all patients with

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ESUS [11,12], a post-hoc analysis of NAVIGATE found that OAC benefitted those with left atrial diameter >4.6 cm but no clinical AF (stroke hazard ratio 0.26) [13]. The prospective, randomised ARCADIA trial is currently investigating whether anticoagulation post-ESUS in those with some evidence of atrial myopathy but no AF will prevent recurrent stroke [14].

Noubiap et al also identified an association between the yield of new AF on monitoring and CHA_2DS_2-VASc scores [6]. The vascular factors that comprise the CHA_2DS_2-VASc score are also factors potentially closely related to atrial myopathy, and some may also have an effect on coagulability. This further supports the premise that AF is more a risk marker of atrial myopathy than a risk factor, requiring a search for atrial myopathy after ESUS. Many of the tests required to diagnose atrial myopathy are commonly performed post-stroke, including, ECHO ECG, and blood biomarkers like NTPro BNP, or even artificial intelligence analysis of the standard 12-lead ECG [15]. Finding such markers would facilitate OAC prescription if ARCADIA is positive. Alternatively, the presence of atrial myopathy could be used to determine who needs further ECG monitoring, and guide the intensity of such monitoring [2,9], with either prolonged wearable technology or insertable devices before discharge from hospital, rather than waiting for weeks to months to implant cardiac monitors when no other cause of the stroke has been identified.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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