Avoiding Stroke: A Continuous Monitoring Challenge

Jakub Gumprecht^{a, c} Magdalena Domek^{a, d} Andrew M. Hill^{a, e}
Gregory Y.H. Lip^{a–c}

^aLiverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool Heart and Chest Hospital, Liverpool, UK; ^bAalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark; ^cDepartment of Cardiology, Congenital Heart Diseases and Electrotherapy, Medical University of Silesia, Silesian Centre for Heart Diseases, Zabrze, Poland; ^dDepartment of Internal Diseases, Diabetology and Nephrology, Medical University of Silesia, Zabrze, Poland; ^eSt. Helens and Knowsley Teaching Hospitals, Whiston, UK

Stroke is a leading cause of death and disability worldwide. Risk factors such as advancing age, hypertension, cigarette smoking, atrial fibrillation (AF), diabetes mellitus and prior cardiovascular disease [1, 2] are well established and provide significant opportunities through public health policy to reduce both the disease burden and the socio-economic cost of stroke care [3]. In approximately 30% of cases, the aetiology is undetermined despite standard investigations [4]. A proportion of these cryptogenic events will be induced by paroxysmal, “silent” AF. However, establishing the relative burden of silent paroxysmal AF upon stroke risk has been challenging, particularly as continuous cardiac monitoring has developed faster than the ability to contextualise the findings upon stroke risk [5]. The minimum duration of arrhythmia detected on prolonged monitoring considered clinically significant enough to influence ischemic stroke risk is unclear. Current American Heart Association guidelines recommend a threshold of 30 s for diagnosis of AF, with attention to temporal AF burden aggregation: the concept that a patient with a small number of prolonged episodes of AF has a higher AF density than one with many brief episodes [6].

Premature atrial contractions (PAC), previously thought to be benign, may also increase ischemic stroke risk. Several studies have shown the relationship between excessive PACs and an increased risk of ischemic stroke

[7–9]. A systematic review and meta-analysis based on 11 studies revealed that frequent PACs were associated with a significantly raised risk of stroke and mortality (risk ratio 1.41, 95% CI 1.25–1.60; risk ratio 2.17, 95% CI 1.13–1.41, respectively) [10]. In line with those results, the findings from a UK case-control study involving 461 patients with ischemic stroke or transient ischemic attack (TIA) also revealed an independent association of excessive PACs burden and ischemic events among individuals without prior AF history [7]. After adjusting the analysis for other common risk factors, the excessive number of PACs, defined as ≥ 200 PACs/24 h, proved to be the superior risk factor for the cryptogenic stroke subtype (OR 1.95; 95% CI 1.16–3.28) [7]. One possible rationale might be the presence of an atrial myopathy with the electroanatomical changes of the left atrium influencing slower conduction velocities or lower atrial voltages [7].

Although the association between PACs and stroke prevalence has been proven, selecting the optimal method of arrhythmia detection is challenging. Traditional clinical practice of 24 h ECG monitoring after stroke or TIA has a low detection rate; increasing this to 72 h or 7 days improves this but still has low sensitivity for shorter episodes of paroxysmal AF or PACs. Prolonged monitoring using standard Holter-ECG devices is likely to be poorly tolerated, causing skin irritations and being strictly dependent

on patients' compliance [12]. Hence, long-term non-invasive monitoring may provide a solution to the problem.

In this issue of the journal, Todo et al. [13] demonstrate an association of excessive PACs detected by the implantable cardiac monitor (ICM) with the new-onset AF following cryptogenic stroke among 66 Japanese patients. The analysis also indicated that in patients with frequent PACs, the time between the ischemic event and establishment of an AF diagnosis was substantially lower. Hence, if we look longer, look harder and with more sophisticated ways, our detection of AF will be correspondingly increased.

The CRYSTAL-AF study, which compared the standard approach of 24 h Holter-ECG monitoring versus ICM after cryptogenic stroke, also confirmed the significant superiority of ICM-arm in AF detection (30 vs. 3.0% in 36 months), emphasizing the need for long-term monitoring [14, 15]. This type of implantable heart electrical activity monitor provides the opportunity of thorough ECG analysis of automatically detected arrhythmias or those indicated by the patients themselves. Thus, an ICM may constitute an accurate and effective diagnostic tool in patients at high risk of cryptogenic stroke [16].

Also, ICM implantation is an invasive procedure carrying the risk of complications. Therefore, it should be considered in patients where the clinical suspicion of AF is high, non-invasive approaches have been considered and a comprehensive risk-benefit ratio assessment has been undertaken.

By comparison, wearable devices (including bands, smartwatches or smartphone apps) offer non-invasive long-term cardiac monitoring and are consumer-purchased rather than medically directed devices. Studies of wearables by Apple [17] and Huawei [18] into their wearable devices demonstrate positive predictive values of 0.84 and 0.91, respectively, for detecting AF when used in conjunction with ECG patches. However, their sensitivity across an asymptomatic population is low, and detection of more complex arrhythmias is limited. Whilst these offer promising approaches for the future, the threshold by which these could be considered medical devices has not yet been reached.

Various types of wearable external loop recorders in the form of jackets, vests or belts have also been developed [8, 19]. They allow a non-invasive prolonged assessment of at least two ECG recording leads, which considerably improves the arrhythmia detection efficiency. A sub-analysis from EMBRACE trial revealed the increase in AF detection rate up to 40% in individuals with $\geq 1,500/24$ h PACs during 90 days of cardiac tracking using the ECG-belt compared to standard care [8].

According to the AF-SCREEN International Collaboration, a pathway that combines the current routine-care approach of 24 h monitoring and intensive ECG monitoring for at least 72 h allows detecting the new-onset AF in around 25% of patients with cryptogenic stroke [20]. The timespan might then be extended up to 90 days of monitoring using wearable non-invasive devices in patients without documented arrhythmia [8, 20].

In patients where ischemic stroke or TIA has already occurred, the treating clinician must balance the probability of cardiac arrhythmia being the cause of the underlying event, taking into account the stroke subtype, and utilizing predictive tools such as the C₂HEST score when considering the best strategy for detection of arrhythmia and the significance of any findings [21]. It is worth noting that there is currently no evidence supporting anticoagulation therapy in patients with cryptogenic stroke but without ECG-documented arrhythmia nor with atrial myopathy only [11]. Prolonged monitoring aiming at an increase in the rate of AF detection seems to be a comprehensive and holistic approach to improve stroke prevention.

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Statement of Ethics

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