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Straw, S orcid.org/0000-0002-2942-4574 and Witte, KK orcid.org/0000-0002-7146-7105 (2021) Closing the loop: Delivering personalised care for patients with cryptogenic stroke. International Journal of Cardiology, 327. pp. 100-101. ISSN 0167-5273

https://doi.org/10.1016/j.ijcard.2020.11.034

This editorial refers to “Real-world experience with implantable loop recorder monitoring to detect subclinical atrial fibrillation in patients with cryptogenic stroke: the value of p wave dispersion in predicting arrhythmia occurrence” by Russo et al., published in the *International Journal of Cardiology* (2020).

Rhythm matters

Atrial fibrillation (AF) is a modifiable risk factors for stroke, which increases the risk to patients five-fold compared to those with sinus rhythm. Stroke caused by AF is associated with higher morbidity, mortality and longer hospital stays compared to other subtypes. In clinical practice the aetiology of around 40% of ischaemic strokes remains unknown, with observational studies confirming subclinical AF as a major cause of ‘cryptogenic stroke’ (CS). Clinical trials show us that oral anticoagulation is superior to antiplatelet therapy, greatly reducing the incidence of stroke in patients with documented AF. On the other hand, we also know that a non-targeted application of anticoagulation for CS does not reduce the rate of recurrence compared to aspirin therapy, and is associated with significantly more bleeding, regardless of whether vitamin K antagonists or direct acting oral anticoagulants are used.[1,2]

Accurate diagnosis is therefore crucial to facilitate personalisation of care. Traditionally, standard of care has consisted of intermittent ad-hoc ECG (Holter) monitoring, however this approach fails to detect most episodes of AF which are often of short duration and infrequent. Insertable cardiac monitors (ICM), also referred to as loop recorders, have the advantage of providing continuous ECG monitoring for the lifetime of the device and in the CRYSTAL-AF trial were shown to be superior to Holter monitoring for detecting subclinical AF in patients with CS, with their use being associated with higher rates of initiating oral anticoagulation.[3] The three-year diagnostic yield was 30%, similar to other studies[4] and as high as 33.6-35.8% in patients fulfilling embolic stroke of undetermined source (ESUS) criteria.[5] Only ten patients need to be implanted to detect one patient with subclinical AF within one-year, compared to only 3% of patients who are diagnosed by standard of care Holter monitoring.

Real world data are reassuring

Despite evidence of their efficacy, the integration of ICM into stroke pathways has been variable. In this issue of the *Journal*, Russo and colleagues report real-world data from patients undergoing ICM following CS.[6] Implantation was at the discretion of the clinical team, rather than being standard of care and we lack criteria for implantation and data on the unimplanted. Hence, although the finding that the proportion of patients with documented AF at one-year was higher than in CRYSTAL-AF (16.2% vs 12.4%) is reassuring, observational real-world data demonstrating the incidence in a protocolised pathway are still warranted.

Physician inertia is prevalent across cardiovascular medicine, and ICM implantation following the diagnosis of ESUS (or CS) is likely to be no different. The present data confirm however, that once AF is detected, physicians are generally comfortable to initiate an anti-thrombotic strategy. Interestingly, neither of the two patients who had recurrent stroke where receiving anticoagulation, but in only one of these was AF detected on device interrogation. These cases highlight that timely initiation of anticoagulation is critical once AF is detected and confirm that not all CS are caused by AF. The caveat that not all episodes of AF will be detected by ICM, especially when the duration is very short is of modest relevance, since short episodes of AF predict longer episodes.[3]

Can we target these devices to patients at the highest risk?

A comprehensive strategy already exists with a proven and quite remarkable pre-test probability of 30% at three years, significantly higher than ICM implanted to investigate syncope.[7] But could we do even better and thereby target the upfront costs of the device even more carefully?

In their article, *Russo* and colleagues describe how p-wave dispersion (PWD), the difference between the widest and narrowest p-wave duration recorded on 12-lead ECG might predict the occurrence of subclinical AF. Around 50% of patients with AF had PWD >40ms, compared to approximately 20% of the patients who did not. Although it is likely that many stroke physicians will be

unfamiliar with this measurement and it is not automatically reported on 12-lead ECGs nor Holter monitoring, it is easily obtainable and simple to calculate. PWD is a marker of atrial remodelling, and so it makes sense this was associated with more instances of AF, although interestingly left atrial diameter was not.

Whilst these data expand our knowledge of the predictors of AF in this population, the positive and negative predictive values do not offer the opportunity to replace an ICM with a resting ECG especially with the background of the RE-SPECT ESUS[1] and NAVIGATE-ESUS[2] trials. Several simple algorithms that use clinical variables already exist, whilst clinical trials and observational data support the efficacy and cost effectiveness[8] of routine early ICM implantation in this population, and the authors' own data suggest that the detection of AF reliably leads to anticoagulation. On the other hand, strategies aiming to select or deselect patients for ICM who fulfil ESUS criteria risk failing to identify patients with AF and thereby failing to prevent recurrent stroke.

Is time running out for implantable cardiac monitors?

Whilst wearable monitors have considerable potential advantages compared to ICM in terms of cost, practicality, patient preference, and also find AF more reliably than Holter monitoring, the rates of detection in both EMBRACE[9] (16.2%) and SPOT-AF[10] (8.5%) were lower than in CRYSTAL-AF and the data presented by the authors. Moreover, it remains to be proven that physicians and their patients will be comfortable with life-long anticoagulation for AF detected on a wearable. Nevertheless, if the specificity is adequate, it is possible that a wearable could be adopted as a precursor to an ICM, although the risks to a delay in anticoagulation consequent upon a delay to confident diagnosis are obvious.

Conclusions

Russo and colleagues have outlined the real-world utility of ICM in detecting subclinical AF in patients with CS. To close the loop and deliver truly personalise care ICM implantation should become a routine and integral part

of stroke pathways, to optimise the utilisation of oral anticoagulation and reduce the risk of recurrent stroke for all CS patients.

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