Prioritising high risk stroke patients for cardiac monitoring

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Meeting Summary/Abstract

The experts presenting during this webinar focused on the latest evidence in high-risk stroke patient identification, prioritisation, and management in the context of the COVID-19 pandemic. Data from several studies on long-term cardiac monitoring shows that the only consistent risk factor for subclinical AF is age. Since risk-factors are not always reliable, long-term monitoring for AF is the basis of ensuring identification of patients at risk. Carefully selecting patients for this methodology is a critical factor to improve outcomes. In general, the longer patients are monitored, the better the chances are of identifying those that need immediate attention. All of this is more relevant in the current pandemic context which has had significant impact on stroke care pathways.

KEYWORDS: ATRIAL FIBRILLATION, CARDIAC MONITORING, IMPLANTABLE DEVICES, WEARABLE DEVICES

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Latest Evidence in Atrial Fibrillation Risk Factors

The main objective in atrial fibrillation (AF) diagnosis is to detect it early enough to treat it and prevent strokes, avoiding the worst-case scenario of finding AF after a stroke occurs. To this end, there are numerous risk factors for incident, clinical AF (Figure 1).[1] However, these are mostly based on 12-channel EKG detection rather than continuous monitoring (CM) with implantable devices (IDs) which are the most sensitive method of detecting AF.

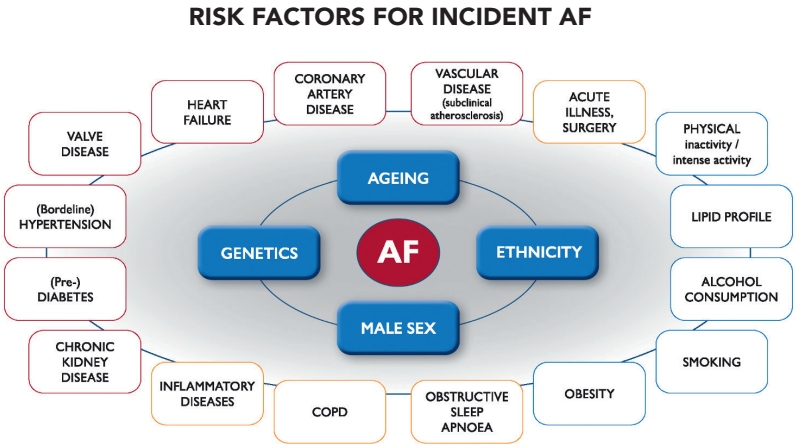

Figure 1. Risk factors for incident atrial fibrillation.

The incident AF risk score based on the Framingham study includes: age, systolic blood pressure (BP), hypertension treatment, body mass index (BMI), PR interval, significant murmur by years of age, and heart failure by years of age.[2] Risk is calculated by adding the number of points. It is worth noting that this score is based on methods available when data started being collected for this study, and that now other parameters such as atrial size are available.

Studies with CM for early AF detection. CM has provided interesting information from patients that were on CM for other reasons, such as pacemakers. Other studies have been conducted to quantify the prevalence of subclinical AF in patients that don't have a pacemaker or who have not had a stroke, for example:

- PREDATE-AF: n=245, using Medtronic Reveal XT and Medtronic Reveal LINQ.[3]
- REVEAL-AF: n=394, using Medtronic Reveal XT and Medtronic Reveal LINQ.[4]
- ASSERT II: n=256, using St. Jude Loop Recorder.[5]

PREDATE-AF showed that during a follow-up of 1.5 years, 20% of patients developed AF. Patients with and without AF (as detected by CM) had similar characteristics: they were 75 years of age on average, had CHA_2DS_2VASc scores between 4.5 and 4.6, preserved ejection fraction, elevated brain natriuretic peptide (BNP), and many of them were on aspirin, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), or statins. In the Framingham Study, age, gender, systolic BP, and heart failure had an impact but according to PREDATE-AF, there are no clear risk factors for subclinical AF on CM.[3]

REVEAL-AF, found a high percentage of patients had subclinical AF; 30% at the primary end-point of 18 months, and 40% at 30 months. The patient population was on average 72 years old, nearly half male and half female. They had several comorbidities: CHA_2DS_2VASc of 4.4, nearly all had hypertension, two-thirds had diabetes, 60% coronary artery disease (CAD), 20% heart failure (HF), and remote stroke or transient ischemic attacks (TIAs). The only AF risk factor identified was age, while BMI was borderline significant.[4]

ASSERT II found a very high percentage of patients with AF during a follow-up of 18 months: 34% had a subclinical AF of ≥5 minutes, and 7% had AF episodes of ≥6 hours. The population was similar to the previous studies (74 years, 34% female, CHA_2DS_2VASc of 4.1, high percentages of cardiovascular comorbidities and diabetes). Three AF risk factors were found: age, systolic BP, and increase in left atrial diameter.[5]

In the CRYSTAL AF trial, patients who had cryptogenic strokes were randomised to CM with insertable cardiac monitors (ICMs) or control. After three years, AF was detected in 30% of patients in the ICM group versus 3% in the control group. ICMs had a significantly higher AF detection rate compared to routine care. No risk factors were detected.[6]

A recently published prospective observational study was conducted in stroke patients with embolic strokes of unknown source (ESUS). In this trial, all ESUS patients (>100) were implanted with an implantable loop recorder (ILR), and

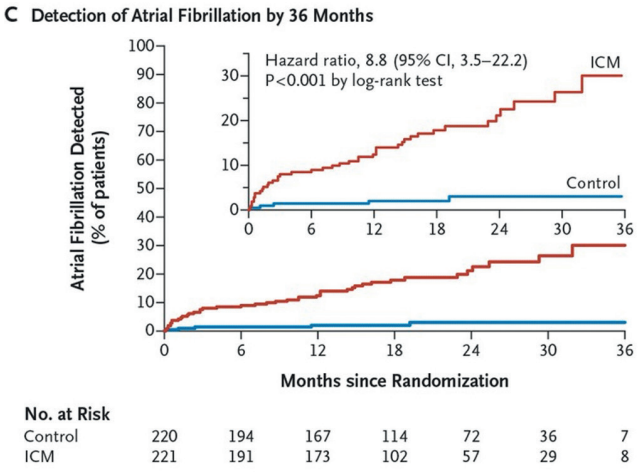

Figure 2. Time to First Detection of AF by 36 months from Sanna et al.[7]

after a follow-up of 3 years, 41% of patients were found to have AF. No AF risk factor was found other than being >70 years of age.[8]

Overall, in these 5 studies, AF was detected in 20–40% of patients. When comparing these populations, subclinical AF was a relevant finding in all studies but the stroke recurrence rate in those that had a stroke (ESUS or cryptogenic, despite anticoagulant treatment) was substantial (10–15%), while it was very low in those with cardiovascular risk factors or IDs. The only risk factor for subclinical AF consistently identified was age.[9] Since risk-factors are not always reliable, long-term monitoring for AF is the basis to ensuring identification of patients at risk.

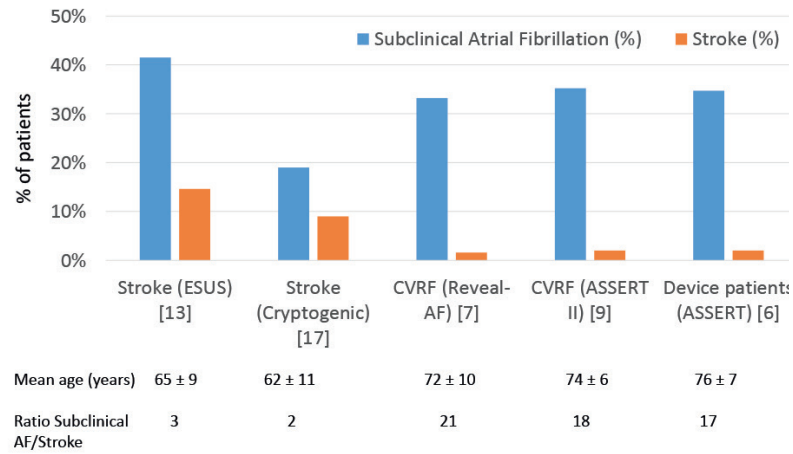

Figure 3. Comparison of subclinical AF and stroke rates in different studies.[9]

COVID-19 Safe Pathways for Stroke Patients

Challenges posed by COVID-19. The COVID-19 pandemic has brought special challenges to everyday clinical work, from admission to the flow through the hospital system. It has impacted:

- Staff, by affecting their well-being, staffing levels (COVID-related absences, absences due to isolation, shielding, or childcare challenges), and causing personal protective equipment (PPE) challenges.
- Decision-making, by restricting family visits and conversations with them about difficult decisions on enteral feeding and complex discharges.
- Patient behaviours, through avoidance of healthcare services by patients with a minor stroke or TIA.
- Stroke care pathways, through COVID-19 transmission prevention with very dependent and vulnerable patients needing significant face-to-face, hands-on contact with nurses and therapists.
- Stroke-specific hospital factors, by reducing scanner capacity, access to stroke units, out-patient services/capacity for FU for secondary prevention, redeployment of staff, and reduced access/barriers to cardiology investigations (Holter, ECHO, TOE).

A study conducted early in the pandemic consisting of a survey sent to 280 hospitals in China investigated the impact of the COVID-19 outbreak on stroke care. It showed that hospital admissions related to stroke dropped by 40% and thrombolysis and thrombectomy cases dropped by 25%. Patients not coming to the hospital for fear of contracting the virus was the key problem.[10]

COVID-19's impact on stroke pathways. Stroke service attendance rates changed substantially. A nationwide analysis of stroke patient care in Germany showed that as COVID-19 cases rose in 2020, there was a dramatic fall in TIA (23%) and acute ischemic stroke (AIS, 17%) hospitalisations compared to 2019. Meanwhile, the patients who did seek care continued to receive acute

recanalisation treatment (thrombolysis or thrombectomy) at approximately the same rate (16%) in 2020 versus 2019. In other words, people with smaller strokes chose to avoid hospitals.[11] Additionally, TIA clinic attendance data from Northwest London show a large attendance drop, starting in March (15%), and worsening in April (40%) as compared to the previous year. Data from the World Stroke Organisation show that stroke admissions fell by up to 80% in many countries.[12] In terms of acute care delivery, registry data from comprehensive stroke centres in the US show a small but significant delay in intravenous thrombolysis. There was a median delay in door-to-needle time of 4 minutes that appeared to be driven by delays from imaging to bolus. Thrombectomy rates were not affected.[13]

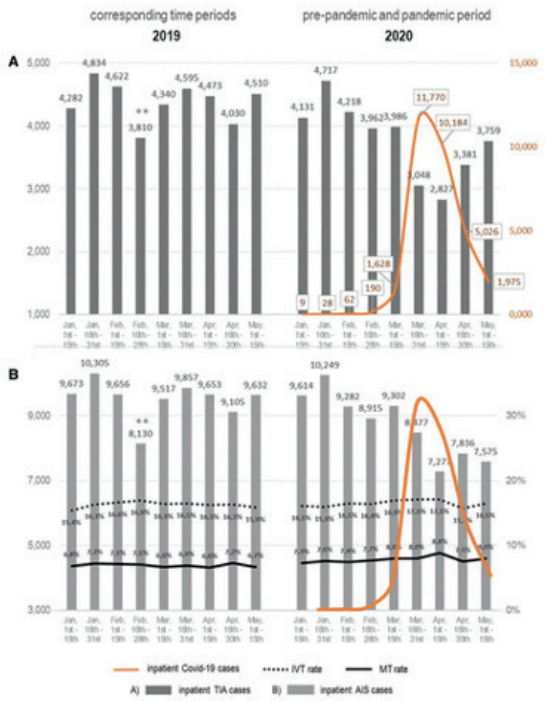

Figure 4. Hospital admissions of patients with TIA and AIS from Richter et al.[11]

Changes in stroke care, potential solutions and innovation. Many measures are implemented during a crisis which may be starting, stopping or changing processes. With these changes, there is opportunity to let go of some practices, to adopt new stroke care innovations, and to maintain new practices once the crisis subsides. Figure 5 shows a summary of changes from a guidance document developed in the UK after the first peak of the pandemic.

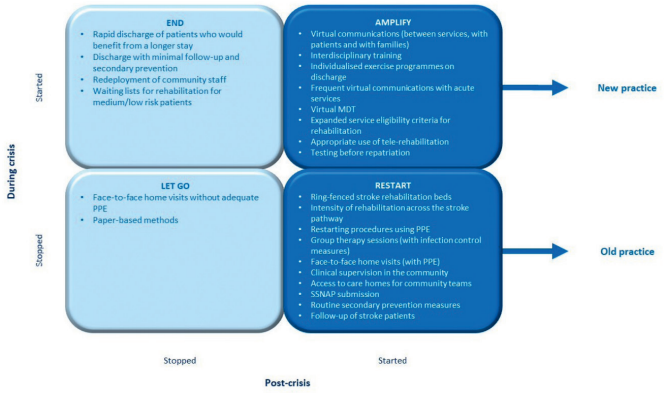

Figure 5. Restoration and recovery of stroke services during the COVID-19 pandemic.[14]

Changes in TIA pathways/services. An international cross-sectional study to describe TIA pathway adaptions in response to the COVID-19 pandemic shows two main changes:

- Patient assessments were performed exclusively through telephone or video-enabled visits in most TIA clinics (63%).

- Carotid ultrasound was replaced by CT angiography in 5 centres (31%), highlighting a move towards one-stop imaging approaches to collect as much information as possible in one imaging environment.[15]

Clearly, there are patients that still require face-to-face visits, but others can be managed initially and have investigations organised using telemedicine.

Changes in rehabilitation services. Limited data are available and experiences differ between countries. There are reports of rehabilitation services being centralised, reductions in follow-up frequency, and a move towards telemedicine.[16] Telerehabilitation has helped in addressing challenges in home visits by staff and patients' access to hospitals. For instance, a randomised trial comparing the efficacy of a home-based telerehabilitation system with in-clinic therapy showed that the two approaches had similar efficacy improving Fugl-Meyer assessments (FMAs) and patient knowledge about stroke.[17] Findings from another randomised study show improved FMAs in patients receiving telerehabilitation versus traditional rehabilitation.[18] Overall,

inpatient rehabilitation services have found ways to cope and adapt but early supportive discharge with rehabilitation at home has faced the most challenges. Simple responses to these challenges include more prolonged treatment plans and working closely with carers.

Changes to secondary prevention. There is also limited data on secondary prevention but major issues were identified since the beginning of the pandemic. A survey by the European Stroke Organisation (ESO) involving 426 stroke care providers from 55 countries, showed that only 20% of patients continued to receive secondary cerebrovascular prevention.[19] Clinicians are encouraged to leverage telemedicine, and empower patients to take ownership of their cardiovascular prevention, to self-evaluate concerning symptoms, monitor their vital signs, report any abnormalities, and adjust medications.[20] Patient empowerment is supported by a pre-pandemic study from the UK, TASMINH4, in which patients requiring follow-up for their BP were randomised to usual care, self-monitoring, or telemonitoring groups. After 12 months, systolic BP was lower in self-monitoring and telemonitoring patients compared with those under usual care.[21]

In summary, the COVID-19 pandemic has had significant impact on stroke care pathways, particularly for minor strokes and TIAs. Fortunately, several innovations have been brought forward and may be kept for future clinical practice.

Prioritising high-risk stroke patients for prolonged cardiac monitoring

Ischemic stroke is a complex entity and the ultimate goal of prevention is to target the underlying disease. However, secondary prevention with anticoagulants is hampered by the undetermined aetiology of 20–40% of strokes since it requires confirmed AF diagnosis; given AF's often paroxysmal and asymptomatic nature, it may not be detected using traditional monitoring techniques making more careful assessments to improve detection a necessity. The CRYSTAL AF study was conducted to compare monitoring techniques and demonstrated that ECG monitoring with an ICM was superior to conventional FU for detecting AF after cryptogenic stroke.[7] The implementation of long-term monitoring requires the prioritisation of stroke patients through early candidate identification, assessment of occult AF risk, and selection of monitoring strategy ideally during the first admission to start monitoring as early as possible.

Early identification of candidates. The following steps can improve identification:

A. Recognise embolic stroke. Vascular invasive and non-invasive imaging pre- and post-thrombolysis facilitates the diagnosis of embolic stroke.

B. Identify the origin of the emboli. Check vascular imaging of large arteries and high-resolution MRI for hidden embolism causes (stenoses, vulnerable-looking plaques) and arterial wall abnormalities.

C. Perform telemetry ECG monitoring in stroke unit for AF detection. Routine staff-based or automated ECG analysis have comparable diagnostic effectiveness. Automated AF detection can improve diagnosis when faced with limited staff and time resources.[22]

When these procedures are performed within the first 24 hours of stroke, and they indicate embolic aetiology with no clear source and no sign of AF, monitoring should be extended.

AF risk assessment. Considering risk factors may help elucidate atrial cardiopathy. As mentioned, the most important clinical factor is age followed by high CHA_2DS_2VASc scores. Other risk factors to consider include: adjusted left atrial volume (LAVI), atrial strain, left atrial diameter, supraventricular abnormalities, p-wave morphology, and blood biomarkers (BNP and N-terminal pro b-type natriuretic peptide (NT-proBNP)).

Additionally, the following criteria may increase long-term monitoring efficiency:

- Criteria favouring long-term monitoring indication: CHA_2DS_2VASc >5, non-lacunar multiple (old and new) arterial territories affected, and AF precursors.

- Criteria not favouring long-term monitoring indication: follow-up not possible, AF detection will not change therapy, poor functional outcome, and life expectancy <1 year.

Device and strategy selection. If the patient is high-risk, a device and a monitoring strategy have to be selected. The choice of device is driven by risk of occult AF, patient

collaboration, need for in-person visits, and availability of resources. External wearable recorders are automatic and tend to be preferred by patients as they are non-invasive but they have the disadvantage of requiring patient collaboration and visits. Also, their precision and monitoring period length is improving. Implantable loop recorders have duration and convenience advantages but their disadvantage is that they require minimally invasive procedures to be implanted. They are the best option to rule-out AF in terms of reliability, precision, sensitivity, positive predictive value and independence from patient compliance.

CM devices are best implemented using a multi-disciplinary approach. For example:

- Cardiology and neurology departments identify patients for prolonged monitoring within the first 24 to 48 hours after admission and they may provide the device at this time.

- Cardiology follow-up is fully remote (internet-based) with records checked by cardiologists. If alert signs of AF are found, neurology is notified.

- Neurology follow-up. Once AF is detected, physical visits at Stroke Prevention Clinics are required ideally within the next 24 to 48 hours to make therapeutic decisions.

Several studies have been conducted to examine the efficacy of implantable and external devices to detect AF in Spain. In a study of cryptogenic stroke patients (N=236) with presumably embolic mechanisms and median follow-up of 32 months, long-term implantable monitoring detected paroxysmal AF in 45% of patients with a median time from implant to AF detection of 90 days.[23] The Crypto-AF multi-centric registry evaluated monitoring with textile wearable holters for 28 days and detected previously undiagnosed AF in 22% of patients; detection increased over time from 5% in the first 0–3 days to 22% at 28 days.[24]

In summary, patient selection is a critical factor when considering long-term monitoring, especially with wearable devices. Medical professionals have to ensure patients and their carers understand what is required of them for the system to work properly and education should start within admission. Usually, during the first 4 weeks compliance is very high, however after the first month, approximately 20% of patients tend to be lost or drop out. Patient education, re-education and reassurance are critical to respond to these challenges.

Conclusion

Limiting AF monitoring to a short time (24–48 hrs) provides only limited information. The ideal way to identify patients at risk is to observe their cardiac rhythm as long as needed, or practically possible, to detect AF. Therefore, long-term ECG monitoring should be the standard of care in cryptogenic stroke patients. Most importantly, candidates for long-term monitoring need to be identified as early as possible prioritising high-risk patients based on AF risk assessment, and monitoring should be initiated within the first admission. In general, the longer patients are monitored, the better the chances are of identifying those that need immediate attention.

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