

Detection and management of subclinical atrial fibrillation in implantable and wearable devices

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Summary

This mini review lists available data on detection of subclinical atrial fibrillation (SCAF) in patients with cardiac implantable electronic devices and underlines uncertainties that remain when it comes to anticoagulation. Ongoing trials will examine the benefit of anticoagulation in these patients when SCAF duration is in the grey zone between 5–6 minutes and 24 hours. Meanwhile, smart and wearable devices may lead to a more patient-driven than physician-driven diagnostic in detection of AF. Wearables come with opportunities and challenges and cardiologists will need to focus on the right balance between using wearables as an additional diagnostic tool in patients at risk while avoiding overdiagnosis in the healthy general population.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with increased mortality, heart failure and stroke [1–3]. It is predicted that AF prevalence in Europe will more than double by the year 2060 [4]. Cardiac embolism due to atrial fibrillation accounts for one third of all ischaemic strokes [5, 6] and about 18% of all ischaemic strokes due to AF are related to subclinical AF (SCAF) [7]. Therefore, early detection of SCAF may be crucial. SCAF, sometimes also referred to as "silent" or "asymptomatic" AF, describes clinically unapparent AF, mostly of short duration, which is detected with an implanted device such as a pacemaker or internal cardioverter-defibrillator (ICD), or a wearable device such as a smartwatch. Atrial high rate episodes (AHREs) in pacemakers and ICDs need to be confirmed by a physician who visually reviews the intracardiac electrograms to be labelled as SCAF. The same applies to the ECG-recorded rhythm in wearables such as smartwatches [8]. Although SCAF is associated with stroke, it is important to note that the increase in risk appears to be lower when compared with symptomatic AF [9, 10]. Stroke prevention by the use of oral anticoagulation in patients with symptomatic AF is well established, but there are no data from randomised trials addressing the question whether patients with SCAF should receive oral anticoagulation, and very few patients

with SCAF have been included in AF anticoagulation trials. Recently, numerous wearable devices to detect clinical and subclinical AF have become available. As a result, technological development may lead to a shift from physician-initiated to patient-initiated screening for AF.

Screening for AF?

Even if very recently, results from the STROKESTOP trial have reported a small clinical benefit in the elderly population when they participated in a screening programme for AF (results presented by Emma Svennberg during EHRA congress on 23 April 2021), the role of systematic screening in the general population remains uncertain and is therefore not recommended by current guidelines. Nevertheless, opportunistic screening by pulse palpation followed by a 12-lead ECG in the case of an irregular pulse has been recommended for patients older than 65 years in European Society of Cardiology (ESC) guidelines since 2012 [11], as well as in the 2020 version of the AF guidelines [8]. In patients with a history of an ischaemic stroke or systemic embolism, secondary screening for AF is challenging because paroxysmal AF episodes often remain undetected. AF detection is related to total AF burden and obviously improves with increasing intensity of monitoring [12]. As an example, wearing a cardiac event monitor belt for 30 days results in higher yield of AF detection than standard 24-hour Holter monitoring as shown in the EMBRACE trial (30-Day Cardiac Event Monitor Belt for Recording Atrial Fibrillation After a Cerebral Ischemic Event) [13]. In patients with cryptogenic stroke, intensified monitoring with an implantable loop recorder leads to an increase in AF detection when compared with standard care: 30% versus 3% after 36 months in the CRYSTAL-AF (Cryptogenic Stroke and Underlying Atrial Fibrillation) trial [14]. Implantable loop recorders are safe and effective tools for detecting AF episodes and the number of implantations of such devices is increasing as a result of technological improvements including miniaturisation [15]. However, when elderly asymptomatic patients are intensively screened for AF one may anyway find a high AF incidence. This was examined in the ASSERT II study (Prevalence of Sub-Clinical Atrial Fibrillation Using an Implantable Cardiac Monitor), where an annual incidence of SCAF lasting >5 minutes was found in 34.4% of elderly asymptomatic patients without pacemakers who were implanted with a loop recorder [16].

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AF detection using cardiac implantable electronic devices

There is no better heart rhythm monitor than a pacemaker or ICD with an atrial lead, since it provides continuous monitoring. Therefore, the detection of SCAF in patients with cardiac implanted electronic devices (CIEDs) is frequent. Prevalence ranges between 25% and 50% during the first 1 to 3 years [10, 17–20]. Several trials have investigated the relationship of SCAF detected in CIEDs and the association with stroke. It is important to note that in patients with continuous monitoring by CIED there is often no strict temporal relationship between AF episodes and occurrence of stroke, suggesting that AF may be a marker rather than a causal factor of stroke risk [17, 21, 22]. In the ASSERT trial (Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial) [10] 10.1% of device patients experienced at least one episode of SCAF >6 minutes duration in the first 3 months. Stroke rate was elevated 2.5 times compared with patients without subclinical AF but this was lower than stroke rate in patients with clinical, symptomatic AF. In the MOST (Mode Selection Trial) study atrial high rate episodes >5 minutes were associated with increased stroke risk [9]. The investigators of the TRENDS study (A Prospective Study of the Clinical Significance of Atrial Arrhythmias Detected by Implanted Device Diagnostics) found that an increased AF burden (>5.5 hours during 30 days) was associated with stroke [17]. In summary, the risk of stroke in patients without anticoagulation increases with SCAF duration and burden, and the strongest evidence for a benefit of anticoagulation was noted when episodes >24 hours duration were

detected [23]. However, a clear threshold when to start with oral anticoagulation is not well defined.

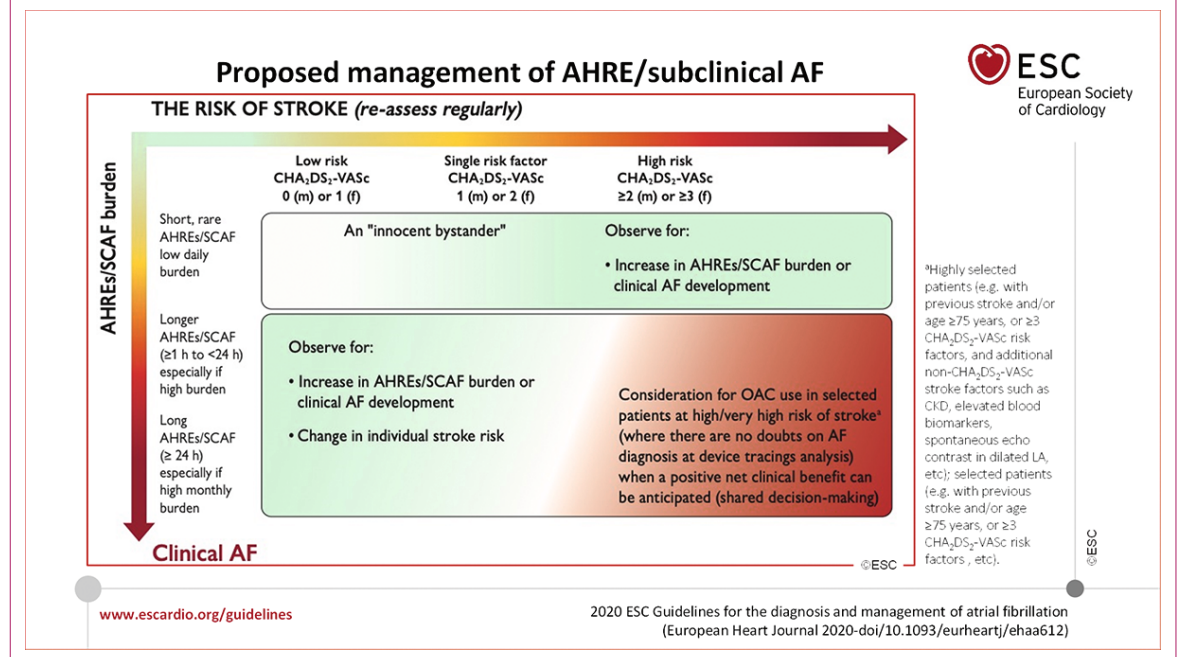
Management of subclinical AF

In contrast to symptomatic AF, evidence on appropriate management of SCAF is limited [12]. In clinical trials, SCAF was associated with increased mortality and stroke when lasting longer than 5 minutes [9, 24] or 6 minutes [10], and in particular when lasting >24 hours [25, 26]. The current ESC AF guidelines state that available evidence is insufficient to justify routine use of oral anticoagulation in patients with SCAF, and modifiable risk factors should be identified and managed in each patient [8]. Patients with SCAF observed during device follow-up should be regularly monitored for progression to clinical AF and changes in individual thrombo-embolic risk. In patients with longer SCAF episodes, especially >24 hours, and a high CHA₂DS₂-VASc-score (≥2 in men or ≥3 in women) it is reasonable to consider the use of oral anticoagulation according to the guidelines [8]. A proposed management approach shown in figure 1.

AF detection in wearable devices

Wearables are smart electronic devices worn close to the skin such as smartwatches, chest straps and ECG patches with connectivity to a smartphone. In comparison to monitoring with Holter ECGs, which usually cover a monitoring period between 24 hours up to 7 days, wearables provide non-invasive cardiac rhythm monitoring without limitation of time. SCAF may occur very infrequently. As an example, mean time to detection of SCAF (by CIED) in the ASSERT trial was 36 days [10] and in ASSERT II (by implantable loop recorder) was 5.1 ± 5.5 months.

Figure 1 : Proposed management of AHRE/SCAF. AF = atrial fibrillation; AHRE = atrial high-rate episode; CKD = chronic kidney disease; CHA2DS2-VASc = Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65–74 years, Sex category (female); f = female; LA = left atrium; LoE = level of evidence; m = male; OAC = oral anticoagulant; SCAF = subclinical atrial fibrillation. (a Highly selected patients (e.g., with previous stroke and/or age ≥75 years, or ≥3 CHA2DS2-VASc risk factors, and additional non-CHA2DS2-VASc stroke factors such as CKD, elevated blood biomarkers, spontaneous echo contrast in dilated LA, etc); selected patients (e.g., with previous stroke and/or age ≥75 years, or ≥3 CHA2DS2-VASc risk factors, etc).



Hence, this is a possible gap where noninvasive monitoring using wearables might be beneficial. Although wearables such as chest strap monitors and ECG patches provide continuous monitoring, they may be less comfortable to wear and recently smartwatches have become more and more popular in the general population. Importantly, smartwatches do not provide continuous rhythm monitoring because of battery limitations. Instead they spot check heart rate and heart rhythm through photoplethysmography (PPG). The PPG technique measures changes in the microvascular blood volume, which converts into pulse wave and tachogram recording. This is achieved by using an emitter that sends a continuous pulse through the skin and a photodetector that measures the variable intensity of reflected photons from the tissue [27]. PPG records are affected by motion artefacts, pressure disturbances and skin pigmentation, but this can be improved using signal processing techniques [27]. Of note, current smartwatch algorithms are not able to detect AF below a heart rate of 50 bpm or above a heart rate of 120 bpm [28], which is a limitation. Smartwatch algorithms notify the user to obtain a single-lead ECG, which resembles lead I, for a duration of 30 seconds as soon as an irregular heart rhythm is detected. To obtain a single-lead ECG, smartwatch users can place a contralateral finger on the crown (negative electrode on the side of the watch), with the back of the watch serving as the positive electrode [29]. Some smartwatches are already officially labelled as medical devices. Recently, the Withings Move[®] smartwatch has received CE marking, whereas the Apple Watch[®], Samsung Galaxy Watch[®] and Fitbit Sense[®] have received CE marking as well as FDA approval for detection of sinus rhythm or AF.

Two large studies with smartwatches were conducted in the general population using the photoplethysmography (PPG) method – the Apple Heart Study [30] and the Huawei Heart Study [31]. In the Huawei Heart Study, the mean age of the participants was 34.7 ± 11.5 years, with only 6% being older than 54 years. In the Apple Heart Study, 15.9% of participants were older than 54 years. In the Apple Heart Study 0.5% of participants received a notification that an irregular rhythm was obtained by the PPG signal. Finally, AF was confirmed in 34% of those patients who did further testing with an ECG patch. In the Huawei Heart Study, 0.2% had an irregular rhythm and 87% of those that underwent follow-up with physical examination, ECG and 24-hour Holter were finally diagnosed with AF. These data emphasise that we have to be cautious using this technique, since the population using smartwatches is generally younger than the group at risk but SCAF episodes with unclear clinical implications might still be revealed. The use of wearables may lead to increasing number of requests to physician from patients presenting with a rhythm strip. Using the smartwatch technology in a population other than in patients at risk may probably increase the risk of false-positive findings in a presumably healthy population [28]. In summary, studies have shown the feasibility to detect AF in smartwatches, however it is still necessary that a physician approves the ECG recorded rhythm. Nevertheless, smart wearables are not a continuous heart rhythm monitor, rather a “spot check” of arrhythmias and currently do not replace the continuous monitors that are prescribed by a healthcare provider [32].

Outlook

Cardiologists play a major role in interpreting electrograms and rhythm strips and in providing guidance towards optimal therapy including anticoagulation. To date, there is still a major knowledge gap in what to do in patients presenting with SCAF recorded by CIED with a duration between 5 or 6 minutes and 24 hours. Even if SCAF duration >5–6 minutes in combination with an elevated CHA₂DS₂VASC score is associated with an increased stroke risk, the risk-benefit ratio of starting anticoagulation in SCAF <24 hours remains unclear [12]. Randomised trials addressing this grey area are ongoing. The NOAH-AFNET 6 trial (Non-vitamin K Antagonist Oral Anticoagulants in Patients With Atrial High Rate Episodes) will investigate whether patients with device-detected atrial high rate episodes/ SCAF >6 minutes will benefit from anticoagulation with edoxaban [33]. The ARTESIA study (Apixaban for the Reduction of Thrombo-Embolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation) will determine whether oral anticoagulation therapy with apixaban compared with aspirin reduces the risk of stroke or systemic embolism in patients with SCAF lasting between 6 minutes and 24 hours [34]. While we are waiting for these trial results, the authors of this review do not anticoagulate patients with device-detected SCAF <6 minutes duration according to available data, whereas in SCAF >24 minutes anticoagulation is started when indicated according to the CHA₂DS₂VASC score. In the grey zone in between, a clinical scenario that often occurs, the authors tend towards anticoagulation when a high CHA₂DS₂VASC score (≥ 2 in men, ≥ 3 in women) is indicative of increased stroke risk and especially when there is no history of bleeding. We recommend a visual review of the electrograms of atrial high rate episodes on a regular base to determine if SCAF is present, assess AF burden, look for a possible progression to clinical AF in which anticoagulation is better established, and to identify and treat comorbidities in AF.

The increasing use of smartwatches comes with opportunities and challenges. Cardiologists will probably encounter an increasing number of patients presenting with suspicion of AF. A visually confirmed episode of clinical AF detected by a smartwatch is already an indication for starting oral anticoagulation when thromboembolic risk is elevated according to the CHA₂DS₂VASC score, but there is a lack of data on whether anticoagulation in patients with SCAF diagnosed by a smartwatch is beneficial. The HEARTLINE trial (A Heart Health Study Using Digital Technology to Investigate if Early AF Diagnosis Reduces the Risk of Thromboembolic Events Like Stroke IN the Real-world Environment) is investigating whether detecting symptomatic or asymptomatic AF with a smartwatch will improve clinical outcomes in people aged 65 and older when embedded in an app-based program including tools to promote adherence to oral anticoagulation. Meanwhile, we recommend dealing with SCAF recorded by a smartwatch in the same way that we deal with SCAF recorded by a CIED.

Cardiologists and other healthcare providers will also play a major role in guiding patients who desire to monitor their heart rhythm with wearables. Smartwatches could potentially fill the diagnostic gap between Holter monitor-

ing and implantation of an implantable loop recorder in patients at increased risk of stroke. However, we opt against AF screening with smartwatches in the general population, and especially in younger, healthy patients given the low prevalence of AF in this population, the risk of false positive results and the possibility of gaining the diagnosis of a cardiac disorder with unclear treatment implications.

Key points

Implantable loop recorders (ILR) and cardiac implantable electronic devices (CIEDs) are considered to have the highest sensitivity to detect atrial fibrillation (AF).

Wearables such as smartwatches are increasingly used and will presumably increase the number of patients diagnosed with subclinical AF.

AF episodes detected by implanted or wearable devices need to be confirmed by visually reviewing the intracardiac electrogram or ECG-recorded rhythm.

Current data does not support anticoagulation in subclinical device-detected AF of < 5–6 minutes duration but does support anticoagulation when the duration is >24 hours

Ongoing studies such as the ARTESIA (Apixaban for the Reduction of Thrombo-Embolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation) trial examine the benefit of anticoagulation in the grey zone between 5–6 minutes and 24 hours

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