The Role of Continuous Monitoring in Atrial Fibrillation Management

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Abstract

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is strongly associated with stroke risk and a variety of cardiovascular conditions. AF early detection is of paramount importance, in order to define proper medical treatment. This can be challenging due to the often silent and intermittent nature of the rhythm disturbance. Long-term external ECG monitoring may be very helpful, but if less than fully continuous and of long duration it will be not reliable. For this reason continuous monitoring is of increased importance, and outcome measurements of AF treatment trials will be based on the AF burden detected by insertable cardiac monitors (ICM) or therapeutic devices such as pacemakers or ICDs, leading to the paradigm that the detection of AF in the presence of thromboembolic risk factors should be performed wherever possible in order to improve patients' chances.

Keywords

Atrial fibrillation, continuous monitoring, rhythm control, stroke, oral anticoagulation

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Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1–2 % of the general population and is increasingly prevalent in older people, occurring in about 10 % of over 80 year olds.¹ AF is associated with a variety of cardiovascular conditions. The arrhythmia is associated with a five-fold rise in stroke risk and frequently coexists with heart failure, both leading to a further increase in mortality.^{2–5}

About 15 % of strokes are attributed to underlying AF, and 50–60 % to documented cerebrovascular disease, but in about 25 % of patients who have ischaemic strokes, no aetiological factor is identified. Subclinical atrial fibrillation is often suspected to be the cause of stroke in these patients.^{3,6–8} A recent study with implantable cardiac monitors in survivors of ischaemic stroke has revealed that far more than expected instances of so-called “cryptogenic stroke” are associated with episodes of AF revealed by continuous ECG monitoring.^{9,10} Concomitant medical conditions have an additive effect on the perpetuation of AF by promoting a substrate that maintains AF. Conditions associated with AF are also markers for global cardiovascular risk and/or cardiac damage rather than simply causative factors.¹¹

Altogether, AF causes a significant economic burden which has grown in recent decades and is expected to grow even further in the future with the increasing trend in AF prevalence and hospitalisations.^{12–14}

Asymptomatic AF and the Low Yield of Intermittent Monitoring

AF can show in several clinical scenarios. Some patients may suffer so much that they seek specialist help to be relieved from the arrhythmia.

Others present with severe symptoms, often including fatigue and shortness of breath, and are found to be in AF on clinical or ECG examination. In yet others, AF is an incidental finding when an irregular heartbeat is detected on physical examination and/or an ECG is recorded for other reasons, such as during preoperative assessment. The problem of early recognition of AF is greatly aggravated by the often silent and intermittent nature of the rhythm disturbance. In about one third of patients with this arrhythmia, patients are not aware of the so-called asymptomatic AF.^{15,16}

The Suppression of Paroxysmal Atrial Tachyarrhythmias (SOPAT) trial¹⁷ showed that only 46 % of episodes recorded during the one-year follow-up period were associated with specific symptoms. The remaining 54 % were asymptomatic AF episodes. Similarly in the Prevention of Atrial Fibrillation After Cardioversion (PAFAC) trial¹⁸ 70 % of all AF recurrences were completely asymptomatic. Arya et al¹⁹ used seven-day Holter recordings before ablation and documented AF in 81 % of the population. All episodes were symptomatic in 38 %. In 52 patients (57 %), symptomatic and asymptomatic episodes were recorded, whereas in 5 patients (5 %), all documented AF episodes were asymptomatic.

Ziegler et al.²⁰ compared continuous monitoring with different strategies of intermittent ECG monitoring in pacemaker patients. All intermittent and symptom-based monitoring resulted in significantly lower sensitivity (range 31–71 %) and negative predictive value (range 21–39 %) for the identification of patients with AF and underestimated AF burden. These results were confirmed by Botto et al.²¹

The Role of Monitoring in Rhythm Control Strategies

In order to measure efficacy of rhythm control approaches and therapeutic techniques, it is widely accepted that continuous information is needed, because spotlight ECGs miss a major part of the AF activity which may lead to a wrong evaluation of therapy efficacy.

The relevance of increasing the Holter observation length from 24 hours to seven days has been demonstrated by Kottkamp et al.²² One hundred patients underwent 24-hour and seven-day Holter monitoring post-pulmonary vein ablation for paroxysmal AF. At 12 months, ablation success rate was 88 % when using the 24-hour Holter data, but only 74 % as indicated by the seven-day Holter. One might argue that this gap in capturing recurrences outside a Holter registration interval could be closed if an external event recorder were used. However, Klemm and co-workers demonstrated that, in 80 post-ablation patients using transtelephonic ECG recordings (minimum one ECG per day and in case of symptoms suggesting AF), during 54 % of transmitted ECGs demonstrating AF patients were asymptomatic.²³ In 11 % of all tracings, the patients indicated symptoms but demonstrated stable sinus rhythm on the tracing. In line with this finding, it was demonstrated that, outside a blanking period of three months, the ablation success in patients with only symptomatic but ECG-documented recurrences was around 70 % whereas, counting all ECG-documented AF recurrences using a tele-ECG concept, the percentage of patients with no AF recurrences was reduced to almost 40 %.

Pokushalov and co-workers published for the first time the wide and routine use of an insertable cardiac monitor (ICM) to perform long-term continuous AF monitoring in their AF ablation patients. Furthermore, they tried to differentiate between sudden-onset and triggered-onset AF recurrence in order to tailor the treatment regimens for AF recurrences after the first catheter ablation.^{24,25} It was shown that an ICM-detected AF burden of >4.5 % during the blanking period was a powerful predictor of ablation failure. This information and correlation could trigger early re-intervention in those patients, shortening the period of time until stable sinus rhythm is reached.²⁶

Similarly to catheter ablation, in surgical procedures there is a relevant proportion of patients with silent and intermittent AF recurrences, whereas a significant number of symptomatic AF episodes are not related to AF. Ip and co-workers report that in about 45 AF patients, who underwent video-assisted epicardial ablation and ICM implantation; as many as 46 % of the AF recurrences were asymptomatic, whereas only 66 % of the symptomatic episodes were AF-related.²⁷

Bogachev-Prokophiev et al.²⁸ reported ablation results for AF with mitral valve surgery after one year of continuous monitoring. Forty-seven patients with mitral valve disease and long-standing persistent AF underwent a left atrial maze procedure with bipolar radiofrequency ablation and valve surgery. At the 12-months follow-up examination, 65.2 % of patients had an AF burden <0.5 % and were classified as responders; 6.5 % of the non-responders had atrial flutter and 27.7 % had documented AF recurrences with an AF burden >0.5 %, and 4.3 % patients with AF recurrences were completely asymptomatic. Among the symptomatic events manually stored by the patients, only 27.6 % were confirmed as genuine AF recurrences according to the concomitant ECG recorded by the ICM. The results in these surgical AF patients again show the usefulness of continuous rhythm monitoring to verify the true amount of successful ablation therapy and to identify

asymptomatic recurrences in order to better discriminate between AF- and non-AF-related symptoms.

If an ICM is implanted for a period before the procedure, this may help the assessment of AF behaviour and improve patient management. In fact Verma et al.²⁹ showed that the ratio of asymptomatic to symptomatic AF episodes increased from 1.1 before to 3.7 after ablation. In addition they demonstrated that the post-ablation state (rate of episodes) is the strongest predictor of asymptomatic AF, and symptoms alone underestimate post-ablation AF burden, with 12 % of patients having only asymptomatic recurrences. In addition Pedrote et al.³⁰ showed that the prevalence of AF prior to an ablation can be highly variable and often lower than expected; therefore post-ablation assessment without knowledge of the pre-ablation burden can overvalue or undervalue the success of the procedure.

The Role of Monitoring in the Risk Stratification for Stroke Prevention

If the risk of stroke is greater than approximately 1 % per annum, oral anticoagulation (OAC) is required for effective prevention of thromboembolic events, but in clinical practice with patients at moderate to high thromboembolic risk OAC is very often underutilised.^{31,32}

Current guidelines for stroke prevention in AF do not differentiate between patients with symptomatic or asymptomatic AF, or between paroxysmal or persistent AF.³³ The vast majority of AF episodes are asymptomatic, including many episodes of clinically significant duration.³⁴

About 20–30 % of patients hospitalised for ischaemic stroke or transient ischaemic attack are discharged with the diagnosis of cryptogenic stroke, meaning that the cause of the clinical event is not diagnosed.^{7,8} Continuous monitoring with ICM is now widely used in patients with cryptogenic stroke to identify those with silent AF and drive the most appropriate antithrombotic therapy.^{35,36,37} In those studies AF was detected in 17–27.3 % of the patients in “real world” clinical practice underlining the limited yield of intermittent monitoring for secondary stroke prevention, where even the smallest amount of AF may play a role in stroke recurrence.³⁸

Risk stratification for stroke prevention has been one of the most relevant issues debated by the medical community in recent years, and continuous monitoring now plays a pivotal role in this assessment. A series of studies performed in pacemaker or ICD patients indicate that longer times spent in AF are associated with a higher stroke risk, and that this increased risk is additional to known risk factors.^{21,39–41}

Recently, the Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial (ASSERT) included 2,580 patients aged 65 years or older, with hypertension and no history of AF, implanted with a pacemaker or ICD.⁴² Episodes of subclinical atrial tachycardia occurred in 10 % of patients in the first three months and were associated with an increased risk of clinical AF (hazard ratio [HR] 5.56) and of ischaemic stroke or systemic embolism (HR 2.49). The conclusions of ASSERT were that subclinical atrial tachyarrhythmia occurs frequently and is associated with a significantly increased risk of ischaemic stroke or systemic embolism.

In addition a pooled analysis of individual patient data from three prospective studies, the Stroke Prevention Strategies based on Atrial

Fibrillation Information from Implanted Devices (SOS AF) project, where more than 10,000 patients were included, evaluated several thresholds for daily AF burden and found that one hour of atrial fibrillation identified the highest thromboembolic risk (HR 2.11).⁴³

Future Perspectives

Continuous AF monitoring has an increased importance, and outcome measurements of AF treatment trials, comparing rhythm versus rate control or different rhythms strategies, will now be based on the AF burden detected by ICM or therapeutic devices such as pacemakers or ICDs. Long-term external ECG monitoring may be very helpful but if less than fully continuous and of long duration will be less convincing than ICM data.

In the last few years it has become evident that it intermittent ECG documentation only captures a minority of the true AF burden. In the current clinical arena, especially in the field of rhythm control, correlation of symptoms and underlying rhythm is still

considered relevant. However, different levels of AF burden captured by continuous monitoring will provide a more solid base for proper assessment and for correct stroke risk stratification.

Implantable long-term ECG monitors offer many advantages but require a change of paradigm focusing on a minimally invasive approach when compared to the current standard of care. It is certainly possible to envision wider adoption of the new, miniaturised, generation of ICMs that are being released; the insertion procedure is minimally invasive reducing to a minimum the burden for the patient and the treating physician, and allowing the possibility of extending its use to new categories of patients.

In any event the detection of AF in patients with thromboembolic risk factors should be performed wherever possible. Even short lasting AF episodes with a low AF burden imply a significant risk increase of thromboembolic risk; therefore any verified AF detection should trigger OAC prophylaxis as recommended. ■

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