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Review

Device-identified atrial fibrillation at pacing clinics. Should it guide anticoagulation?

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ABSTRACT

In recent years, there has been a significant increase in the number of devices implanted following improvement in their safety profile, extension of indications and reduction in cost. Although the reason remains largely the beneficial effect on heart rhythm stabilisation, implanted devices might also have additional advantages, notably identification of silent arrhythmia. Should clinicians therefore act on device-identified atrial fibrillation (AF) and should such identification be used to guide anticoagulation management? This review evaluates the current evidence on the management of device-identified asymptomatic AF.

1. Introduction

Atrial fibrillation (AF) is one of the commonest cardiac arrhythmias, with an overall prevalence of 1–2% in the general population and an estimated lifetime risk of about 25% [1,2]. It is associated with many risk factors including valvular heart disease, hypertension, left ventricular dysfunction, coronary artery disease, aging, obesity, diabetes mellitus, obstructive sleep apnoea and alcohol consumption. It is well known that AF confers significant morbidity and reduction in quality of life and increases the mortality of patients through a variety of mechanisms such as altered hemodynamics, atrial and ventricular dysfunction and increased thromboembolic risk [2]. The two key aspects in the management of AF are firstly, appropriate anticoagulation for prognostic benefit and secondly, rate control for predominantly symptomatic benefit. Embolic stroke accounts for a large percentage of the morbidity/mortality seen with AF. It is estimated that, in the absence of adequate anticoagulation, AF increases the risk of stroke five-fold, while dose-adjusted warfarin reduces this risk by approximately 64% [3,4]. In terms of controlling the patient's symptomatology and preventing the development of complications such as tachycardiomyopathy, rate control is the other important aspect of management. So far, studies have not demonstrated a significant, consistent benefit of rhythm control over rate control with respect to cardiovascular mortality or quality of life in patients with AF [3]. By contrast, a subgroup analysis of the AFFIRM study showed that a rhythm-control strategy in patients with a permanent pacemaker (PPM) and AF increased the all-cause mortality compared with rate control [5].

It is known that 10–40% of all patients with AF are asymptomatic and asymptomatic (silent) AF confers similar morbidity and mortality to symptomatic AF. This makes screening for AF in clinical practice critically important in order to prevent some of its serious complications. Despite this, there is no consistency in clinical practice on how to screen for silent AF [6,7]. In this review, we will discuss the potential role of PPMs and other implantable devices (referred to as 'devices' from here onwards) in screening for silent AF and how this can potentially aid in the modification of medical therapy to reduce the thromboembolic risk. Silent atrial flutter can also be identified by devices, confers similar thromboembolic risk to AF and is managed in a similar way to what is described here for AF.

2. Identification of atrial fibrillation with devices: the advantages

Although the gold standard for diagnosing AF is the manual interpretation of an electrocardiogram (ECG), the paroxysmal and silent nature of AF in many patients decreases the sensitivity of detection significantly. Non-invasive cardiac monitoring using tools such as the 24–48 h Holter monitor and patient-triggered event recorders play a significant role in identifying AF but are limited with respect to short monitoring time and

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the requirement of patient awareness to activate the device. A PPM implantation purely for cardiac monitoring is not indicated, however for patients with PPMs and other devices for other reasons, they can be an excellent resource for continuous lifelong cardiac monitoring. With an aging population, the number of patients with devices continues to increase. Furthermore, patients with devices tend to be of advanced age and have comorbidities similar to the risk factors for AF, making screening in this group of patients appropriate. In addition to patient characteristics, the pacing mode could also play a role in a person developing AF. It has been shown for example that a pacemaker in VVI-mode could precipitate AF through asynchronous left ventricular (LV) contraction due to right ventricular pacing, which in turn can lead to papillary muscle dysfunction, mitral regurgitation and left atrial enlargement [8]. It has been shown that the incidence of AF can be up to 50% in patients with PPMs and a significant proportion of the patients develop AF after PPM implantation, making monitoring during pacing checks even more important [9,10].

Dual-chamber pacemakers can help detect AF through their automatic mode switching (AMS) algorithms and intracardiac electrogram interpretation. AMS algorithms were initially developed to prevent tracking of supraventricular tachycardias but their data can also be used to diagnose paroxysmal atrial tachycardias. Most modern devices also provide the ability to record intracardiac electrograms of high-rate episodes for manual interpretation in order to increase the diagnostic accuracy by reducing false readings due to oversensing of far-field R wave (Fig. 1) or noise on the atrial lead. The exact sensitivity and specificity depend on the programmable values for atrial rate, duration of episode and also the manual verification of the stored electrograms. In general, the sensitivity is 57–98% and specificity is 85–100% [11]. An analysis of the ASSERT study has demonstrated that 17.3% of atrial high-rate episodes >6 min and >190 beats/min were false positives (mainly repetitive non-re-entrant ventriculoatrial synchrony) when the electrograms were reviewed. False positives were reduced to 6.8%, 3.3% and 1.7% when the threshold duration was increased to 30 min, 6 h and 24 h respectively. Therefore, it is important to verify subclinical AF with a manual interpretation of the electrogram and not to simply rely on the detection of an atrial high-rate episode by the pacemaker, especially for episodes of short duration. [12].

3. Identification of atrial fibrillation with devices: the clinical significance

The relationship between traditionally identified AF and the risk of stroke is well known: identification of any AF in the context of someone at high risk of thromboembolism merits consideration of anticoagulation. Accordingly, both the European and the recently published American guidelines make recommendations for anticoagulation according to the established CHA_2DS_2-VASc and HAS-BLED scores, regardless of whether the AF is paroxysmal, persistent or permanent, symptomatic or silent [13,14]. In the absence of lifelong monitoring, it is impossible to quantify the burden of the disease and it is assumed that patients have further episodes of AF and recommendations for anticoagulation are being made as per guidelines.

However, the development of pacemakers/devices which can provide lifelong cardiac monitoring made it possible to quantify the burden of AF. It raised the question of whether there is a critical value of device-detected AF over which the risk of stroke increases significantly, and if there is a small, safe threshold under which anticoagulation can be avoided. We review the available studies to date below.

The ASSERT study from 2012 attempted to investigate the relationship between device-detected AF and the risk of stroke. The authors defined device-detected AF as any episode with an atrial rate >190 beats per minute (bpm) lasting >6 min. They found that subclinical device-detected AF for >6 min in the first three months after device implantation was significantly associated with a risk of stroke (HR = 2.5; 95% CI = 1.28–4.89; p = 0.008). This risk was independent of other risk factors of stroke and also independent of clinical presentation of symptomatic AF. Interestingly, the time-dependent analysis showed that increased burden of device-detected AF (i.e. >24 h vs. >6 h vs. 6 min) was not associated with a significantly greater increase in the risk of stroke. Even though the study was underpowered for such an analysis, the stratification of patients in quartiles based on the duration of longest device-detected AF episode showed that patients at the highest quartile had a significantly higher risk of stroke, with episodes of >17.7 h attributing risk of stroke of 4.89%/year (95% CI = 1.96–10.07). As expected, the higher the $CHADS_2$ score, the higher the risk of stroke. However, it is important to appreciate that the rate of stroke in the ASSERT study was lower than what would be expected according to the $CHADS_2$ score. There are two possible explanations for this. Most likely, a higher proportion of patients were anticoagulated promptly upon identification of the high atrial rates as a result of the frequent clinic consultations during the study and the potential clinicians' feeling that this would be appropriate. Alternatively, another likely explanation might be that not all high atrial rates were truly atrial fibrillation hence the risk was lower [15].

A secondary analysis of the TRENDS study from 2009 showed that 30-day periods with zero and low device-detected AF burden were

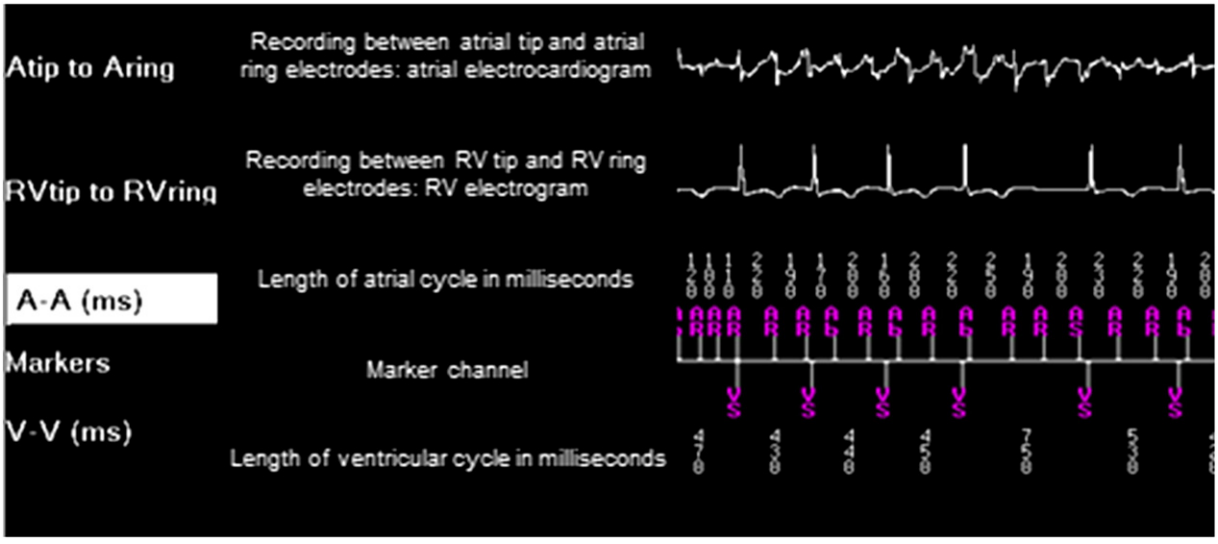

Fig. 1. The intracardiac electrogram can give accurate interpretation of the rhythm of the patient. In this case the atrial electrogram rate ranges from 160 ms to 290 ms suggesting an atrial rate of 200–375 bpm. The ventricular conduction is variable leading to an irregularly irregular rate of 110–140 bpm.