Are implantable cardiac monitors the ‘gold standard’ for atrial fibrillation detection? A prospective randomized trial comparing atrial fibrillation monitoring using implantable cardiac monitors and DDDRP permanent pacemakers in post atrial fibrillation ablation patients

Steven J. Podd, Conn Sugihara, Stephen S. Furniss, and Neil Sulke*

Cardiology Research Department, East Sussex Healthcare NHS Trust, Eastbourne Gen Hospital, East Sussex, UK

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Aims

Implantable devices are widely accepted, but not proven, to be the most reliable monitoring method to assess atrial fibrillation (AF) therapies. We compared REVEAL™XT implantable cardiac monitors (ICMs) and permanent pacemakers (PPMs).

Methods and results

Fifty patients with paroxysmal AF were randomized to ICM or PPM implant 6 weeks prior to pulmonary vein isolation. Permanent pacemakers were programmed to monitoring only (ODO). Device downloads were performed at 0, 3, 6, 9, and 12 months. All patients underwent 7-day external loop recorder. Device ECGs and EGMs were compared for AF burden. A total of 20 744 and 11 238 arrhythmia episodes were identified in the ICM and PPM groups, respectively. Correct identification of AF was significantly better in the PPM group (97 vs. 55% \( P \), 0.001). In the ICM group, 26% of ECGs were un-interpretable. Sensitivity and specificity for each episode of AF was significantly better in the PPM group (100 vs. 79% and 98 vs. 66%, respectively, \( P < 0.001 \)). The positive predictive value for the detection of any AF was significantly better in the PPM than the ICM (100 vs. 58%, \( P = 0.03 \)). The negative predictive value for the absence of all AF was not significantly different between the PPM and ICM (100% vs. 92%, \( P = 0.76 \)).

Conclusion

Permanent pacemakers Holters are the most accurate method of evaluating arrhythmia burden and the therapeutic efficacy of novel AF therapies. ICM has a high degree of artefact, which reduces its specificity and sensitivity. Despite the deficiencies of ICM monitoring the negative predictive value of the ICM is satisfactory if zero AF burden is the aim of therapy.

Keywords

Atrial fibrillation • Atrial fibrillation burden • Implantable cardiac monitoring • Loop recorders • Atrial fibrillation ablation

Introduction

Atrial fibrillation (AF) is the most frequent arrhythmia and is a major risk factor for stroke.\(^1\)–\(^3\) It is also reported to double the risk of death due to cardiovascular diseases. Medical therapies have had moderate symptomatic success, and novel therapies such as pulmonary vein isolation have significant inherent risks. Evaluations of these novel techniques have relied on symptomatic reporting and sparse ECG monitoring, both of which are unreliable assessments of true AF burden.\(^4\)–\(^6\) Approximately 95% of AF episodes are
Asymptomatic in patients with paroxysmal AF. The presence of asymptomatic AF still carries significant morbidity. Recent assessments trying to evaluate the relationship between AF burden and the risk to patients suggest that as little as 5 min of arrhythmia may convey an increased stroke risk. A position paper regarding AF monitoring states that implantable devices are widely accepted, but not proven, to be the most reliable monitoring method to assess AF therapies—a ‘theoretical gold standard’. An accurate assessment of AF burden and episode patterns may give clues to the natural history of AF, complications, and response to treatments.

This study compared the AF monitoring capability of implantable cardiac monitor (ICM) often referred to as an implantable loop recorder or implantable loop recorder (ILR) and DDDRP permanent pacemaker (PPM) with advanced AF detection. Concurrent validation with a 7-day external loop recorder was undertaken. We hypothesise that ICMs are not as accurate at AF detection as PPM.

**Methods**

**Setting**

The study was performed at Eastbourne District General Hospital.

**Patients**

Fifty consecutive patients with drug refractory symptomatic paroxysmal AF were invited to participate in the study. Exclusions included pregnancy, unstable angina or myocardial infarction within the last 2 months, NYHA class III or IV heart failure, severe valvular dysfunction, and previous left atrial ablation.

**Interventions**

The local research ethics committee approved the study. Written informed consent was obtained from all participants. Participants were randomized 1:1 to either implantable cardiac monitor or dual-chamber permanent pacemaker (DDDRP PPM) with advanced AF detection algorithms implantation at least 6 weeks prior to pulmonary vein isolation. An independent clinician using computer-generated random numbers performed randomization. Clinical follow-up was performed at 1 month and at 3, 6, 9, and 12 months post ablation with device Holter downloads. In addition, all participants underwent a full disclosure 7-day external monitor within the 12-month follow-up period to corroborate device derived recordings to allow evaluation of positive and negative predictive values for the device monitor.

**Implantable cardiac monitor group**

Participants in the ICM group were electrically mapped in a sitting position prior to implantation as per the manufacturer’s instructions (Reveal XT). The devices were implanted subcutaneously and all parameters were programmed to manufacturer’s advised settings. The device has a 27 min automated electrocardiogram (ECG) recording capability and a 22.5 min patient activated ECG recording capability. Episodes of AF are detected by irregular R–R intervals as detected on a double-sector Lorenz plot. Episodes of AF must be at least 2 min in duration to be detected and recorded. Text details (start date, time and episode duration) are recorded for up to 30 episodes. Atrial fibrillation burden is derived from all detected episodes. When the device memory is full, earlier episodes are overwritten by later episodes.

**DDDRP permanent pacemaker group**

Participants in the DDDRP PPM group were implanted with dual-chamber PPMs. Preferred lead access was via the axillary vein. The ventricular lead was actively fixed in the inter-ventricular septum. The atrial lead was actively fixed in the right atrial appendage. All pacemakers were programmed to ODD mode (i.e. monitoring mode only) with all anti-AF algorithms switched off. These devices provide 22 min of intracardiac electrogram (EGM) recording capability. Atrial fibrillation burden is derived from all episodes of AF. Atrial fibrillation episodes are detected from high rate atrial episodes lasting more than 3 s. When the device memory is full, earlier episodes are overwritten by later episodes.

**Pulmonary vein isolation**

Pulmonary vein isolation was performed under conscious sedation at least 6 weeks post device insertion. All procedures utilized either phased multipolar radiofrequency ablation technology (pulmonary vein ablation catheter, PVAC®, Medtronic, Minneapolis, MN, USA) or conventional irrigated tip radiofrequency ablation technology (Navistar Thermocool®, Biosense Webster, CA, USA) guided by a 3D electroanatomical mapping system a multipolar circular mapping catheter. All procedures were performed with the participants on uninterrupted warfarin therapy (target INR 2–3) and with a target activated clotting time above 300 s once successful access to the left atrium was achieved.

**7-Day full disclosure external monitor**

Del Mar Reynolds Lifecard CF monitors were used for the 7-day full disclosure external monitoring. A device Holter download was performed at the start and end of the 7-day external monitoring period.

**Measurements**

**Comparison of implantable cardiac monitor and permanent pacemaker groups**

Atrial fibrillation burden from each device was recorded at baseline and each follow-up stage.

All EGMs from the PPM group and ECGs from the ICM group were examined independently by two electrophysiologists and identified as true AF, false AF, or un-interpretable.

**Comparison of implantable cardiac monitor and permanent pacemaker groups with 7-day full disclosure external monitoring**

Two independent electrophysiologists identified all episodes of AF lasting more than 2 min in duration. The episodes from the external monitor were compared with the episode list from the implantable device and classified as AF episode detected (true positive), AF episode not detected (false negative), AF episode incorrectly detected (false positive).
The remaining time from the external monitor was classified as an episode of sinus rhythm (true negative) or un-interpretable.

Statistical analysis

All continuous variables were reported as a mean with standard deviation for normally distributed data and median with interquartile range for non-normally distributed data. Unpaired Student t-test was used for comparisons of continuous normally distributed variables between the groups. Chi-squared test was used for comparison of all categorical data. A two-tailed P-value of <0.05 was considered statistically significant. PASW statistics 18™ for windows was used for all data analysis.

Results

Patient demographics

Twenty-five patients were recruited to each group. Patient characteristics are displayed in Table 1. There were no significant differences between the two groups. The devices implanted in the PPM group were 24 Advisas and 1 Enrhythm (Medtronic).

Arrhythmia episodes detected

A total of 20 744 arrhythmia episodes were identified by the device in the ICM group. Of these 12 864 (62%) were identified as AF by the device and a total of 894 ECGs were examined. A total of 20 744 arrhythmia episodes were identified by the device in the PPM group. Of these 12 864 (62%) were identified as AF by the device and a total of 870 EGMs were examined.

Comparison of implantable loop recorder to permanent pacemaker

The AF burdens for the ICM and PPM patient groups at the pre-ablation, 1, 3, 6, 9, and 12 months post ablation are shown in Figure 1. No significant difference was seen in the average AF burden recorded from the ICM and PPM groups at any stage.

The positive predictive value (PPV) for correctly identifying an AF episode was significantly better for the PPM than the ICM (97 and 55%, respectively, P < 0.001). For AF episodes exceeding 6 min the ICM PPV for correctly identifying an episode of AF was significantly better than those episodes of 6 min or less (62%, P = 0.03) but remained inferior to the PPM PPV (100%, P < 0.001).

The number of un-interpretable ICM recorded ECGs were significantly higher than un-interpretable PPM recorded EGMs (26 and 0%, respectively, P < 0.001). The number of patients with a complete dataset that was un-interpretable was significantly higher in the ICM group compared with the PPM group (5 vs. 0, respectively, P = 0.049).

Seventeen (68%) patients in the PPM group and 18 (72%) patients in the ICM group reported a symptomatic success from the ablation procedure (P = 0.74). Post ablation 15 (60%) patients in the ICM group and 12 (48%) in the PPM group had zero AF burden as recorded by their device (P = 0.7).

There was a significant difference in the symptom success rate and zero AF burden as recorded by the device in the PPM group (P = 0.03) but not in the ICM group (P = 0.18).

Comparison of each device to 7-day full disclosure monitor

A total of 167 episodes of AF of over 2 min duration were detected by the 7-day full disclosure monitor in the PPM group. A total of 173 episodes of AF of over 2 min duration were detected by the 7-day full disclosure monitor in the ICM group. The true positive, false positive, false negative, true negative episodes and the sensitivity, specificity, PPV, and NPV for each device are shown in Table 2.

The PPV for the presence of any AF for the ICM was significantly lower than the PPM (58 vs. 100%, respectively, P = 0.03). However, the NPV for the absence of all AF for ICM was not significantly different to the PPM (92 vs. 100%, respectively, P = 0.76).

Patient experiences with implantable cardiac monitor and permanent pacemaker and complications

In the ICM group, one patient experienced some discomfort from the device and one patient required 5 days of antibiotics for a wound infection.

Table 1 Displays demographics for each group

<table>
<thead>
<tr>
<th></th>
<th>PPM (n = 25)</th>
<th>ICM (n = 25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66.8 ± 7.0</td>
<td>64.5 ± 10.6</td>
<td>0.35</td>
</tr>
<tr>
<td>Male</td>
<td>12 (50%)</td>
<td>10 (40%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (40%)</td>
<td>11 (44%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease /asthma</td>
<td>3 (12%)</td>
<td>3 (12%)</td>
<td>1</td>
</tr>
<tr>
<td>IHD</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
<td>0.31</td>
</tr>
<tr>
<td>OSA</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Previous stroke/TIA</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
<td>1</td>
</tr>
<tr>
<td>Alcohol misuse</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1</td>
</tr>
<tr>
<td>Biplane EF</td>
<td>62 ± 7.2%</td>
<td>61 ± 7.0%</td>
<td>0.48</td>
</tr>
<tr>
<td>LA size</td>
<td>3.7 ± 0.9 cm</td>
<td>3.8 ± 0.7 cm</td>
<td>0.66</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.3 ± 0.4</td>
<td>1.1 ± 0.4</td>
<td>0.07</td>
</tr>
</tbody>
</table>

**Figure 1** AF burdens as recorded by each device, pre-ablation, 1, 3, 6, 9, and 12 months post ablation.
infection. All patients in the ICM group would opt for an ICM again. The most common reason given was, they felt reassured, that any palpitation symptoms could easily be clarified by use of the implanted monitor.

In the PPM group, two patients required atrial lead revisions due to displacement. All patients in the PPM group would opt for a PPM again. The most common reason given was, they felt reassured, that any palpitation symptoms could easily be clarified by use of the device Holter function.

**Discussion**

This study suggests that changes in AF burden measured by ICM do correlate with those of the significantly more sensitive and specific PPM Holters in patients undergoing pulmonary vein isolation for paroxysmal AF. However, the PPV of the ICM per episode of AF is only just above 50% and up to 20% of episodes of at least 2 min duration and all episodes of below 2 min duration (contributing ~9.9% of the total AF burden) are not detected at all by their device. This implies that for individual patients the ICM AF burden assessment may be inaccurate, but the average population burden may represent a reasonable estimate as the false-positive episodes are effectively neutralized by false-negative episodes and AF episodes of less than 2 min duration in our population.

There was a significant difference in the symptomatic success rate and the device-recorded success rate across all of the patients. This suggests that symptomatic follow-up alone of patients post-AF ablation is insufficient when the absence of AF is the desired end point. This result was seen in the PPM group but not in the ICM group.

The European Heart Rhythm Association Position Paper identified implantable devices as the theoretical gold standard for detection of AF recurrence. This hypothesis has been extrapolated to AF burden and ICMs are being increasingly utilized to measure the efficacy of novel therapies. Presently there are 13 trials registered on ClinicalTrials.gov using ICMs to measure the primary endpoint of AF burden. The assumption that ICMs accurately measure AF burden is partially refuted by our data and this has implications for the use of ICMs in both the clinical and research setting.

From a clinical perspective, the NPV for the absence of all AF is similar in ICMs and PPMs and thus the ICM could be useful in a number of scenarios, e.g. post cerebrovascular accident or transient ischaemic attack for the detection of silent AF or in post AF ablation patients where accurate confirmation of complete AF extinction, may influence anticoagulation use. Furthermore, it is becoming accepted that patients with a high CHADS2-VASc score but without documented AF should be intensively investigated for the presence of AF, which may include the use of an ICM. Results from large trials such as CABANA, EAST, and CRYSTAL AF will aid our decisions on the use of intensive AF interventions and AF monitoring. In a general population, implantable devices currently have a relatively narrow use. Other non-invasive screening tools for AF have shown promise. One such example analyses a single ECG lead, via a patient’s grip, for R-R interval irregularity and has excellent sensitivity and specificity (100 and 95.9%, respectively). These easy-to-use, non-invasive devices are ideally suited to opportunistic sampling and therefore large screening programmes. The ease of use and impressive sensitivity and specificity must be weighed against the short sampling time (1 min) and hence applies only to patients in persistent AF. External loop recorders used for relatively long periods (49–191 h) showed significantly higher rates of AF recurrence detection post surgical AF ablation than conventional 24–48 h external monitors or spot ECGs (31 vs. 16 vs. 11%, respectively). Detection of AF recurrences in the ICM group was 40%. It is difficult to directly compare these values given the different ablation technologies used in each study, but it does suggest that the longer period of monitoring the higher the detected rate of AF recurrence post ablation. The PPM group had detected an AF recurrence rate of 52%, suggesting that detection is not just a function of time monitored but also the quality of the recording.

The XPECT trial compared ICM with ELR monitoring over a 46 h period. The study reported a similar NPV (98%) for the absence of AF but a higher PPV (79%) for the presence of AF with the ICM. This trial significantly differed from our design and this may explain the disparity in the PPV and also highlight some of the ICMs weaknesses in accurate AF episode recording. The XPECT trial population was selected due to their high risk of AF recurrence (patients known to have ‘active’ PAF) and as such the average AF burden at the time of recording was 14% with 65% of patients having some AF during the 46-h monitoring period. In contrast, our study recruited patients at lower risk of AF recurrence and recorded an average AF burden at the time of monitoring of 4.8 with 26% of patients having any AF during the 7-day ELR monitoring period. The percentage of erroneously recorded AF should be constant regardless of the underlying real AF burden; thus the higher the real AF burden the less the influence of erroneous AF burden on the PPV. Therefore ICMs perform better with respect to PPV as the true AF burden increases. This exposes one of the ICM’s shortcomings; the device is designed to be ‘oversensitive’ and therefore not miss important arrhythmic episodes. This device bias for over detection of arrhythmia will result in it performing well when PPV is measured in patients with high AF burdens. In clinical use however, these devices are more likely to be used with patients where the diagnosis of AF is in doubt and the AF burdens may be extremely low but still of clinical importance.

An AF burden as low as 0.75% in the prior 30 days, as measured by pacemaker Holters has been shown to double a patient’s cerebrovascular risk. In clinical scenarios where ICMs are likely to be

| Table 2  Positive predictive value, NPV, sensitivity and specificity per episode of AF for the PPM and ICM groups |
|-----------------------------------------------|---------------|
|                                              | PPM (n = 25)  | ICM (n = 25)  |
| True positives                              | 167           | 136           |
| False positives                             | 3             | 62            |
| False negatives                             | 0             | 37            |
| True negatives                              | 174           | 121           |
| PPV                                          | 98%           | 69%           |
| NPV                                          | 100%          | 77%           |
| Sensitivity                                  | 100%          | 79%           |
| Specificity                                  | 98%           | 66%           |


used, cryptogenic stroke, and post AF ablation, the AF burden is likely to be low or zero to have escaped previous diagnosis. Our study, as compared to the XPECT trial, better reflects this real-life population and therefore in practice the PPV is likely to be similar to, if not lower than, that recorded in this trial as the erroneous arrhythmic episodes are exposed more frequently in a low AF burden population.

If low AF burden carries increased cerebrovascular risk is this still the case for differing patterns of AF. For example do two patients with similar AF burdens (1.4%) but one with twenty 60 s AF episodes occurring daily have the same stroke risk as a patient with a single 10 h episode over a period of a month? The ICM in its current format is poorly equipped to answer this question. The PPM Holter however does provide such information. Furthermore, the temporal relationship between stroke and episodes of atrial arrhythmia is poor with AF episodes occurring up to 30 days prior having an influence on cerebrovascular risk. Both PPMs and ICMs are equipped to detect and store AF episodes occurring over several years. Unfortunately the poor specificity and PPV for AF episodes combined with a limited storage capacity in the ICMs has been shown in this study to saturate the ECG storage with aberrant data in a significant proportion of patients. The PPM Holter EGM storage is less prone to this effect due to the high specificity and PPV for AF episodes. Recent and future technological advances in automated remote storage of information utilizing Bluetooth technology may alleviate the shortcomings of current ICMs. It has previously been commented that PPM EGMs are a powerful tool in the detection of silent AF. Remote monitoring of PPM EGMs will increase our capability for earlier detection of silent AF episodes, which may have important clinical implications regarding anticoagulation and stroke prevention.

In contrast, the NPV for the absence of all AF is not influenced in the same manner as PPV. The oversensitivity which the ICM suffers gives rise to its impressive NPV for the absence of all AF which is arguably its most salient feature. This is supported by the similar NPV found in the ICM group of this study and the XPECT trial.

Many previous studies have shown the superiority of the ICM over spot, 24 h, 7-day ECG monitoring and telephonic monitoring at detecting recurrences of AF. This study has revealed some of the weaknesses of ICMs in AF burden evaluation compared with PPM. Other studies have highlighted that pacemaker algorithms that rely upon atrial high rate episodes alone or mode switch episodes for atrial arrhythmia detection have a false-positive rate of up to 17.3%. The pacemakers used in the PPM group utilized advanced AF detection algorithms that incorporate atrial rate stability in addition to atrial rate and therefore would be expected to, and did perform better than those reported from studies using atrial high rates alone. In practical terms, however, PPMs are not used as pure monitoring devices nor are they appropriate to do so and therefore the ICMs remain the primary tool for the detection of AF recurrence. Permanent pacemaker implantation for AF detection alone should not be used outside of a research setting.

This study demonstrates that, in a clinical context, the ICM can be of use in patients with suspected low burden AF, either in the context of undiagnosed infrequent palpitations or post AF therapy where AF extinction is the required endpoint. The ICMs are useful for evaluating study endpoints including freedom of AF and estimates in changes of AF burden. With current technology, more detailed understanding of the relationship between clinical AF phenotypes, clinical AF risks, AF patterns, initiations, and other electrical behaviour are beyond the reach of the current ICMs and should be reserved for PPM populations. A recent study has shown interesting insights from patients with pacemakers and AF in terms of AF patterns and progression that differs from conventional definitions. These novel categorizations may have clinical implications that influence treatment outcomes and AF progression.

The use of currently available ICMs in the long-term assessment of AF burden should be undertaken with caution. This is not the case if the absence of AF is the trial or clinical endpoint as is the case in many trials evaluating AF ablation technologies.

**Study limitations**

The PPM devices used in this study had advanced AF detection algorithms, which are not available in all PPM systems. Surrogates such as time in mode switch are often used but give estimations of AF burden that are less accurate. Implantable cardiac monitors were programmed at nominal settings for the duration of the study to prevent operator bias. This may differ from their use in clinical practice. For the majority of this study, the patients were post ablation, and therefore the recurrence rate of AF, was likely to be low. This does not represent all patient populations in which detection and evaluation of AF episodes may be desired. However, the post-ablation population is steadily growing and the certainty of arrhythmia extinction is invaluable in the evaluation of ablation technologies and may prove to be of paramount importance in the clinical context of stroke reduction and anticoagulation use.

**Conclusion**

Dual-chamber PPMs are the gold standard for AF detection and monitoring but are not primarily implanted as cardiac rhythm monitors. Implantable cardiac monitors have an excellent NPV for AF extinction. This potentially makes it a powerful tool in both research and clinical settings where confirmation of AF extinction is desirable especially when considering cessation of anticoagulation therapy. However, the high false-positive rate for AF episode detection limits its use for precise AF burden monitoring in individual patients.

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**References**

Are implantable cardiac monitors the ‘gold standard’ for AF detection?


