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Management of atrial fibrillation –

What are the possibilities of early detection with Home Monitoring?

Summary A large number of patients implanted with dual-chamber pacemakers exhibit symptoms of recurrent or new atrial fibrillation. Scheduling follow-up visits for every 6–12 months in this setting may be disadvantageous on three grounds. First, delayed information about the onset of atrial fibrillation does not allow an immediate reaction with pharmacological or dedicated pacing therapy. Second, the efficacy of the chosen therapy cannot be evaluated until the next scheduled follow-up. Third, real-time awareness of a significant atrial fibrillation burden is critical to use appropriate anticoagulation therapy for the prevention of thromboembolic events. The new Home Monitoring technology (Biotronik, Berlin) offers real-time transmission of diagnostic data stored in the pacemaker memory to the physician. This may represent a useful tool for the detection and treatment of patients with atrial fibrillation. Daily documentation of atrial rhythm via Home Monitoring allows a quick reaction to the onset of atrial fibrillation and real-time control of the therapeutic efficacy. The ongoing, international, randomized Home-PAT clinical trial aims at defining and quantifying the importance of Home Monitoring for the diagnosis and treatment of atrial fibrillation in patients with dual-chamber pacemakers.

Key words Atrial fibrillation – cardiac pacing – Home Monitoring – telecardiology

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Introduction

Atrial fibrillation is the most common arrhythmia in clinical practice and is associated with increased morbidity, and mortality rates twice as high as in sinus rhythm subjects [7]. With the number of elderly patients growing and incidences increasing, the clinical and financial burden of the treatment of atrial fibrillation will progressively rise in the future [14]. Early detection and treatment of this arrhythmia could substantially influence health-care related costs. In many patients, atrial fibrillation is associated with symptomatic bradycardia and/or significant pauses, which might be responsible for arrhythmia recurrences. Bradycardia can be the consequence of antiarrhythmic drug treatment and may require pacemaker implantation.

Continuous technological development over recent decades has led to a significant improvement in the diagnosis and treatment of atrial fibrillation in pacemaker patients. Enhanced pacemaker diagnostic memory in terms of event counters, histograms and stored electrograms allows optimal monitoring of arrhythmia, including detection of asymptomatic episodes. Furthermore, new pacing algorithms may prevent or interrupt early atrial tachyarrhythmia episodes.

However, benefits of the internal, continuous monitoring of atrial fibrillation by implanted devices is limited if follow-up controls are scheduled every 6

months (routine controls) or initiated by patients' symptoms. In these situations, the arrhythmia cannot be controlled in real-time, causing the following unfavorable consequences:

- delayed information about the onset of paroxysmal atrial fibrillation (i.e., asymptomatic episodes) obviates an immediate therapeutic reaction, which may lead to a higher rate of adverse clinical events, facilitating the progression to permanent atrial fibrillation;
- the use of an effective anticoagulation therapy may be delayed in patients with asymptomatic episodes;
- particularly during the early postoperative period, the optimization of antiarrhythmic therapy and pacemaker programming may require additional follow-ups, inconveniencing the patient;
- the efficacy of rate control therapy cannot be consistently evaluated, neither in patients with permanent atrial fibrillation nor in those with frequent recurrences.

A technology called Home Monitoring has recently been implemented in Biotronik pacemakers. Home Monitoring is an automatic, long-distance telemetry system that provides frequent, regular transmission of data in the pacemaker memory to the Patient Unit (CardioMessenger). This device is capable of relaying data received from the implants to a Service Center via a GSM (mobile phone) network in the form of encrypted SMS messages. The Service Center decodes, analyzes and organizes the data and posts them on a secure website, which can be accessed by the patients' physicians.

This paper's objective is to analyze and discuss how important Home Monitoring technology may be for the diagnosis and treatment of atrial fibrillation in pacemaker patients.

Detection of asymptomatic atrial fibrillation episodes

Although most patients with atrial fibrillation experience multiple symptoms such as palpitations, dizziness, breathlessness, anxiety, chest discomfort, and pre-syncope, atrial fibrillation can also be asymptomatic and incidentally discovered during routine physical examination, preoperative assessment, or following a stroke. Ambulatory cardiac monitoring in paroxysmal atrial fibrillation has demonstrated that asymptomatic episodes are common in patients with a history of symptomatic episodes and may involve 20% of patients during a 2-year follow-up [13]. This figure is likely to be higher due to shortcomings of the applied detection technique. In the Prevention of Atrial Fibrillation after Cardioversion (PAFAC) trial, about 95% of all atrial fibrillation recurrences were initially detected by ECG recordings that were transmitted transtelephonically on a daily basis, and 70% of all recurrences occurred completely asymptomatically [6].

The high incidence of asymptomatic episodes has been confirmed by using implantable device diagnostics for atrial fibrillation detection. Israel et al. [9] studied a group of patients receiving pacemakers equipped with advanced diagnostic and therapeutic options for atrial fibrillation. Over a mean period >18 months, atrial fibrillation recurrences were asymptomatic in more than one-third of patients with a history of paroxysmal or persistent atrial fibrillation. Moreover, a recent multivariate analysis of the Mode Selection Trial (MOST) demonstrated that the presence of atrial high rate events recorded by pacemaker diagnostics is an independent predictor of total mortality, stroke, and chronic atrial fibrillation in patients with sinus node dysfunction [8]. In the cohort of patients at high risk for a stroke, Home Monitoring technology may be crucial in early detection of asymptomatic episodes and in allowing physicians to select the optimal clinical approach for each individual patient.

Drug therapy control

Although nonpharmacological options for atrial fibrillation have been considerably expanded in recent years, medical management still remains the first-line therapy in most cases. In patients with short paroxysms of atrial fibrillation, therapeutic strategies should generally concentrate on providing rhythm control. In these patients, Home Monitoring may help to continuously control rate and duration of arrhythmia episodes and promptly provide effective therapy if the arrhythmia persists. In patients with persistent atrial fibrillation, the clinician is often faced with the dilemma whether to restore and then maintain sinus rhythm (rhythm control), or to accept the arrhythmia (permanent atrial fibrillation) and control the ventricular rate (rate control). Benefits of rhythm control include a better clinical outcome, an improved quality of life and a reduced risk for stroke.

On the other hand, antiarrhythmic drugs, commonly used to gain rhythm control, have important adverse effects and limited efficacy. Rate and rhythm control strategies were compared in the AFFIRM (Atrial Fibrillation Follow-up Investigation in Rhythm Management) [1] and RACE (Rate Control

Clinical Research in Cardiology, Volume 95, Supplement 3 (2006)

vs Electrical Cardioversion for Persistent Atrial Fibrillation) [17] trials. Despite different study populations and designs, no significant differences in the major endpoints (total mortality, cardiac death, stroke, bleeding, etc.) were observed between the two strategies. In fact, only about 60% of the patients in the rhythm control arm in the AFFIRM trial were in sinus rhythm after 5 years, while rate control was obtained in >90% of patients in the rate control group. These results confirmed the ineffectiveness of antiarrhythmic drugs in sinus rhythm preservation, while rate control may be easily achieved by beta-blockers and calcium antagonists. It should not be forgotten that non-pharmacological therapies were applied in both studies only in a small fraction of patients assigned to rhythm control. A major finding of the AFFIRM trial is that anticoagulation represents a key factor for improving clinical outcome both in patients with paroxysmal or persistent atrial fibrillation [4]. The fact that less patients in the rhythm control group received anticoagulation may have impacted the clinical outcome.

A recent revision of the AFFIRM findings, relying on treatment instead of intention-to-treat analysis, demonstrated an improved clinical outcome when rhythm control could be reached [4]. The presence of sinus rhythm was associated with a lower risk of death than the warfarin use. Antiarrhythmic drugs were associated with increased mortality only after adjustment for the presence of sinus rhythm. Consistent with the original intention-to-treat analysis, antiarrhythmic drugs were no longer associated with mortality when sinus rhythm was removed from the model.

An optimal drug treatment in patients with atrial fibrillation is not easy to establish and requires strict control by clinicians. Olshansky et al. evaluated 2027 patients randomized to the rate control arm in the AFFIRM study and concluded that most patients had an adequate response to the available drug classes, although frequent medication changes may be necessary and combinations may be needed [12]. Others analyzed the risk of arrhythmic events in the antiarrhythmic drug arm of the AFFIRM study [10]. The main results showed that in patients treated with antiarrhythmic drugs, the overall proarrhythmia risk is relatively low, if the drug selection is appropriate and carefully monitored.

In this clinical setting, Home Monitoring technology may become an important tool for physicians in the following ways:

- in patients with paroxysmal atrial fibrillation, to control frequency and duration of arrhythmia episodes and to detect persistent atrial fibrillation in order to allow prompt and early reaction;
- in patients with persistent atrial fibrillation and rhythm control therapy, to react early to atrial fibrillation episodes with cardioversion to prevent atrial remodeling; device reprogramming may be required;
- in patients with persistent or permanent atrial fibrillation to continuously control ventricular rate.

Device therapy control

The number, duration and frequency of arrhythmia episodes, including asymptomatic ones, can nowadays be retrieved from the enhanced pacemaker diagnostic memory [5, 8, 20]. In recent generation devices, several atrial overdrive pacing algorithms have been developed to suppress atrial fibrillation episodes by pacing at a rate that is slightly above the intrinsic rate and by adjusting pacing rate for physical activity and for autonomic nervous system imbalance. Although some studies showed a decrease in the burden of atrial fibrillation, using suppressing algorithms, there is no validated evidence of their clinical efficacy [2, 3, 15, 16]. Patients with low percentages of atrial pacing during conventional dual-chamber pacing seem to benefit more from the activation of preventive algorithms [16]. On the other hand, a high percentage of ventricular pacing may exert a deleterious effect on hemodynamics, thus, inhibiting the benefit of atrial overdrive pacing [2]. In the ADOPT trial, the atrial fibrillation suppression algorithm was effective mainly in decreasing the symptomatic arrhythmia burden in patients with sick sinus syndrome [3]. Interestingly, a significant reduction in the total atrial fibrillation burden was observed in brady-tachy patients when a rate-adaptive algorithm driven by the autonomic nervous system activity was applied. This system is based on the evaluation of cardiac impedance, which reflects cardiac contractility (closed loop stimulation system). In the same patients, overdrive algorithms did not prevent atrial fibrillation [15]. Negative results have been obtained in the ATTEST trial, in which a prevention algorithm was combined with atrial antitachycardia pacing [11].

In optimizing device therapy for atrial fibrillation, Home Monitoring technology may be useful to:

- minimize ventricular pacing;
- set an optimal atrioventricular delay;
- set rate responsiveness;
- optimize prevention algorithms and antitachycardia pacing therapies.

Home Monitoring and atrial fibrillation: clinical application

First clinical experience

The initial clinical experience on atrial fibrillation detection by Home Monitoring was reported by Varma et al. [18]. The authors retrospectively analyzed data from 276 consecutive patients implanted with Home Monitoring pacemakers to define atrial fibrillation patterns and associated ventricular rate. Twenty-nine patients (10.5%) experienced at least one "atrial fibrillation day", defined as a mode-switch burden >20% within 24 hours, during 12±2 months of follow-up. In addition, the following occurred:

- a wide scatter of atrial fibrillation day distribution, ranging from <5 days to >90 days;
- 80% of the patients had relatively few (<30) atrial fibrillation days;
- only 30% of the patients had atrial fibrillation days characterized by a 100% mode switch;
- 79% of patients had a ventricular rate >80 bpm during atrial fibrillation days (mean 25±30 days, median 11 days).

The authors concluded that automatic wireless data transmission by Home Monitoring may be a useful tool to detect atrial fibrillation and to assist in arrhythmia management and clinical decisions.

Perspectives: the Home-PAT trial

The "*Home* Monitoring for the Management of *P*atients with *A*trial *T*achyarrhythmia (Home-PAT)" trial is an ongoing, multicenter, prospective, single-blind, randomized study investigating diagnostic effectiveness of the telemetrically transmitted data in the detection and treatment of atrial arrhythmias, especially paroxysmal atrial fibrillation. The incidence of atrial fibrillation will be compared between patients who are supervised by Home Monitoring and those who are not. The comparison is based on pacemaker memory data, symptom score data, and 24-hour ECG monitoring. In addition, the study will evaluate the influence of Home Monitoring on the patient's quality of life and gather data on the impact of Home Monitoring on cost-effectiveness of combined pacemaker and antiarrhythmic therapy.

The primary objective is to investigate whether continuous diagnosis of paroxysmal atrial fibrillation with the aid of Home Monitoring may result in an improved efficacy of drug and device therapy. The investigation will compare two groups:

- Cardio Report group, in which the Home Monitoring function is enabled and the transmitted data (Cardio Reports) are sent to the physicians according to predetermined specifications;
- Control group, in which the Home Monitoring function is also enabled, but Cardio Reports are not forwarded to the physicians, except for the notification of lead failure, which is not directly related to any endpoint but may jeopardize patient safety.

The efficacy of anthiarrhythmic therapy will be regarded as increased by Home Monitoring if the incidence of significant atrial fibrillation in the Cardio Report group is lower than that in the control group. The incidence of atrial fibrillation and the total atrial fibrillation burden for each patient will be calculated from the mode-switch counters interrogated during follow-up controls.

Secondary goals include atrial fibrillation symptom score, differences in quality of life for the two study groups, and differences in the overall costs of device and drug therapy due to the use of Home Monitoring.

Atrial fibrillation symptom score: According to a symptom questionnaire, patients will be asked whether they have experienced shortness of breath, pain or pressure in the chest area, heart palpitation, dizziness, etc., and to what extent these perceptions have limited their daily activity.

Quality of life will be evaluated by comparing the SF-36 health survey results for baseline and follow-up [19]. The corresponding secondary endpoint tests the alternative hypothesis that the improvement in quality of life from preimplantation to the 6-month follow-up will be different between Cardio Report and control groups. Furthermore, the analysis will comprise the evaluation of baseline and follow-up data among all patients according to age, gender, and pacemaker indication.

Costs of therapy: The economic aspects of Home Monitoring for the management of patients with atrial tachyarrhythmia will be analyzed by estimating direct and indirect costs for scheduled and unscheduled (additional) follow-up examinations, costs for antiarrhythmic medication and for arrhythmia-related adverse events such as cardioversion and stroke. The cost endpoint is investigated with the alternative hypothesis, which postulates no difference in costs between the two groups because it is not expected that the impact of Home Monitoring may result in an overall cost reduction after only 6 months. The additional costs of Home Monitoring will probably be balanced by associated savings in therapy and by reduced costs of arrhythmia-related events.

Clinical Research in Cardiology, Volume 95, Supplement 3 (2006)

A total of 490 patients with any kind of sinus node dysfunction, either in conjunction with impaired atrioventricular conduction or not, will be enrolled in the study and implanted with a Philos DR-T or a Philos II DR-T pacemaker. The patient's general medical condition has to be stable in order to allow him/her to attend the follow-up examination according to the protocol. Patients living in an area with insufficient access to the GSM network are excluded.

After pacemaker implantation and hospital discharge, all participating patients should attend the standard 3- and 6-month follow-up controls. At the 3-month follow-up, a 24-hour ECG recording will be taken for a close comparison of atrial fibrillation data in the standard Holter ECG and in the Home Monitoring messages. The patient has to fill in the SF-36 quality of life questionnaire before the implantation and at the 3- and 6-month follow-ups. The atrial fibrillation-related symptoms questionnaire is to be completed before the implantation, at the 3- and 6-month follow-ups, and during every additional (unplanned) follow-up examination. Data concerning medications, pacemaker programming, and direct and indirect costs of follow-up are to be collected during every follow-up control. The antiarrhythmic therapy choice is left to the physicians, but should comply with the ACC/AHA/ESC Guidelines for the Management of Patients with Atrial Fibrillation [7]. Pacemaker programming can be performed at the physicians' discretion, except for the automatic mode-switch function, which has to be enabled, and atrial sensing configuration, which has to be bipolar. Besides, intrinsic atrioventricular conduction has to be preserved as much as possible, and the overdrive pacing algorithm has to be activated after the first episodes of atrial fibrillation.

Case report on arrhythmia management with the aid of Home Monitoring technology

Fig. 1 illustrates the case of a 74-year old man with sick sinus syndrome. The patient was implanted with the first prototype of a DDDR pacemaker with the Home Monitoring feature, capable of sending atrioventricular synchronism data and without mode-switch counters. No atrial fibrillation episodes had been documented before implantation. Two weeks after the hospital discharge, the patient was re-admitted due to atrial flutter. Following successful electrical cardioversion, Home Monitoring was activated and the patient was discharged. Four days later, Cardio Report showed significant increase in the ventricular rate in conjunction with the deterioration of atrioventricular synchronism. The physician called the patient for an additional follow-up. The ECG and the pacemaker's diagnostic memory data revealed a prolonged asymptomatic atrial fibrillation episode that was subsequently treated by cardioversion and the administration of antiarrhythmic and anticoagulation drugs. Several days later, Home Monitoring data indicated a loss of atrioventricular synchronism, apparently caused by another prolonged atrial fibrillation episode. However, the ventricular rate remained normal due to adequate rate control drug therapy initiated during the previous follow-up. In this case, Home Monitoring allowed:

- an early recognition of asymptomatic atrial fibrillation that would have otherwise remained unnoticed until the next follow-up;
- prompt administration of cardioversion and pharmacological therapy to reduce the risk of progressive heart failure (due to high ventricular rate), progression to persistent atrial fibrillation, and stroke;
- verification of the effect of medication therapy.

Conclusions

Telecardiology represents the most effective future treatment for new patients with implantable devices. Real-time monitoring of pacemaker patients with atrial fibrillation will aid in achieving optimal drug and device therapy and will allow early reaction to changes in a patient's clinical status. Home Monitoring pacemakers seem to be a particularly promising tool in this context. Major updating in health care organization is, however, needed to maximize the benefit of this new technology. In some cases, it might be a challenge to maintain the human relationship between health care personnel and patients when a remote control system is in charge of gathering diagnostic data.

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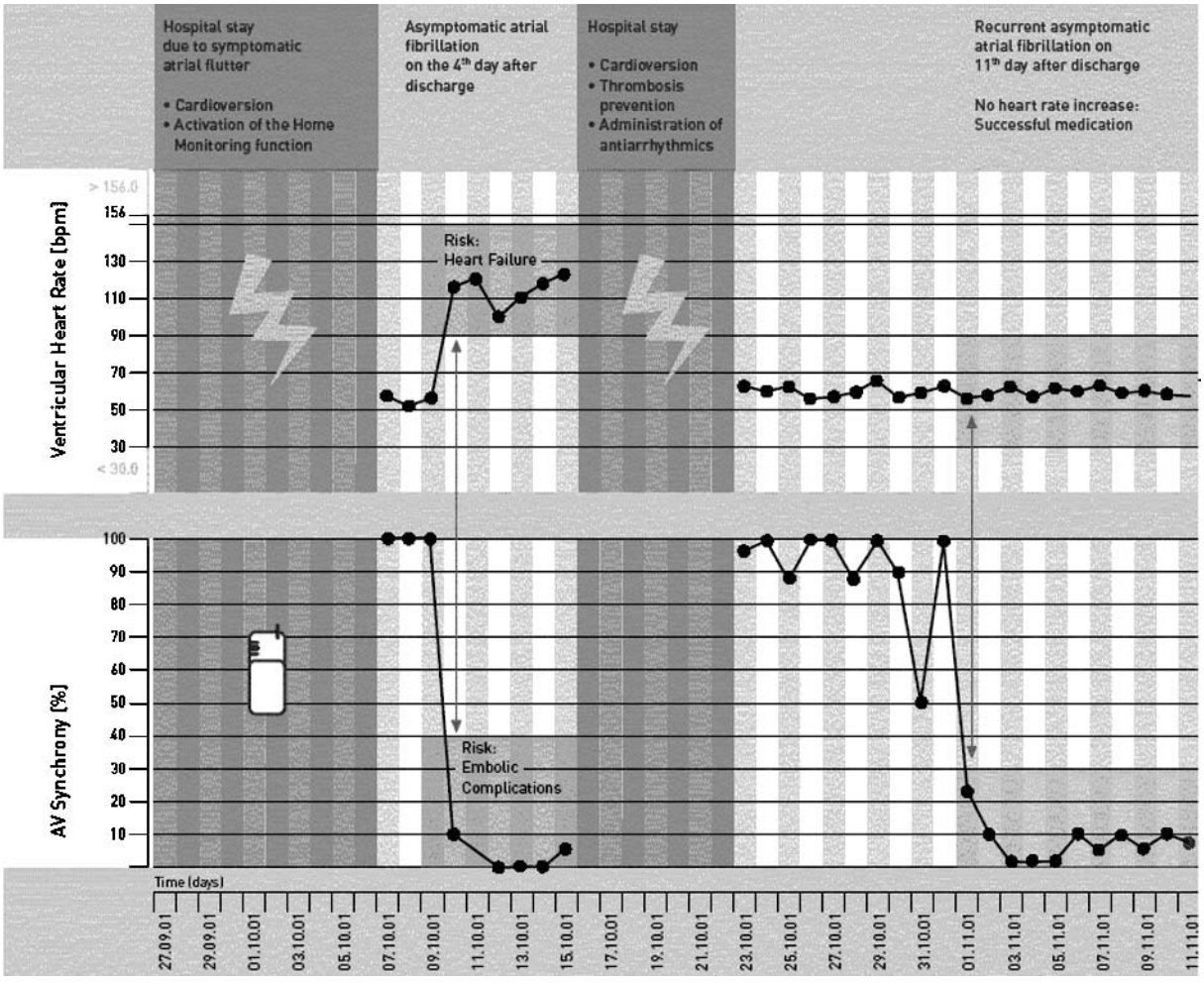

Fig. 1 Thanks to Home Monitoring data, the onset of a persistent atrial fibrillation episode on Oct. 10, 2001 could be recognized through a sudden loss of atrioventricular (AV) synchrony and a significant increase in the ventricular heart rate. Atrial fibrillation reoccurred on Nov., 2001 (loss of AV synchrony), but the stable ventricular rate proved the efficacy of the previously administered rate control medications

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