Potential Applications of Home Monitoring in Pacemaker Therapy – A Review with Emphasis on Atrial Fibrillation and Congestive Heart Failure

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Summary

Currently, the quality of the medical supervision of patients with implanted pacemakers depends solely on regularly scheduled follow-up visits. This is a considerable drawback for continuous therapy optimization and prevention of disease progression as well as early recognition of device-related complications. To overcome this restriction, the concept of Home Monitoring in pacemaker therapy has been developed. This new system involves the periodic automatic transmission of standard pacemaker data to the attending physician via a mobile patient device and a service center. It enables the daily surveillance of a patient's cardiac status, enhances the success of the initiated therapy, and helps determine the necessity for further therapeutic measures. The Home Monitoring system is now under clinical evaluation to reveal its potential for everyday clinical use. In this article, we present a detailed description of the system and the first investigation of its efficacy. Furthermore, we present an analysis of the future use and the potential benefits of Home Monitoring in patients prone to atrial fibrillation and congestive heart failure. In this patient population, we expect significant advantages for diagnosis and therapy with Home Monitoring due to highly detailed patient supervision.

Key Words

Home Monitoring, telemetry, clinical trial, congestive heart failure, atrial tachyarrhythmia

Introduction

Since the first implantation of an artificial cardiac pacemaker over 40 years ago [1], implantable pacemaker technology has undergone a remarkable development. Pacemakers have been transformed from devices that were pre-defined in all their functionalities and could not be modified after implantation into programmable devices that can be tailored to the needs of the individual patient. This tailoring is supported by data about the patient's rhythm, AV-conduction, or activity that are collected in the pacemaker memory for subsequent analysis by the attending physician. Nevertheless, one aspect in the follow-up of pacemaker patients has not changed during these four decades: The patient has to visit the physician for examination and pacemaker follow-up.

Today, pacemaker patients are normally seen every 6 to 12 months for follow-up. One of the greatest disadvantages of these very long follow-up intervals is the significant delay in the physician's awareness of changes in the patient's cardiac status. As a first attempt to address this situation, the idea of TransTelephonic Monitoring (TTM) was introduced in the early 1970's [2]. TTM allows diagnostic data to be transmitted via a telephone line to a TTM service center, which then relays the information to the physician. The data is interrogated from the pacemaker with the help of a special device that the patient has to apply over his/her pacemaker. Hence, TTM relies on the active cooperation of the patient, an arrangement that cannot be expected to work properly for the majority

of pacemaker patients. Therefore, TTM has gained little acceptance in pacemaker therapy in Europe.
In the following we will present the concept of Home Monitoring (HM), which is now available for the first time in a pacemaker. HM shall allow a frequent regular transmission of implant data to the attending physician. It relies only to a minor extent on the patient's cooperation and should thus open the door to innovation in patient supervision and therapy optimization. We will explain the concept of the first clinical investigation, which started in April 2001, and present ideas on the possible impact of HM on pacemaker therapy in patients with atrial tachyarrhythmias or congestive heart failure.

The Home Monitoring System
Successful telemetric inter-follow-up patient supervision, i.e., reliable monitoring of the patient's cardiovascular status between two standard follow-ups, relies mainly on the following:

- Transmission of relevant cardiac data, which may indicate the need for a detailed evaluation of the patient's cardiac situation;
- Transmission of relevant system data, indicating the system's integrity;
- Rapid information in case immediate intervention is required;
- Transmission of data at short intervals, providing a reliable patient history;
- Transmission without delay;
- Concise information without unnecessary repetitions or meaningless data;
- Ease of system handling for the physician and the patient;
- Minimal technical maintenance.

The current HM realization provided by Biotronik (Berlin, Germany) incorporates these aforementioned demands in the following way (Figure 1):
The pacemaker periodically creates an HM message from the standard pacemaker data, i.e., trend data, event counters, histograms, etc. The attending physician can specify the interval in the pacemaker program. Additionally, the possibility of a patient-activated message can be enabled; every time the patient applies a magnet over the pacemaker a message is generated.
The message is transmitted via the pacemaker's long distance telemetry to a patient device, a kind of mobile phone without any controls except an "On/Off" button. The patient device relays the message as an encrypted SMS (Short Message Service) transmission across the GSM network to the Home Monitoring Service Center. There, the SMS message is decrypted, combined with the patient's history, and forwarded via fax to the attending physician as a so-called "Cardio Report". The Cardio Report contains a table with the latest transmitted values, the means of the previously transmitted values, and a graphical representation of the history of selected parameters.
Independent of the frequency of pacemaker message transmission, the attending physician may specify a standard time interval for the reception of a Cardio Report, e.g., every 14 days. Additionally, a Cardio Report may be sent immediately after every patient-activated message.
The attending physician can also specify parameter-related criteria for transmission in order to ensure rapid receipt of information in case of severe changes in the cardiac status. Examples are the occurrence of indicators for atrial fibrillation, ventricular tachycardia, or bradycardia in chronotropically competent patients, or an increase in the incidence of ventricular extrasystoles (VES).
To tailor the messaging to the needs of both the physician and the patient, the clinic and the patient must be registered at the Service Center. Presently, this is realized by the faxing of a clinic/practice application and a patient application, wherein the physician states his/her preferences for Cardio Report transmissions: e.g., frequency, time of day, and fax numbers for routine and event Cardio Reports. The patient's privacy is strictly maintained, as the Service Center does not receive any personal data; the patient is referred to only by pacemaker serial number.
The first system to use this HM scheme is the combination of a dual-chamber rate-adaptive pacemaker BA03 DDDR and a patient device RUC 1000, consisting of the mobile RUCM 1000 and the loading tray RUCL 1000 (all Biotronik, Germany). The BA03 DDDR is based on the Actros DR pacemaker but incorporates additional hardware and software for telemetry (Figure 2).
The transmitted HM data is derived from the standard counters for heart rate, event classification, VES analysis, and from the activity chart. Hence, the attending physician is likely already acquainted with this kind of information and its analysis.

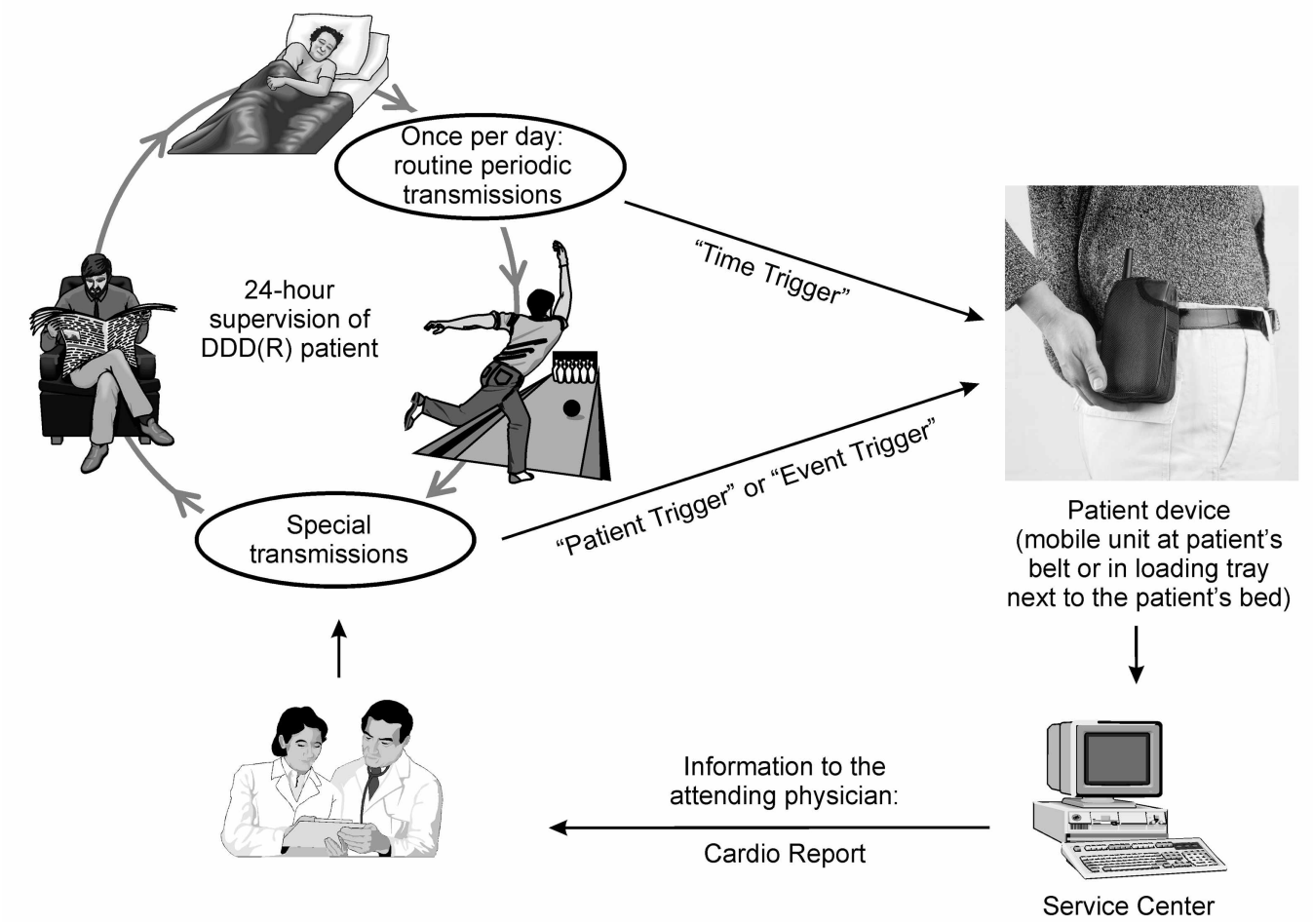

Figure 1. 24-hour supervision of pacemaker patients with a Home Monitoring System.

First Investigation on Reliability and Clinical Use

The first step in establishing the HM system in a clinical setting is to prove its technical reliability. We designed a clinical study that investigates the type, origin, and consequences of possible technical pitfalls and patient-associated difficulties. Additionally, the study intends to provide the first indications of the usefulness of HM for patient inter-follow-up supervision and, thus, lay the foundation for further HM investigations.

Technical Aspects

The primary goal of the technical part of the study is to determine the percentage of patients that can be supervised by the physician thanks to HM messages received correctly as Cardio Reports. This is tested with the following hypothesis:

- The percentage of patients that can be successfully supervised by the physician due to the reception of Cardio Reports is at least 95 % of the patients included into the study.

Patients will be classified as unsuccessfully supervised if the sequence of Cardio Reports is interrupted for more than 3 consecutive days or if there are more than 2 interruptions of 2 or 3 consecutive days (Figure 3). For the analysis concerning the primary technical endpoint, only patients will be considered that have sent at least one message within the first 3 days after discharge.

The details concerning interrupts in the sequence of Cardio Reports will be analyzed with the help of secondary technical endpoints:

- Percentage of patients for whom HM operates correctly immediately upon first use, i.e., after the system has been explained to the patient by the clinic's service team and activated.

Figure 2. Home Monitoring system comprising pacemaker and mobile unit (Biotronik, Germany).

- Percentage of patients with successful transmission only after repeated instruction.
- Percentage of patients with several successful transmissions and subsequent transmission failure that can only be corrected by a physician's intervention.
- Percentage of periodic and patient activated messages received as Cardio Reports by the physician for every successfully supervised patient.
- Transmission time, i.e. the time delay between reception of implant data at the patient device and reception of the associated patient device message at the Service Center.
- Correctness of the transmitted data, i.e., the content of the Cardio Reports is identical to the content of the messages transmitted, and the data is also stored in the pacemaker for later cross-checking.

Clinical Aspects

The primary goal of the clinical part pertains to the clinical relevance of the telemetrically transmitted data. The relevance is derived from therapeutic interventions that are considered by the physician following the reception of a Cardio Report. The number and scope of the intended interventions are compared with the interventions performed during the subsequent follow-up.

The focus is on the following therapeutic interventions:

- Necessity of a follow-up;
- Pacemaker reprogramming;
- Pacemaker or lead revision;
- Changes in type, dose, or daily distribution of medication;
- Exercise testing, long-term ECG, echocardiography;
- Changes in the classification of the patient's cardiac situation, irrespective of direct therapy, e.g., concerning chronotropy or arrhythmia.

The analysis concerning this goal is performed via a questionnaire about the physician's expectations originating from the Cardio Reports with respect to the patient's treatment. His or her expectations and intentions on the day before the follow-up are compared to the real results of the follow-up.

As secondary endpoints, we investigate the values taken by selected HM counters and hypothesize that they are between certain indication-specific limits for at least 80 % of all transmissions during the final 4 weeks (weeks 8 through 12) of the patient's study participation. For example, a chronotropically competent patient in sinus rhythm with permanent 3rd degree atrioventricular block should have more than 90 % atrial sensed events and fewer than 10 % ventricular sensed events. We investigate the counters for the mean ventricular heart rate, percentage of atrial and ventricular sensed events, atrioventricular conduction (AsVs, AsVp, ApVs, ApVp), and time at maximum sensor rate. Limits are specified for combinations of:

- sinus rhythm, with or without paroxysmal atrial fibrillation;
- chronotropic competence or incompetence and
- intrinsic AV conduction or permanent AV block of 1st, 2nd, or 3rd degree.

The other HM counters (max. ventricular heart rate, max. frequency of ventricular extrasystoles, number of VES, couplets, triplets and runs, occurrence of VT) are not investigated within this endpoint, as we do not expect a significant correlation to indication.

Details of the Study

Based on the primary technical endpoint, we calculated that a number of 105 patients would yield a statistically significant result on the probability of successful patient supervision with HM with an expected α error of 5 %. Therefore, 120 patients will be included

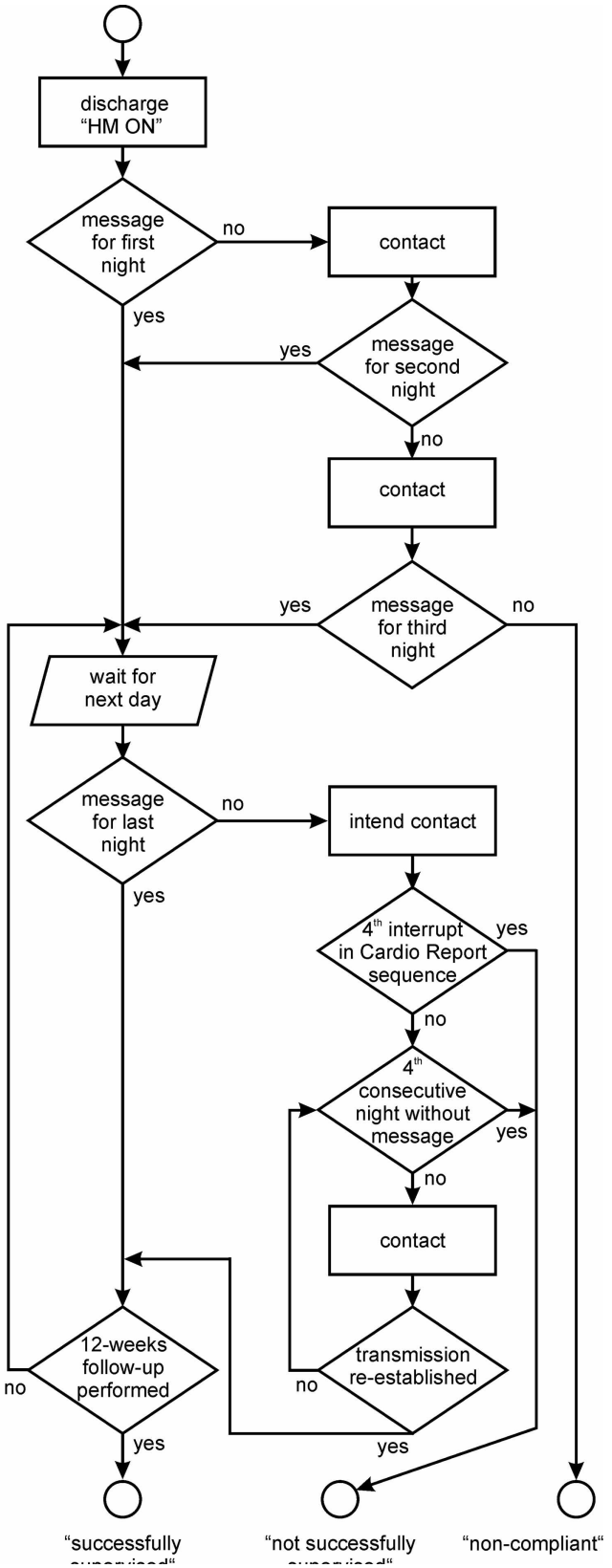

Figure 3. Decision tree for success and failure of Home Monitoring (HM) supervision.

in 11 clinical centers in Great Britain, Italy, and Germany. The inclusion criteria are:

- Indication for DDD or DDDR pacemaker implantation;
- Patients that have been informed about the investigation, have read and understood the patient information, and have signed their informed consens.

The most important exclusion criteria are:

- Contraindication for dual-chamber pacing;
- Patients living outside the area with sufficient access to the GSM network according to a map of access provided by the GSM net provider.

The patients are followed for 12 weeks, with follow-ups occurring at 2, 4, 8, and 12 weeks after discharge (Figure 4). The HM functionality is activated at discharge. For the first 2 weeks, periodic and patient-activated messages are enabled. Between the 2-week and the 12-week follow-ups, only periodic messages are enabled. At the 12-month follow-up, HM is switched off. With the help of a questionnaire, the patients are asked to describe their personal impressions and attitudes regarding HM.

During the study, the physician must evaluate the patient's situation by analyzing the Cardio Reports on the day before a follow-up is performed. Therefore, the physician gets a Cardio Report based on a periodic message once a day per patient, provided that a periodic message has been received in the Service Center. Additionally, a Cardio Report for a patient-activated message is immediately forwarded after the message has been received at the Service Center.

The study is projected to last 12 months including 6 months of patient inclusion, 3 months participation, and 3 months data analysis. Hence, the final results are expected to be published in spring 2002.

Perspectives for Home Monitoring in Pacemaker Therapy

For the further development and use of the HM functionality in pacemaker therapy, we see two major fields of clinical interest: Supervision of patients prone to atrial tachyarrhythmias, especially atrial fibrillation (AF) and optimization of pacemaker and medication therapy in patients with congestive heart failure (CHF). Both groups will probably benefit from close supervision of the therapeutic compliance, high-resolution monitoring of the cardiac status, and a quick reaction time to gradual or abrupt changes in the underlying

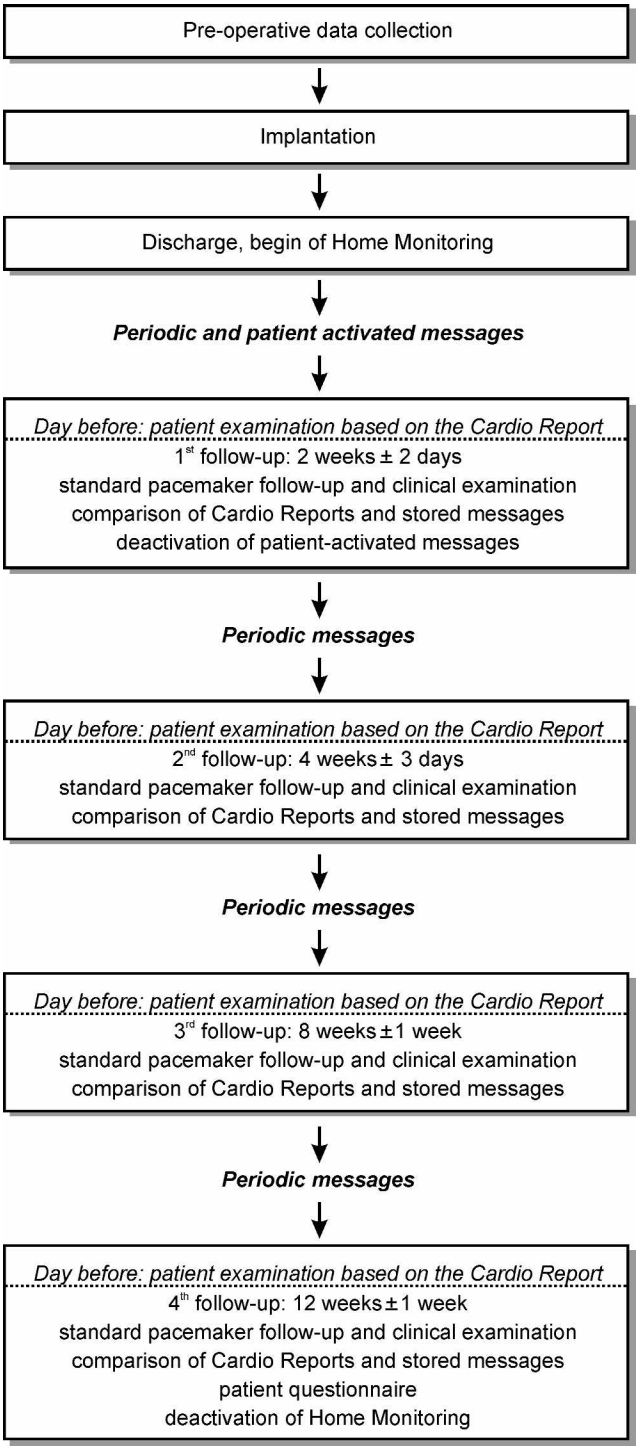

Figure 4. Flow chart of the study.

cardiac disease. Apart from its application in pacemaker patients, HM may also be very useful in the future as a means of screening on patients with implanted cardioverter defibrillators.

Home Monitoring in Patients with Atrial Tachyarrhythmia

The usefulness of HM supervision in patients prone to AF stems from the relative importance of a fast reaction to the onset of AF.

A mean incidence of AF of 2 % within 2 decades was derived from the Framingham study [3]. For the elderly, which significantly contribute to the pacemaker patient population, the incidence rate greatly increases to 19.2 cases of first AF occurrence per 1000 person-years. Men aged over 75 years have an even higher risk: 42.7 first AF cases per 1000 person-years are reported [4]. Concerning the results for pacemaker patients, the studies indicate only a slightly increased risk for development of AF, depending on the pacing mode: With physiologic pacing (DDD or AAI), the annual rate for AF incidence is 5.3 %, compared to 6.6 % with VVI pacing [5]. The annual incidence is, however, not evenly distributed: Mattioli, et al. report an AF incidence of 10 % for the 1st year after implantation, 23 % after 3 years, and 31 % after 5 years, again with an increased risk for patients paced in VVI mode [6].

The data on the incidence of supraventricular tachycardia (SVT) in patients with sick sinus syndrome (SSS) versus those with high-degree atrioventricular block (AVB) are somewhat conflicting: In the AIDA study, 50.5 % of all patients had experienced at least one SVT by the 28th day after implant. In the AVB subgroup, the incidence of SVT was 56.3 % [7].

For the first 1000 patients in the MOST study with SSS as the inclusion criterion, the incidence of SVT including AF prior to implant was 53 % [8]. In another study, no difference in the AF incidence was detected between SSS patients and AVB patients, but the risk for cerebral ischemia was twice as high for SSS as for AVB (18 % vs. 9 %) [9].

With respect to the detection of SVT, Defaye et al. reported from the AIDA study group that 65 % of all SVT episodes documented within the first 28 days were asymptomatic. In 21 % of the patients, asymptomatic SVT episodes were documented as the patients' first SVT events ever [7].

The need for permanent and highly detailed information about the atrial rhythm in pacemaker patients is further stressed by the observation that in permanently or predominantly paced patients, AF is systematically underdiagnosed compared to the case in unpaced patients. Anticoagulation therapy is less common in permanently

paced patients than in intermittently or unpaced patients [10].

The rapid detection of AF has practical implications. In AF that lasts more than 48 hours, anticoagulation with warfarin is recommended for 3 weeks before and at least 4 weeks after attempted cardioversion [11]. A treatment alternative is intravenous heparinization followed by trans-esophageal echocardiography to exclude thrombosis in the left atrial appendage, and early cardioversion [11]. Hence, fast and reliable information about the onset of AF would help to minimize treatment burden and associated costs.

Longer AF durations with loss of AV synchrony may help cause the arrhythmia to become chronic due to electrical remodeling, and also lead to a decrease in atrial contractility due to mechanical remodeling, which may increase the chance for thromboembolic complications [12-14]. Thus, rapid detection and termination of AF may help to reduce the incidence of chronic AF and thromboembolic complications in pacemaker patients.

Home Monitoring in Patients with Congestive Heart Failure

Heart failure (HF) is nowadays regarded as the result of a dynamic process in which mechanisms that compensate for an impairment in cardiac function result in further disease progression. After an initial myocardial injury, the attempt to preserve stroke volume entails a neurohumoral activation, ventricular dilation, and cardiac remodeling [15-18]. Activation of the renin-angiotensin-aldosterone system and the increased expression of NO, vasopressin and cytokines mediate the progression of heart failure. Programmed myocyte death (apoptosis) is further promoted by angiotensin II and dilation stress, thus amplifying ventricular dilation [19,20]. Therefore, it is generally accepted that heart failure is a vicious cycle, and it is of vital importance to interrupt this cycle as early as possible.

For the typical pacemaker patient population, i. e. aged 65 years and older, the incidence of congestive heart failure is estimated at 2 – 5 %; in patients aged over 80 years, it even increases to about 10 % [21-24]. For more than 80 % of HF patients, symptoms are due to ventricular dysfunction [25].

State-of-the-art therapy in HF patients with systolic dysfunction is a combination of angiotensin-converting enzyme (ACE) inhibitors or AT1 receptor blocking, beta-adrenergic blocking agents, diuretics, spironolactone, and digoxin [26]. Despite the indisputable usefulness of these drugs in HF treatment, they may sometimes cause severe side effects such as AV conduction disturbances with beta-blocking agents [27] or an increased incidence of ventricular arrhythmias with diuretics [28]. The incidence and severity of these effects can be supervised directly with HM. Several of the desired effects of this medication are also mirrored by parameters monitored by HM, e.g., a change in mean ventricular heart rate for beta-blockers and digoxin, or a reduction in the incidence of ventricular premature complexes at rest, and arrhythmia under physical load with spironolactone [29,30]. As an additional feature, by regular transmission of activity indicators, HM allows the supervision of the patients' compliance with physical training programs, which were shown to have beneficial effects on exercise tolerance and symptoms [31,32].

Direct monitoring of ventricular function or geometry is not yet possible with HM. However, the initial pilot investigations show that hemodynamic parameters and NYHA classification correlate with the ventricular evoked response, and that evaluating the cardiac functional status based on the recording and analysis of the ventricular evoked response is promising under well-defined conditions [33]. This may also apply to heart rate variability as a measure of para- / sympathetic activity [29]. Incorporation of such new parameters in the HM system may pave the way to an early recognition of HF even in asymptomatic patients, thus enabling preventive therapy [26].

References

[1] Elmqvist H, Senning A. Implantable pacemaker for the heart. In: Smith CN (editor). Medical electronics; Proc. Sec. Int. Conf. on Medical Electronics; June 1959; Paris. London: Iliffe. 1960.

[2] Furman S, Escher DJW. Transtelephone pacemaker monitoring. In: Schaldach M, Furman S (editors). Advances in Pacemaker Technology. Berlin: Springer. 1975: 177-194.

[3] Kannel WB, Abbott Rd, Savage DD et al. Epidemiologic features of chronic atrial fibrillation: The Framingham study. N Engl J Med. 1982; 306: 1018-1022.

[4] Psaty BM, Manolio TA, Kuller LH et al. Incidence of and risk factors for atrial fibrillation in older adults. Circulation. 1997; 96: 2455-2461.

[5] Connolly SJ, Kerr CR, Gent M et al. Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. Canadian Trial of Physiologic Pacing Investigators. N Engl J Med. 2000; 342: 1385-1391.

[6] Mattioli AV, Vivoli D, Mattioli G. Influence of pacing modalities on the incidence of atrial fibrillation in patients without prior atrial fibrillation. A prospective study. Eur Heart J. 1998; 19: 282-286.

[7] Defaye P, Dournaux F, Mouton E. Prevalence of supraventricular arrhythmias from the automated analysis of data stored in the DDD pacemakers of 617 patients: the AIDA study. The AIDA Multicenter Study Group. Automatic Interpretation for Diagnosis Assistance. PACE. 1998; 21: 250-255.

[8] Lamas GA, Lee K, Sweeney M, et al. The mode selection trial (MOST) in sinus node dysfunction: design, rationale, and baseline characteristics of the first 1000 patients. Am Heart J. 2000; 140: 541-551.

[9] Mattioli AV, Castellani ET, Vivoli D et al. Prevalence of atrial fibrillation and stroke in paced patients without prior atrial fibrillation: a prospective study. Clin Cardiol. 1998; 21: 117-122.

[10] Patel AM, Westveer DC, Man KC et al. Treatment of underlying atrial fibrillation: paced rhythm obscures recognition. J Am Coll Cardiol. 2000; 36: 784-787.

[11] Prystowsky EN, Benson W Jr, Fuster V et al. Management of patients with atrial fibrillation. A statement for healthcare professionals from the Subcommittee on Electrocardiography and Electrophysiology, American Heart Association. Circulation. 1996; 93: 1262-1277.

[12] Allessie MA, Konings K, Kirchhof CJ et al. Electro-physiologic mechanisms of perpetuation of atrial fibrillation. Am J Cardiol. 1996; 77: 10A-23A.

[13] Sparks PB, Mond HG, Vohra JK et al. Electrical remodeling of the atria following loss of atrioventricular synchrony: a long-term study in humans. Circulation. 1999; 100: 1894-1900.

[14] Sparks PB, Mond HG, Vohra JK et al. Mechanical remodeling of the atrium after loss of atrioventricular synchrony: a long-term study in humans. Circulation. 1999; 100: 1714-1721.

[15] McMurray JJ, Ray SG, Abdullah I et al. Plasma endothelin in chronic heart failure. Circulation. 1992; 85: 1374-1379.

[16] Shan K, Kurrelmeyer K, Seta Y et al. The role of cytokines in disease progression in heart failure. Curr Opin Cardiol. 1997; 12: 218-223.

[17] Middlekauff HR. Mechanisms and implications of autonomic nervous system dysfunction in heart failure. Curr Opin Cardiol. 1997; 12: 265-275.

[18] Cohn JN, Ferrari R, Sharpe N. Cardiac remodeling - concepts and clinical implications: a consensus paper from an international forum on cardiac remodeling. Behalf of an international forum on cardiac remodeling. J Am Coll Cardiol. 2000; 35: 569-582.

[19] Sabbah HN, Sharov VG. Apoptosis in heart failure. Prog Cardiovasc Dis. 1998; 40: 549-562.

[20] Anversa P, Kajstura J, Olivetti G. Myocyte death in heart failure. Curr Opin Cardiol. 1996; 11: 245-251.

[21] Kannel WB, Belanger AJ. Epidemiology of heart failure. Am Heart J. 1991; 121: 951-957.

[22] McKee PA, Castelli WP, McNamara PM et al. The natural history of congestive heart failure: the Framingham study. N Engl J Med. 1971; 285:1141-1146.

[23] Eriksson H. Heart failure: a growing public health problem. J Intern Med. 1995; 237: 135-141.

[24] Cowie MR, Mosterd A, Wood DA et al. The epidemiology of heart failure. Eur Heart J. 1997; 18: 208-225.

[25] Consensus recommendations for the management of chronic heart failure. On behalf of the membership of the advisory council to improve outcomes nationwide in heart failure. Am J Cardiol. 1999; 83: 1A-38A.

[26] Hoppe UC, Erdmann E. Leitlinien zur Therapie der chronischen Herzinsuffizienz, herausgegeben vom Vorstand der Deutschen Gesellschaft für Kardiologie - Herz- und Kreislaufforschung. 2000. Available from: URL: http://www.dgkardio.de/Leitlinien/LeitlinienHerzinsuffizienz.pdf.

[27] Hall SA, Cigarroa CG, Marcoux L, et al. Time course of improvement in left ventricular function, mass and geometry in patients with congestive heart failure treated with beta-adrenergic blockade. J Am Coll Cardiol. 1995; 25: 1154-1161.

[28] Cooper HS, Dries DL, Davis CE, et al. Diuretics and risk of arrhythmic death in patients with left ventricular dysfunction. Circulation. 1999; 100: 1311-1315.

[29] Krum H, Bigger T, Goldsmith RL, et al. Effect of long-term digoxin therapy on autonomic function in patients with chronic heart failure. J Am Coll Cardiol. 1995; 25: 289-294.

[30] Ramires FJ, Mansur A, Coelho O, et al. Effect of spironolactone on ventricular arrhythmias in congestive heart failure secondary to idiopathic dilated or to ischemic cardiomyopathy. Am J Cardiol. 2000; 85: 1207-1211.

[31] Coats AJ, Adamopoulos S, Meyer TE, et al. Effects of physical training in chronic heart failure. Lancet. 1990; 335: 63-66.

[32] Wilson JR, Groves J, Rayos G. Circulatory status and response to cardiac rehabilitation in patients with heart failure. Circulation. 1996; 94: 1567-1572.

[33] Ebner E, Krätschmer H. The ventricular evoked response as clinical marker in patients with dilative cardiomyopathy. Prog Biomed Res. 2000; 5: 239-244.

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