Paroxysmal atrial fibrillation in patients paced for atrioventricular block. Comparison between DDD and VDD single-lead pacing system

Carlo Pignalberi, Renato Ricci, Gaetano Canale, Giovanni Testa, Domingos Diogo, Luca Santini, Francesco Miraglia, Massimo Santini

Department of Cardiology, San Filippo Neri Hospital, Rome, Italy

Key words:
Atrial fibrillation;
Atrioventricular block;
DDD pacing;
VDD pacing.

Background. **Paroxysmal atrial tachyarrhythmias have been frequently detected in patients paced for atrioventricular block. However, it is not yet clear which is the actual incidence of such arrhythmias and if they were preexisting but not recognized, or if they could be related to the device.**

Methods. **One hundred and forty-five patients with a diagnosis of second or third degree atrioventricular block were enrolled into the study. One hundred and twenty-four received a pacemaker Medtronic Thera DDD and 21 a Medtronic Thera VDD. High rate atrial episodes were evaluated for 3 months after enrollment. Atrial electrograms documenting paroxysmal atrial fibrillation (AF) were stored and programming of atrial sensitivity and pacemaker diagnostics was very strict in order to exclude short and false positive AF episodes.**

Results. **Thirty-six patients (35%) in the DDD group and 8 (42%) in the VDD group presented with AF (p = NS). The mean number of AF runs was 29.8 ± 66.4 in the DDD group and 6.8 ± 5.9 in the VDD group; the episode duration was 300 ± 1680 min in the DDD group and 1200 ± 3480 min in the VDD group. Dividing the patients into subgroups according to the number or length of episodes, both the DDD and VDD groups showed a very similar distribution (p = 0.5 and p = 0.8, respectively). Patient evaluation on the basis of an episode number ≤ 10 or of an episode duration ≤ 60 min revealed a non-significant difference between the DDD and VDD groups (number 2.9 ± 2.4 vs 5.0 ± 3.0, p = 0.09; length 3.2 ± 2.7 vs 3.0 ± 2.3, p = NS).**

Conclusions. **Patients paced for isolated atrioventricular block showed a high prevalence of AF. The contact between the lead tip and the atrial wall does not seem to be related to arrhythmia occurrence.**

(Ital Heart J 2001; 2 (10): 772-777)

Received April 24, 2001; revision received July 13, 2001; accepted August 9, 2001.

Address:

Dr. Carlo Pignalberi

Dipartimento delle Malattie del Cuore Azienda Ospedaliera San Filippo Neri Via Martinotti, 20 00135 Roma E-mail: c.pignalberi@libero.it

Introduction

The widespread use of diagnostic functions of implanted pacemakers has shown an unexpectedly high recurrence rate of paroxysmal atrial tachyarrhythmias in patients wearing a dual-chamber pacing system for atrioventricular block. Atrial arrhythmias have often been documented even in patients who were asymptomatic and who did not show any arrhythmia before implantation[1-6]. However, no data are available regarding the possibility of the presence of undiagnosed arrhythmias prior to implantation or if they were actually due to the presence of the atrial lead. In order to evaluate the role played by the atrial lead, we compared the occurrence of atrial fibrillation (AF) in patients receiving a DDD pacing system for atrioventricular block with that observed among patients implanted with a VDD single-lead pacing system in which physiologic pacing does not require that the lead be in contact with the atrial wall.

Methods

Patient population. One hundred and forty-five consecutive out-patients (86 males, 59 females, mean age 74 ± 11 years) were enrolled into the study. All patients had a diagnosis of second or third degree atrioventricular block and had been implanted with a DDD or VDD single-lead pacing system both equipped with the same diagnostic features at least 3 months before. Baseline variables, cardiac and concomitant diseases are summarized in table I.

One hundred and twenty-four patients (group 1) received a DDD pacing system Medtronic Thera DR 7940-7944, 7960-7964 (Medtronic Inc., Minneapolis, MN,

Table I. Patient characteristics.

No. patients	145
Sex (M/F)	86/59
Age (years)	74 ± 11
Heart disease (%)	
Ischemic	17.9
Hypertensive	20
Valvular	2.8
Failure	9.0
No structural disease	50.3
Transient ischemic attack/stroke (%)	2.8

USA). The atrial lead was bipolar in 19 (15%) and unipolar in 105 (85%). The ventricular lead was unipolar in all patients. Twenty-one patients (group 2) were implanted with a VDD pulse generator Medtronic Thera 8948 connected to a single-pass lead Medtronic 5032, which is a ventricular bipolar, tined and steroid eluting lead equipped with a floating bipolar atrial ring dipole 12.5 mm^2 in surface area and with an interelectrode distance of 8.6 mm.

Pacemaker features. Automatic mode switching from the atrial tracking to the non-atrial tracking modality in case of atrial tachyarrhythmias is available in Medtronic Thera VDD and DDD devices. The algorithm continuously monitors the intrinsic atrial rate and calculates (in ms) a mean atrial cycle value. The current atrial interval is compared beat by beat with the stored mean atrial cycle. When the current atrial interval is longer than the stored mean atrial cycle, the latter is increased by 8 ms, and when the current atrial interval is shorter than the stored mean atrial cycle, the latter is decreased by 23 ms. When the stored mean atrial cycle is shorter than the atrial tachycardia detection interval, tachycardia is detected and the pacing mode switches from VDD to VDIR or from DDD to DDIR according to the device. The device switches back to VDD or DDD when the stored mean atrial cycle becomes longer than the atrial tachycardia detection interval or after five consecutive paced atrial events. An automatic mode switching episode counter may be used to obtain raw data on atrial arrhythmia episodes.

To identify sustained episodes of atrial tachycardia and to confirm appropriate arrhythmia detection, pacemaker diagnostics may be programmed on high rate atrial episode detection. High rate atrial episode onset is defined by a preselected number of sequential spontaneous atrial beats (detection number) over a specified rate (detection rate). The episode ends when a programmed number of sequential atrial impulses below the detection rate (termination number) is noticed. In its memory the device can analyze and store information on the overall number of tachycardia episodes and detailed information on the last seven, including time and date, maximal atrial rate, duration of each episode, analysis of the last eight atrial events before tachycardia onset, analysis of the first eight atrial events after tachycardia onset, and analysis of the first eight atrial events after termination of tachycardia. For each of the twenty-four atrial events, the cycle length and the paced or sensed class are available. For one episode, a 2.3 s atrial electrogram is recorded at the onset of arrhythmia (Fig. 1).

In our study the detection rate was programmed at 150 b/min, the detection number at 50 beats, the termination number at 20 beats, and the electrogram collection "on". Detection at 50 beats (maximum available) was selected in order to increase the algorithm specificity for long-lasting arrhythmias. Termination at 20 beats (maximum available) was selected in order to prevent inappropriate episode termination due to intermittent undersensing of AF (Fig. 2).

Pacemaker programming. At enrollment, the pacing mode was programmed in DDD or VDD according to

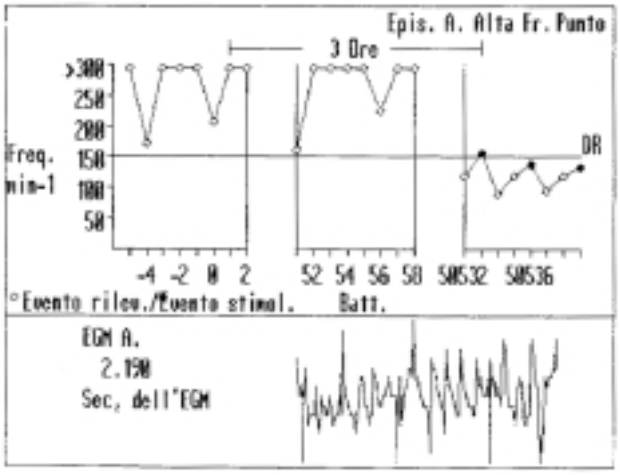

Figure 1. *Atrial fibrillation episode stored in the device memory: the atrial events before and after the onset of arrhythmia are drawn. The atrial electrogram documenting appropriate detection can be appreciated.*

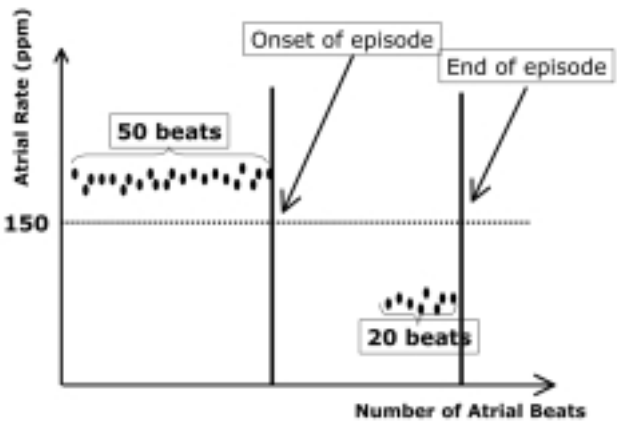

Figure 2. *Diagnostic programming: high rate atrial episodes were defined as a sequence of 50 atrial beats occurring at a rate > 150 b/min; the occurrence of a sequence of 20 beats at a rate < 150 b/min defined the end of the episode.*

the implanted device and the automatic mode switching algorithm was activated; the lower rate was set at a value inferior to the spontaneous sinus rate; the upper rate was selected according to patient age and physical training; the atrioventricular interval was individually programmed according to the patient's hemodynamic picture. In order to program atrial sensitivity, the atrial electrogram in sinus rhythm and the far-field R wave oversensing were measured. The programmed value was set at one third of the measured atrial electrogram or less if far-field R wave oversensing could be prevented by the selected value. If not, atrial sensitivity could be set at one half of the measured atrial electrogram; in figure 3 the guidelines for programming of atrial sensitivity are shown. In the VDD pacing system, programmed atrial sensitivity had to allow a 1:1 atrioventricular conduction during normal and forced breathing in the supine and sitting positions. The minimum atrial sensitivity setting allowed in VDD was 0.5 mV. Bipolar polarity for atrial sensing was programmed whenever possible. The pacing energy was set at 3 times the threshold energy.

Follow-up visits and study protocol. At enrollment, overall clinical evaluation was carried out and optimal functioning of the implanted system was verified. Patients were discharged after pacemaker and diagnostic function programming. A 3-month follow-up was planned.

At the end of follow-up all patients were clinically evaluated, particularly as far as symptomatic AF occurrence was concerned. Diagnostic data stored in the device memory were collected. These included the total number of automatic mode switching episodes, the total number of high rate atrial episodes, including detailed analysis of duration, atrial rate and circadian distribution. The registered atrial electrogram was checked. A reliable atrial signal documenting atrial tachyarrhythmias was mandatory to classify the detection of arrhythmia as appropriate. The atrial pacing/sensing and the ventricular pacing/sensing percentages were analyzed.

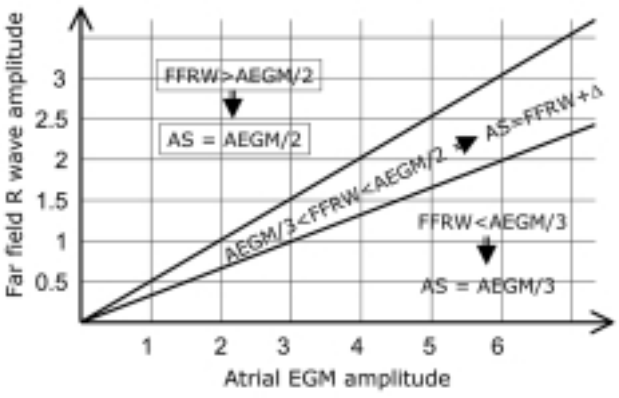

Figure 3. *Diagram to program atrial sensitivity (AS). When the intersection between the atrial electrogram (AEGM) and the far-field R wave (FFRW) amplitudes fell within the inferior triangle and consequently the FFRW was lower than one third of the AEGM, the AS threshold was set at one third of the AEGM; when the intersection fell in the middle triangle and the FFRW was between one third and one half of the AEGM, the AS threshold was set at one third of the AEGM plus a Δ value, sufficient to cut the far-field, but still between one third and one half of the AEGM; finally, when the intersection fell in the superior triangle and the FFRW was higher than one half of the AEGM, the AS threshold was still set at one half of the AEGM.*

Statistical analysis. Data are expressed as mean values ± SD, unless stated otherwise. Patients with AF which was not confirmed by the stored electrogram were considered as false positive, but not excluded from the general population. Each study group was twice divided into subgroups: first, according to the number of AF episodes (seven subgroups), second, according to the duration of the AF episode (five subgroups). The homogeneity of patient distribution between the two groups, the incidence of AF runs and other differences between groups were assessed by the Mann-Whitney U test for continuous variables, where data did not show a normal distribution. The correlation between the number and length of AF episodes was verified using the Pearson test. Multivariate analysis was performed to isolate independent preoperative predictors for AF. All analyses were performed using the SPSS 6.0 version Software (SPSS Inc., Chicago, IL, USA). A p value < 0.05 was considered statistically significant.

Results

The mean time interval between implant and enrollment into the study was 26 ± 18 months (range 3-65 months). In group 1, 8 patients with coexisting documented sinus node disease at implant and 2 with brady-tachy syndrome were excluded from further analysis. Similarly, 10 patients from group 1 and 2 patients from group 2 with documented episodes of paroxysmal AF before implant were also excluded. Eight patients from group 1 (2 without AF prior to pacemaker implantation) were in permanent AF at enrollment. So, 121 patients (102 in group 1 and 19 in group 2) were enrolled into the prospective phase of the study. In group 1 the atrial lead was bipolar in 16 patients (16%) and unipolar in 86 (84%). Fifteen of 121 patients (12%) were on antiarrhythmic drug treatment and 9/121 (7%) on anticoagulant therapy for reasons unrelated to AF.

Pacing measurements and actual programming. At enrollment, in the DDD group, the atrial pacing threshold was on average 0.10 ± 0.07 ms at 1.5 V, while the atrial pacing impedance at 2.5 V/0.5 ms was 562 ± 81 Ohms. The measured atrial electrogram amplitude was 3.5 ± 1.6 mV and the far-field R wave amplitude 0.9 ± 0.5 mV. The ratio between the atrial electrogram and the far-field R wave was on average 6.5 ± 12. A ratio

< 2 (not allowing appropriate programming of atrial sensitivity according to the protocol) was found in 19/102 (19%) DDD patients. The mean programmed atrial sensitivity value in the DDD group was 0.9 ± 0.4 mV (range 0.5-2.0 mV). In the VDD group the mean atrial electrogram amplitude was 1.1 ± 1.0 mV, while the far-field R wave sensing was negligible. The mean programmed atrial sensitivity value in the VDD group was 0.3 ± 0.2 mV (range 0.18-0.5 mV). Other pacing parameters were: the lower rate 61 ± 8 b/min, the upper rate 116 ± 14 b/min, the paced atrioventricular interval 183 ± 42 ms (DDD only) and the sensed atrioventricular interval 151 ± 44 ms.

Pacemaker stored memory data. In the period between implant and enrollment, 11/102 patients (10.7%) of group 1 and 2/19 (10.5%) of group 2 developed symptomatic paroxysmal AF (p = NS).

After 3 months, memory stored data showed appropriate detection of AF as documented by the high rate atrial episode collection plus atrial electrogram confirmation in 36 cases (35%) in the DDD group and in 8 cases (42%) of the VDD group (p = NS) (Fig. 4). AF detection was excluded by the atrial electrogram in 18 cases (18%) in the DDD group and in 1 case (5%) in the VDD group.

The mean number of AF episodes among DDD patients was 29.8 ± 66.4 while in the VDD group it was 6.8 ± 5.9; the episode duration was 300 ± 1680 min in the DDD group and 1200 ± 3480 min in the VDD group. The mean atrial rates were 309 ± 89 and 222 ± 84 b/min respectively (p < 0.01). The episodes did not show circadian distribution. The atrial pacing percentage in the DDD group was 35 ± 33%. The atrioventricular association level in the VDD group was 94 ± 10%.

The automatic mode switching raw data counter reported 153 ± 112 episodes in the DDD group and 46 ± 98 in the VDD group (p = NS). Thirty-two DDD and 4 VDD patients showed automatic mode switching episodes in spite of no sustained atrial tachyarrhythmia episode detection at high rate atrial episode analysis.

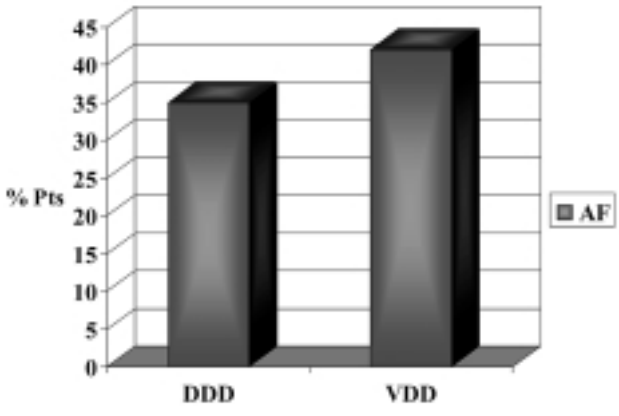

Figure 4. *High rate atrial fibrillation (AF) episode number in the DDD and VDD groups.*

Dividing the patients into 7 subgroups according to the AF episode number (expressed as percentage) (Table II), and comparing the DDD and VDD groups, a strong similarity in the distribution of the two populations could be observed (p = 0.5) (Fig. 5A). In fact, as shown in figure 5A, the percentage of patients included in each subgroup was very similar in both the DDD and VDD populations. Similarly, dividing the patients into 5 subgroups according to the episode duration (Table III), a similar behavior in patient distribution was noted (p = 0.8) (Fig. 5B). No cross-correlation between the number and duration of arrhythmia episodes was observed in any group (p = NS).

In fact, in patients with a high number of episodes, their duration was usually short and vice versa, but the two variables were independent and randomly distributed. Subgroup analysis allowed us to compare patients implanted with a DDD or VDD pacing system and with a small number of AF episodes (≤ 10) to those with short episodes (≤ 60 min) of AF. Considering patients with an AF episode number ≤ 10, the VDD patients showed an incidence of AF runs slightly higher than that of the DDD group, but the difference was not statistically significant (5.0 ± 3.0 vs 2.9 ± 2.4 respectively, p = 0.09). According to run duration, no significant difference between the DDD and VDD groups was observed (3.2 ± 2.7 vs 3.0 ± 2.3, p = NS). Patients with an episode number > 10 and an episode duration > 60 min were excluded from the last analysis because of their scarcity in the VDD group (> 10 runs: DDD 18 and VDD 1 patient; > 60 min: DDD 11 and VDD 2 patients).

Multivariate analysis showed that there was no independent risk factor which was capable of exerting a significant influence on the incidence and duration of AF.

Table II. Patient distribution into seven subgroups according to the number of atrial fibrillation (AF) episodes.

AF number	DDD patients	VDD patients
1	12 (33.3%)	2 (25%)
2-10	16 (44.4%)	5 (62.5%)
11-20	0	0
21-30	1 (2.8%)	0
31-40	4 (11.1%)	1 (12.5%)
41-50	2 (5.6%)	0
51-255	1 (2.8%)	0

Table III. Patient distribution into five subgroups according to the duration of atrial fibrillation (AF) episodes.

AF duration (min)	DDD patients	VDD patients
0-2	12 (33.3%)	3 (37.5%)
2.1-4	6 (16.7%)	2 (25%)
4.1-8	6 (16.7%)	1 (12.5%)
8.1-60	2 (5.5%)	0
> 60	10 (27.8%)	2 (25%)

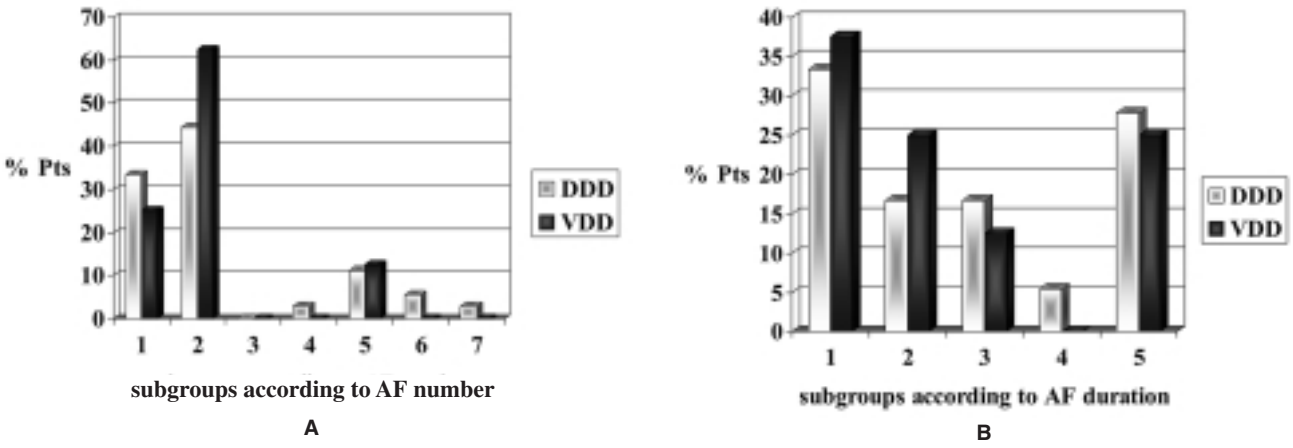

Figure 5. A: *distribution of the DDD and VDD groups into seven subgroups according to the number of atrial fibrillation (AF) episodes.* B: *distribution of the DDD and VDD groups into five subgroups according to the duration of AF episodes.*

Discussion

During the last years, the expanded memory of implanted pacemakers has allowed continuous monitoring of cardiac rhythm in paced patients thus leading to arrhythmia identification and to collection of data on their recurrence and duration and on triggering factors. Specific software has been developed and endocavitary electrograms have been stored thus facilitating arrhythmia interpretation by physicians[7,8]. The sensitivity and specificity of the diagnostic features have been tested and confirmed as valuable parameters in clinical studies[9-11] comparing stored data with those obtainable from conventional Holter monitoring. The clinical application of pacemaker diagnostics demonstrated a high rate of AF in paced patients, regardless of the indication to pacing[2-4,6,12]. The AF incidence was found to be as high as 50% and in many patients neither symptoms nor a pre-implant AF history could be documented.

While the proarrhythmic role of ventricular pacing on AF has been documented in both retrospective[13-16] and prospective[12] studies, dual-chamber pacing was expected to exert a protective effect, on the basis of studies involving patients with sinus node disease[17,18].

The identification of the causes of these unexpected arrhythmias has not yet been established. The first hypothesis is that undiagnosed AF runs were already present before implant; the second possibility is that the atrial lead itself could be responsible for the development of arrhythmia. In patients with sinus node dysfunction, AF is related to the natural history of the disease[1,19]. An increase in the sympathetic or parasympathetic tone and anatomic alterations of the atrium such as areas of fibrosis can create a background for macro and microreentry, hence facilitating AF. In patients with atrioventricular block, the proarrhythmic role of ventricular pacing may be explained on the basis of the dissociation between atrial and ventricular contractions. In dual-chamber pacing systems the hypothesis that the atrial lead could play a role in the development of AF is related to the chronic irritation resulting from the contact between the lead tip and the atrial wall. This irritating action of both passive fixation and screw-in leads was commonly observed during positioning of the device.

We compared the AF occurrence in two groups of patients implanted respectively with a DDD and VDD pacing system for atrioventricular block. All patients received the same device with the same diagnostic features; the main difference was the contact of the lead with the atrial wall in the first group and the presence of a floating dipole in the second group. The results of our study confirmed the presence of symptomatic and asymptomatic AF episodes. In patients without documented prior episodes, no significant differences were found in the incidence of arrhythmia between the DDD and VDD groups. The AF rate during follow-up was 35% among DDD and 42% among VDD patients (p = NS). In view of the very strict programming of atrial sensitivity and of AF detection parameters that was performed in order to exclude very short and false positive AF episodes in patients without prior arrhythmias, the results can be considered as being quite significant. In particular, so as to reduce false positives, atrial sensing was planned to cut the far-field wherever possible; furthermore, the high rate atrial episode detection algorithm was programmed in such a way as to record only the episodes lasting > 50 beats; finally we classified all the patients in whom the electrogram did not confirm the diagnosis as not having AF, although other episodes could possibly be true. The higher incidence of inappropriate AF detection in the DDD group was probably related to the presence of many unipolar atrial leads, in spite of the individually tailored programming. On the other hand, in the VDD group oversensing episodes were extremely rare.

The incidence of AF in the DDD and VDD subgroups was also found to have a similar distribution in the two populations as far as the number and duration of runs were considered (Fig. 5). Independently of the pacing mode, a small number of episodes was recorded in some patients whereas in others such episodes were much more

frequent; analogously, in both groups, some patients had long episodes and some others short ones. These data indicate that the contact between the lead tip and the atrial wall plays only a minor role in the development of arrhythmia since even patients with the VDD system, in which the floating single lead does not produce a continuous irritating stimulus on the atrial wall, episodes of similarly characterized AF still occurred. Such a final statement should not be considered surprising, particularly in view of the fact that the prevalence of atrial tachyarrhythmias observed in our study was not significantly different from that observed in other subgroups of patients not submitted to cardiac pacing, but with similar overall characteristics. In fact, aging, hypertension, left ventricular hypertrophy, and left ventricular dysfunction have been associated with a high prevalence of AF[20,21].

A potential benefit of atrial pacing in the prevention of AF would have been expected in the DDD group, but it was not confirmed by our results. However, the actual atrial pacing percentage obtained in patients wearing a DDD system was only 35% which is very far from the values (> 80-90%) which were associated with the prevention of arrhythmia in sinus node disease patients[18]. Furthermore, the different pacing mode after automatic mode switching activation (VVI or DDIR) did not influence the occurrence of AF.

Study limitations. Atrial tachyarrhythmia detection was based on atrial rhythm analysis performed by the atrial lead fixed to the right atrial wall or floating in the right atrium. Such an analysis, in contrast to electrophysiological evaluation, does not always allow appropriate discrimination between AF, atrial flutter and atrial tachycardia. Thus, all forms of atrial tachyarrhythmia have been included in our analysis. Anyway, only sustained episodes were taken into account. Furthermore, the clinical significance of frequent and long-lasting episodes of arrhythmia and the need of further investigation in such cases have not been analyzed.

In conclusion, the prevalence of AF during follow-up of patients paced for atrioventricular block but without prior atrial tachyarrhythmias was rather high; the rate of arrhythmias was not related to the presence of an atrial lead in contact with the atrial wall; further studies are required in order to better evaluate the clinical significance of these arrhythmias and to establish the need of antiarrhythmic drug treatment.

References

1. Sgarbossa EB, Pinski SL, Maloney JD, et al. Chronic atrial fibrillation and stroke in paced patients with sick sinus syndrome. Relevance of clinical characteristics and pacing modalities. Circulation 1993; 88: 1045-53.
2. Jordaens L, Robbens E, Van Wassenhove E, Clement DL. Incidence of arrhythmias after atrial and dual-chamber pacemaker implantation. Eur Heart J 1989; 10: 102-7.
3. Morsi AMR, Lau C, Nishimura S, Goldman BS. The development of sino-atrial dysfunction in pacemaker patients with isolated atrioventricular block. Pacing Clin Electrophysiol 1988; 21: 1430-4.
4. Wiegand UKH, Bode F, Schneider R, et al. Development of sinus node disease in patients with AV block: implications for single lead VDD pacing. Heart 1999; 81: 580-5.
5. Mattioli AV, Castellani ET, Vivoli D, Sgura FA, Mattioli G. Prevalence of atrial fibrillation and stroke in paced patients without prior atrial fibrillation: a prospective study. Clin Cardiol 1998; 21: 117-22.
6. Garrigue S, Cazeau S, Ritter P, et al. Incidence des arythmies atriales chez les patients stimulés au long cours en mode double chambre. Arch Mal Coeur Vaiss 1996; 89: 873-81.
7. Seidl K, Meisel E, Vanagt E, et al. Is the atrial high rate episode diagnostic feature reliable in detecting paroxysmal episodes of atrial tachyarrhythmias? Pacing Clin Electrophysiol 1998; 21 (Part I): 694-700.
8. Ricci R, Puglisi A, Azzolini P, et al. Reliability of a new algorithm for automatic mode switching from DDDR to DDIR pacing mode in sinus node disease patients with chronotropic incompetence and recurrent paroxysmal atrial fibrillation. Pacing Clin Electrophysiol 1996; 19 (Part II): 1719-23.
9. Limousin M, Geroux L, Nitzsche R, et al. Value of automatic processing and reliability of stored data in an implanted pacemaker: initial results in 59 patients. Pacing Clin Electrophysiol 1997; 20: 2893-8.
10. Defaye P, Dournaux F, Mouton E, for the AIDA Multicenter Study Group. Prevalence of supraventricular arrhythmias from the automated analysis of data stored in the DDD pacemakers of 617 patients: the AIDA study. Pacing Clin Electrophysiol 1988; 21: 250-5.
11. Botto GL, Ricci R, Bonini W, et al. Effect of intermittent or continuous overdrive atrial pacing in paroxysmal atrial fibrillation related to brady-tachy syndrome. G Ital Cardiol 1999; 29 (Suppl 5): 90-3.
12. 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: 282-6.
13. Feuer J, Shandling A, Messenger J, Castallanet C, Thomas J. Influence of cardiac pacing mode on the long-term development of atrial fibrillation. Am J Cardiol 1989; 64: 1376-9.
14. Sasaki Y, Shimotroi M, Akehane K, et al. Long-term follow-up of patients with sick sinus syndrome: a comparison of clinical aspects among unpaced, ventricular inhibited paced, and physiologically paced groups. Pacing Clin Electrophysiol 1988; 11: 1575-83.
15. Rosenqvist M, Brandt J, Schuller H. Long-term pacing in sinus node disease: the effects of stimulation mode on cardiovascular morbidity and mortality. Am Heart J 1988; 116: 16-22.
16. Furman S, Coper JE. Atrial fibrillation during AV sequential pacing. (abstr) Pacing Clin Electrophysiol 1982; 5: 133.
17. Bellocci F, Spampinato A, Ricci R, et al. Antiarrhythmic benefits of dual chamber stimulation with rate-responsive in patients with paroxysmal atrial fibrillation and chronotropic incompetence. A prospective, multicentre study. Europace 1999; 1: 220-5.
18. Ricci R, Santini M, Puglisi A, et al. Impact of consistent atrial pacing algorithm on premature atrial complexe number and paroxysmal atrial fibrillation recurrences in brady-tachy syndrome: a randomized prospective cross over study. J Interv Card Electrophysiol 2001; 5: 33-44.
19. Brandt J, Anderson H, Faraheus S, Shuller H. Natural history of sinus node disease treated with atrial pacing in 213 patients: implications for selection of stimulation mode. J Am Coll Cardiol 1992; 20: 633-9.
20. Chugh SS, Blackshear JL, Shen WK, Hammill SC, Gersh BJ. Epidemiology and natural history of atrial fibrillation: clinical implications. J Am Coll Cardiol 2001; 37: 371-8.
21. Hennersdorf MG, Strauer BE. Arterial hypertension and cardiac arrhythmias. J Hypertens 2001; 19: 167-77.