EDITORIAL

What is the role of the pacing rate in the prevention of atrial tachyarrhythmias?

Carsten W. Israel

Division of Clinical Electrophysiology, Department of Cardiology, J.W. Goethe University, Theodor-Stern-Kai 7, 60590 Frankfurt, Germany

Online publish-ahead-of-print 3 October 2007

This editorial refers to ‘Increased base rate of atrial pacing for prevention of atrial fibrillation after implantation of a dual chamber pacemaker: Insights from the Atrial Overdrive Pacing (AOP) study’ by B.K. Kantharia et al., doi:10.1093/europace/eum170

In 1998, Delfaut et al. reported about 30 patients with drug-refractory atrial fibrillation (AF) which recurred in all individuals despite continuation of antiarrhythmic drugs within approximately 1 month, but was suppressed by pacing for a mean of 143 days. Although the main scope of this study was the assessment of dual-site right atrial pacing (which further prolonged the arrhythmia-free interval to 195 days), this observation stimulated interest in atrial overdrive pacing as a potential therapy of AF. Of note, all patients in this study had spontaneous or drug-induced bradycardia, and the investigators carefully adjusted pacing rate and drug dose until a proportion of atrial pacing during sinus rhythm of >80% was achieved. Similarly, Garrigue et al. calculated the mean 24 h heart rate in 22 patients with a dual-chamber pacemaker via the memory of the device and programmed the lower pacing rate just 10 bpm above this value to perform atrial overdrive at an individually optimized rate. Again, overdrive pacing, in this case at a mean of 75 bpm, was associated with a reduction or complete prevention of AF recurrences. These and other observations led to the hypothesis that atrial overdrive pacing, i.e. pacing faster than the sinus rate, for a significant proportion of time may prevent AF. As the PA trial showed, atrial pacing in the DDDR mode with 70 bpm achieved atrial pacing for only 67% of the time in patients without sinus bradycardia and was unable to prolong the time to AF recurrence. Pacing at higher rates such as 90 bpm can achieve atrial overdrive for >80% of the time but is not tolerated by a number of patients. Therefore, pacing algorithms that maintain the atrial pacing rate just above the sinus rate were developed, thereby providing >90% atrial pacing during sinus rhythm without a significant rate increase. These pacing algorithms, providing ‘dynamic-rate’ instead of ‘fixed-rate’ atrial overdrive, were tested against conventional dual-chamber pacing (DDD or DDDR) at 60 bpm but failed to demonstrate a significant impact on AF recurrences in a number of studies, whereas only one study found a reduction in the number of days with symptomatic AF.

Therefore, the question arises if the percentage of atrial pacing or rather the lower rate limit is the key to atrial preventive pacing. In individual patients, an association between the occurrence of atrial premature beats or the initiation of AF and a rate decrease below an absolute value can be observed. Figure 1 shows such an example using a pacemaker monitoring function. In this patient, an atrial overdrive algorithm maintains the pacing rate above the intrinsic value, slowly decreasing the pacing rate as long as no intrinsic events are seen towards a minimum value of 60 bpm However, whenever the pacing rate approaches 60 bpm, intrinsic activity appears in form of atrial premature beats. This manoeuvre reiterates until premature beats finally trigger AF. Programming the lower rate limit to 70 bpm abolished AF recurrences in this patient. A detailed analysis of the atrial rate and rhythm just before AF initiation using an implanted dual-chamber pacemaker revealed that 39% of AF episodes seemed to be triggered by some form of bradycardia.

These observations suggest that at least in some patients, programming the lower pacing rate may play a role in the prevention of AF. Therefore, the Atrial Overdrive Pacing (AOP) study addresses an important and insufficiently studied question. In this study, 145 patients received dual-chamber pacing at 60 bpm before they were randomized to a lower pacing rate of (i) 70 bpm, (ii) 70 bpm with a rate decrease to 65 bpm at rest, or (iii) 80 bpm with a rate decrease to 65 bpm at rest. In a cross-over design completed in 99 patients, each programming was applied for 3 months. The authors did not find any difference in the number of mode-switching episodes between the three settings.

The opinions expressed in this article are not necessarily those of the Editors of Europace, the European Heart Rhythm Association or the European Society of Cardiology.

*Corresponding author. Tel: +49 69 6301 6512; fax: +49 69 6301 6341. E-mail address: c.w.israel@em.uni-frankfurt.de

© The European Society of Cardiology 2007. All rights reserved. For permissions, please e-mail: journals.permissions@oxfordjournals.org
One of the problems associated with device-derived parameters for quantification of AF recurrence becomes rapidly evident looking at the results of this study: AF occurs at a highly variable rate and does not occur at random but in clusters as has been shown before. In the present study, the mean number of mode-switching episodes was 126, 378, 357, and 136 in the four study periods of 3 months each. At the same time, the standard deviation was 596, 1403, 1482, and 400, illustrating this problem. Owing to this variability, the number of patients and the study period in each pacing mode are most likely unable to detect any treatment effect. Additionally, the authors chose a parameter less useful to assess the treatment effect: Mode switching critically depends on programmed settings; if atrial sensitivity is not sufficiently high to continuously detect AF to an extent sufficient for the maintenance of mode switching, a single, long AF episode may be cut into hundreds of short mode-switching episodes distorting this outcome parameter. For this reason, current studies with device-based monitoring of AF recurrence typically use the 'AF burden', i.e. the device-derived cumulative time in AF as a percentage of the total follow-up period, together with an AF detection algorithm independent of mode switching.

Figure 1  Atrial fibrillation associated to a low-paced atrial rate. In this example, atrial premature beats and atrial fibrillation start despite atrial pacing but only if the atrial rate falls below a critical value slightly above 60 bpm. (A) Monitor showing the atrial rhythm 500 s before atrial fibrillation onset. Every 10 atrial paced cycles, the atrial pacing rate is decreased if no intrinsic beats occur. (B) The blow-up of the last 45 s before atrial fibrillation onset shows that whenever the pacing rate approaches 60 bpm, atrial premature beats appear, which finally trigger AF. During pacing at a slightly higher rate, no atrial premature beats occur.
Several other aspects of this study have to be considered. First, the cross-over study design carries the risk of carry-over effects that affect every successive study period. Secondly, the mean value for mode-switching episodes may be not representative for the treatment effect under investigation. It may be clinically more important how many patients were free of AF >30 sec than to compare some mean values without any clear clinical implication (what does a reduction in the number of mode-switching episodes from 357 to 136 mean clinically)? Thirdly, the concept of a rest rate as evaluated in this study may be unsuccessful in patients with vagally induced or bradycardia-dependent AF. Vagal predominance will be most prominent in periods of rest which are least covered by overdrive pacing in this concept, and the rate decrease from the normal lower rate (e.g. 80 bpm in study phase C) to the rest rate (65 bpm in study phase C) may act as a trigger of AF.

Fourth, atrial leads were implanted in the right atrial appendage, which is most likely less successful in preventing AF than pacing from the atrial septum.16, 17 Finally, unnecessary right ventricular pacing was not systematically avoided in this study. There is emerging evidence that right ventricular stimulation in context with dual-chamber pacing in sinus node disease increases the risk of developing AF18 and that the efficacy of atrial preventive pacing may be reduced by ventricular pacing.8, 19 Dual-chamber devices have to be programmed in an unusual way to avoid ventricular pacing during atrial overdrive (e.g. to an AV delay of 350 ms) or should even better be fitted with dedicated algorithms providing mode switching between AAIR and DDR pacing to prevent unnecessary right ventricular pacing.20, 21 It is important to note in this context that AAIR, instead of DDR overdrive pacing, has been successful in reducing the number of AF episodes in the PAF-PACE study.22

However, it is easy to criticize a study, particularly if results are not welcome. It has to be realized that the AOP study did not show a significant effect of lower rate programming on the efficacy of atrial pacing for AF prevention. Further studies, however, seem to be justified to assess the value of pacing optimized according to current concepts: atrial septal lead position, prevention of ventricular pacing, AF burden as study endpoint, and atrial electrograms to verify correct detection of the beginning and the end of AF.

Conflict of interest: C.W.I. is a member of the Advisory Board and Speaker’s Bureau of Guidant Germany, Medtronic Inc., Sorin Group, and St. Jude Medical; and participates in studies sponsored by Medtronic Inc. and St. Jude Medical.

References