Higher rates to reduce irregularity: the use of overdrive pacing in atrial fibrillation

N.M. van Hemel*

Department of Cardiology, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands

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This editorial refers to 'Dynamic ventricular overdrive stimulation in atrial fibrillation: effects on ventricular rate irregularity, ventricular pacing, and fusion beats' by G. Nölker et al., on page 1688

For a long time, it was a matter of debate whether fast rate or ventricular irregularity during atrial fibrillation (AF) was primarily responsible for the perception of palpitations, development of cardiomyopathy, and system emboli from the fibrillating atria. Recent studies have shown that ventricular irregularity associated with AF and manifested by random QRS intervals that constitute the diagnostic clue in scalar electrocardiography, can elicit symptoms and cardiomyopathy regardless of the rate. Reduction of ventricular irregularity in AF patients in addition to control of fast ventricular rates, therefore, appears sensible to reduce symptoms and minimize the risk of cardiomyopathy. The underlying mechanisms of ventricular irregularity are uncertain and include concealed conduction within the atrioventricular (AV) node secondary to decremental conduction or electrical modulation of AV nodal propagation or pacemaker activity in the AV node.

If rate control is preferred to rhythm control, suppression of AV conduction with pharmacologic treatment and ablation of the AV junction are nowadays the established methods according to guidelines. However, the side effects and non-compliance associated with drug treatment or pacemaker dependency after ablation with potentially unfavourable effects of long-term right ventricular apical pacing often undermine the effectiveness of these therapies. These disadvantages urge the search for other therapeutic modalities for a safe and easy reduction of ventricular irregularity in AF.

In 1983, Wittkampf and De Jongste showed that continuous pacing in the right ventricle reduced the irregularity of QRS intervals during AF; faster pacing rates produced even more regularity by elimination of a large proportion of longer QRS intervals observed during slower ventricular rates. This phenomenon of rate stabilization is attributed to suppression or delay in AV nodal conduction by retrograde penetration of ventricular stimuli. This concept was incorporated in rate smoothing pacing algorithms that indeed significantly reduced variability of successive QRS intervals in AF patients. Unfortunately, the application of this algorithm was associated with a concomitant increase in mean heart rate by 21–29%. This drawback limited the widespread use of rate smoothing algorithms in paced patients with paroxysmal or permanent AF.

In 1997, we tested a new rate smoothing programme delivered by the former Vitatron company, that uses a dynamic average of successive sensed or paced heart rates as a reference point. The pacing rate followed the average heart rate and started pacing when the average ventricular rate dropped by 2.5 bpm. In addition, the algorithm prevented the occurrence of sudden brady- or tachyarrhythmia by pacing at a decelerating or accelerating rate at 2 bpm. In the acute pacing study, we observed that variability of the RR intervals could be reduced by 73% while the heart rate during pacing did not increase significantly (2%) compared with the preceding period without pacing.

In the unpublished randomized, single-blinded cross-over trial of patients with permanent (n = 91) and paroxysmal AF (n = 93), we observed a significant reduction in the variance of RR intervals in both patients categories. However, quality of life, measured with instruments specific for pacemaker patients, did not change significantly with ventricular rate smoothing. A preference for rate smoothing pacing was observed in patients with paroxysmal AF. These dissatisfying findings prevented further clinical exploration.

Treatment and specifically prevention of AF with atrial pacing was also investigated in the mid-90s. Assuming that atrial overdrive of the atria would suppress triggering atrial premature beats, short—long intervals and atrial pauses, thereby diminishing potentially arrhythmogenic increased dispersion of atrial refractoriness, one- or two-site atrial pacing has been extensively studied. The results of many studies are very conflicting because of differences in overdrive pacing algorithms, profiles of included AF patients, calculation of AF burden based on the number of mode switches, and other methodological differences including control groups and duration of follow-up. For example, Carlson et al. showed the
efficacy of right atrial appendix stimulation with respect to AF burden, but only symptomatic AF was detected with an event recorder.

However, de Voogt et al.\(^9\) applying overdrive pacing from the low right atrial septum or right atrial appendix, combined with anti-arrhythmic drugs, did not demonstrate any reduction in AF burden if the total time in pacemaker mode switch was measured. Since 2000, the number of reports on atrial overdrive for treatment or prevention decreased markedly reflecting shrinking interest for this approach.\(^10\) Nowadays, these pacing algorithms are switched on often with a trial-and-error approach.

In this issue of the journal, Nölker et al.\(^11\) present the results with a dynamic ventricular overdrive pacing algorithm in the acute AF study that had been originally developed for atrial pacing in AF. This algorithm aims at reducing the variability of RR intervals as well as to promote ventricular stimulation to allow for continuous and stabilized pacing in cardiac resynchronization therapy for congestive heart failure. The programme is primarily focused on the detection of intrinsic QRS complexes in AF and after their detection, the pacing rate is initially increased and later gradually decreased to the programmed basic rate of ventricular on demand pacing (VVI). The increments and decrements in the pacing rates at 60–150 bpm can be programmed with several slopes resulting in various levels of dynamic ventricular overdrive. Programmed pacing is interrupted by intervening of intrinsic QRS complexes and afterwards the pacing sequence restarts.

This pilot study showed that all settings significantly diminished the variance of QRS intervals while the proportion of paced beats clearly increased favouring the application of cardiac resynchronization pacing. However, the mean heart rate increased significantly compared with the intrinsic rate and on demand VVI pacing at 60–80 bpm and lower overdrive levels. The haemodynamic changes during various overdrive pacing protocols and the accompanying increase in heart rate were not measured in this acute study. Thus, compared with previous algorithms, no further progress is achieved except for an elegant method to calculate the percentage of fused paced beats.\(^11\)

After almost 30 years of efforts to regulate the random ventricular irregularity associated with AF or its prevention with programmable atrial pacing algorithms, at present, the therapeutic target of automatic electrical intervention therapy in the right ventricle or the right atrium has not yet been achieved. Regarding AF prevention, it can be explained by the variably long initially asymptomatic AF intervals\(^12,13\) creating left atrial arrhythmogenic substrate that hardly can be modified by right atrial appendix or low right septal pacing despite highly sophisticated pacing features.

Regarding lowering the ventricular irregularity with overdrive pacing, the unfavourable effects of increased ventricular rates hamper further clinical exploration. It is unclear as to whether right ventricular septal pacing can prevent this side effect. In my opinion, it is not the efforts of the device engineers but, rather, our insufficient knowledge about AF and its conduction through the AV junction that is responsible for these imperfect pacing algorithms developed in the past three decades. We need much more insight into AF in order to guide engineers in the proper direction.

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**References**