Atrial antitachycardia pacing: do we still need to talk about it?

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This editorial refers to ‘Impact of atrial antitachycardia pacing and atrial pace prevention therapies on atrial fibrillation burden over long-term follow-up’ by A.M. Gillis et al., on page 1041

Since first described in 1968,1 sick sinus syndrome (SSS) has become one of the most frequent indications for pacemaker implantation. Although in early days, the presence of atrial fibrillation (AF) limited the use of pacemakers in patients with SSS, nowadays pacemakers play an important role in the management of AF in patients with SSS. Highly sophisticated devices have been developed with increased Holter capabilities allowing continuous rhythm monitoring. Although the prevalence of AF prior to pacemaker implantation has been found in the range of 40–45%,2 AF detection during follow-up using pacemaker Holter data is reported in 50–65% of patients with SSS.3,4 In the Mode Selection Trial (MOST), pacemaker-detected paroxysmal AF was a strong independent predictor of stroke, death, and persistent AF, whereas symptoms as a clinical comparator could not reliably predict AF recurrence.4 The known limited success rate of drug therapy for rhythm control and the overwhelming number of pacemaker patients with paroxysmal AF prompted interest in using pacing therapy to treat AF. Therapy options developed included alternative single-site atrial pacing, multisite atrial pacing, pacing algorithms to prevent AF by increasing the amount of atrial pacing suppressing triggers of AF, and atrial antitachycardia pacing (ATP) to terminate AF.

Many clinical trials have been conducted over the past 10 years studying the efficacy of pacing algorithms for AF prevention and termination. The present paper by Gillis et al.5 reports the first long-term data on atrial ATP. Neither ATP alone nor ATP in combination with preventive pacing algorithms could successfully suppress atrial tachycardia (AT)/AF during a follow-up period of 3 years. The trial was early terminated due to phasing out of the AT500/501 pacemaker and study results may have been underpowered to detect any differences. However, the results correlate well with other ATP studies like the ATTEST trial or the Italian AT500 registry. In all these trials, ATP showed at best moderate efficacy in terminating slow regular ATs, low efficacy in terminating fast regular AT, and was ineffective in established AF.

The concept of ATP is based on the idea that early terminating atrial tachyarrhythmias may limit atrial remodelling. Atrial antitachycardia pacing is delivered at an atrial cycle length shorter than the detected arrhythmia in order to access the re-entrant circuit during any excitatory gap and to extinguish the arrhythmia. Successful therapy application is therefore limited to about one-third of the patients with AF who have a history of atrial flutter or show intermittently more organized atrial macroreentrant tachycardias susceptible to ATP. Furthermore, it is under debate whether the application of right atrial ATP can be effective in interfering with left atrial re-entrant circuits.

Besides the need for organized atrial tachyarrhythmias, ATP success is crucially reliant on correct device functioning, e.g. early detection of AT, correct rhythm classification, and therapy application by the device. Gillis et al.5 point out in their paper that manual inspection of stored IEGMs of detected AT/AF episodes did not show any atrial undersensing, far-field R-wave sensing, or inaccurate classification of an episode termination in their study. Nevertheless, one needs to keep in mind that the number of stored electrograms is small compared with the total number of detected events and rhythm strips are short, often not showing the onset nor the termination of AT/AF. One can imagine that intermittent far-field sensing detected by the device as AF, for example, may lead to false application of ATP which in turn may be proarrhythmic and lead to a significant increase in AF burden over time.

Interestingly, Gillis et al.5 report indeed an increase in AT/AF burden over time in the ATP arm only, compared with DDD pacing alone or ATP in combination with preventive pacing algorithms. This difference may be partially due to slight imbalances in clinical characteristics among patient groups as suggested by the authors. One may also hypothesize that the beneficial effects of preventive pacing algorithms may have counteracted the
proarrhythmic effects of ATP during long-term follow-up and stabilized AF burden over time comparably to DDD pacing alone. It demonstrates the need to interpret the effects of ATP and of preventive pacing algorithms separately. Unfortunately, the study designed by Gillis et al. did not include a study arm with preventive pacing algorithms only and, therefore, does not allow to conclude on the efficacy of preventive pacing algorithms during long-term follow-up.

Although ATP works when atrial arrhythmias occur, the concept of preventive pacing algorithms is based on the detection of triggers, their elimination by different pacing manoeuvres, and the prevention of AF onset. A substantial number of clinical trials assessing the efficacy of preventive pacing algorithms have been published in the last 10 years. Although their patient populations, study designs, and pacing strategies and algorithms varied widely, device-detected AF was usually used as a primary endpoint in almost all trials. Of note, no other AF therapy trial ever had used continuous beat-to-beat rhythm monitoring to detect AF recurrences during follow-up. The study outcomes reported on overall efficacy in reducing device-detected AF burden with pacing fell short of everybody’s expectations. No pacing strategy proved generally efficacious to reduce AF and to be generally recommended in patients with a bradycardia indication for pacing and paroxysmal AF. These negative results unjustly slackened off the general interest in AF pacing trials. But still, important insights on how to pace SSS patients with paroxysmal AF were gathered in these trials and one may wonder how efficacious atrial preventive pacing could be applied in the modern state of the art setting of atrial-based pacing.

The study reported by Gillis et al. was designed back in 2000. Several accomplishments in pacing from the past years, therefore, were not considered in their study protocol. First, patient selection plays a crucial role for pacing efficacy in AF prevention. In several trials, patients with true paroxysmal AF were better candidates for preventive pacing. Clinical markers for the presence of substantial atrial remodelling may be a history of cardioversion and long-lasting AF. In the SAFARI (Study of Atrial Fibrillation Reduction) trial, patients with recent cardioversions or with a history of persistent AF were strictly excluded; these, the greatest benefit from pacing was demonstrated in patients with an AF burden of at least 6% at baseline. Selected patients with identifiable triggers prior to the onset of AF may have had a greater benefit from pacing than patients without. As a subsystudy of the Atrial Fibrillation Trial (AFT) has shown, 46% of AF episodes were preceded by atrial premature beats and 39% by bradycardia. In the VIP [Vorhofflimmer (atrial fibrillation) prevention by Individualized pacemaker Programming] registry, an AF burden reduction of 28% could be achieved in patients with frequent premature atrial beats prior to AF using triggered algorithms only designed to suppress premature atrial activity.

Many different preventive algorithms have been developed and are commercially available today. Most of them are continuous atrial overdrive pacing algorithms and only a few pacemakers have intermittently activated, so-called triggered algorithms on board. As the 3:4 study demonstrated, the type of algorithm, the timing, and duration of pacing may significantly influence the outcome. Although the use of continuous overdrive pacing may have a detrimental effect, the use of only triggered algorithms was so far always associated with a beneficial effect on AF burden reduction.

To date, the effects of various pacing modes on atrial tissue are not well understood. The study of Gillis et al. randomized patients to different pacing strategies between 2 and 30 months after pacemaker implantation, thus leaving us with an undefined inhomogeneous patient population in respect to atrial susceptibility for atrial pacing manoeuvres and with difficulties to interpret study results. Experimental studies are currently lacking, showing how pacing may alter ion currents and cellular haemostasis in normal as well as in diseased atrial myocardium. Future research on this topic may help to develop pacing algorithms that may support physiological atrial activation rather than stress atrial tissue and trigger electrophysiological changes leading to AF.

Considering our limited knowledge on pacing effects, it is finally worth mentioning that a substantial number of patients with SSS will already benefit from conventional atrial pacing. As noted in SAFARI, 40% of the patients with a history of ECG-documented AF were lost for randomization because they were free of any AF recurrences up until 4 months after pacemaker implantation. The effect may be even greater if ventricular pacing can be omitted. As Sweeney et al. have demonstrated, dual-chamber minimal ventricular pacing yields a 40% reduction in the relative risk for developing persistent AF when compared with conventional dual-chamber pacing. Thus, modern device technology offering AAI pacing with DDD backup only in cases of pauses and AV block appears superior to older pacemaker technology.

In conclusion, SSS is recognized today not only as a disorder of the sinus node but also as a substrate for the development of atrial tachyarrhythmias. Pacing therapy plays an important role in the management of patients with SSS and, therefore, is an integral part in the management of AF in these patients. Whether pacing therapy successfully prevents AF recurrences will depend on the selection of a pacemaker, the mode of pacing, the programming of the device, the experience of the treating physician, and last but not least on the state of disease. Current study results demand an individual approach to pacing therapy. More trials are needed to better identify pacing responders, to understand pacing effects on the cellular level, and to study new pacing applications for the prevention of AF in patients with SSS.

Conflict of interest: none to declare.

References


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The externally placed ‘temporary-permanent’ generator

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At first glance, this chest X-ray appears to show a standard, right-sided permanent pacemaker. Further scrutiny, however, shows that the right internal jugular vein is the portal of entry for the active-fixation, ventricular septal electrode. This unusual X-ray appearance actually represents a ‘permanent’ generator being used as a temporary pacemaker. The lead exits the skin overlying the internal jugular vein (or can be tunnelled to exit in the subclavian region) and is connected to an externally placed, reusable pacing generator. The small size of the generator allows for greater patient mobility and the electrode’s active-fixation promotes lead stability. This technique is primarily used in pacing-dependent patients undergoing pacemaker explant for infection prior to re-implantation of a new pacing system.

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