Biatrial Stimulation and the Prevention of Atrial Fibrillation

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Summary

The conventional drug therapy for paroxysmal atrial fibrillation or atrial flutter poses several unresolved problems. Non-pharmacological therapies for these rhythm abnormalities, such as radiofrequency ablation, biatrial pacemaker stimulation, or hybrid therapy, are promising. Biatrial pacing helps lengthen arrhythmia-free intervals by means of atrial resynchronization and overdrive atrial pacing. Nowadays, implantation of a biatrial or septal atrial pacing system is mostly undertaken to prevent paroxysmal atrial fibrillation and/or flutter, to treat sick sinus syndrome in the presence of interatrial conduction block, to achieve total right ventricular activation by means of ultrashort atrioventricular delays in patients with hypertrophic obstructive cardiomyopathy, and to optimize atrioventricular resynchronization in patients with dilative cardiomyopathy. The initial results of ongoing multicenter, randomized clinical trials encourage clinical use of these pacing modalities. However, final results of these studies are awaited to judge on the overall effectiveness and indications for biatrial pacing.

Key Words

Cardiac pacing, biatrial stimulation, atrial resynchronization

Introduction

Atrial fibrillation is the most common rhythm disturbance that has posed many unresolved problems. Drug therapy for supraventricular tachycardias, especially in cases of atrial fibrillation, has often failed due to the development of various forms of side effects and proarrhythmic effects. Paroxysmal or permanent atrial fibrillation requires continuous anticoagulation due to the risk of cerebral embolism, but it can produce its own complications. Despite the ability of drugs to prevent atrial fibrillation and maintain sinus rhythm in the long-term, more than 50 % of patients atrial fibrillation develop before the one-year follow-up [1]. In addition to radiofrequency ablation, treatments such as dual-site atrial pacing [2], septal atrial pacing [3,4], biatrial pacing [5-7], and continuous atrial overdrive from the right atrium have been developed to treat this disease by non-pharmacological means. The purpose of using pacemakers in patients with atrial fibrillation is to prevent this arrhythmia, achieve longer arrhythmia-free intervals, decrease drug intake, and improve quality of life of the patients.

The aim of our paper is to discuss different forms of pacemaker application to prevent atrial fibrillation and their hemodynamic effects. The emphasis is placed on the role and indications for biatrial pacing. We also analyzed the results of prospective randomized clinical trials and pertinent data from Hungary.

Structural factors	Functional factors	Substrate	Triggers
Fibrosis	Autonomic tone	Abnormal repolarisation Refractoriness Dispersion of refractoriness	Premature Atrial Complexes
Dilatation	Ischaemia	Abnormal conduction Conduction velocity IaACB, IACB Anisotropy Dispersion of conduction velocity	Pauses
Infarction	Acid-base balance	Chronotropic incompetence	Specific initiation sequences – short-long-short
Cardiac surgery	Stretch		
Cardiomyopathy	Drugs		
	Rhythm disturbances		

Table 1. Mechanism of atrial fibrillation. IaACB = intraatrial conduction block, IACB = interatrial conduction block.

Managing Atrial Fibrillation through Cardiac Pacing

The initiation of atrial fibrillation can be described as an interaction of structural and functional factors affecting the atrial substrates that triggers atrial rhythm disturbances (Table 1). Different forms of pacing for biatrial stimulation have been developed in recent years (Table 2).
There are several advantages of biatrial stimulation using DDD pacemakers (AAD mode):

- bipolar coronary sinus pacing from the ventricular port facilitates programming of the pacing output at a level slightly above the pacing threshold, with simultaneous right atrial pacing;
- possibility of independent programming of the right atrial and left atrial pacing parameters;
- no dependency from the global impedance of atrial leads;
- favorable sensing characteristics in bipolar sensing configuration, with no far-field sensing of R- or T-waves;
- precise and easy diagnosis of atrial arrhythmias via recorded intracardiac electrograms;
- continuous left atrial synchronization to sinus or ectopic beats from the right atrium (triggered AAD pacing).

However, major shortcomings of the AAD mode is inability to pace the ventricle in case of atrioventricular block development and the lack of resynchronization on premature beats coming from the left atrium.
The four primary effects of biatrial stimulation are:

- hemodynamic benefits from resynchronization, due to shortened total atrial activation time and P-wave duration, reduced dispersion of atrial refractoriness, and limiting anatomical substrates involved in the generation of supraventricular extrasystoles;
- overdrive suppression of supraventricular rhythm disturbances and prevention of special proarrhythmic sequences, such as short-long-short cycles;
- halting atrial remodeling;
- potential reduction of antiarrhythmic drug intake.

The acute hemodynamic effects of the right atrial appendage pacing, coronary sinus pacing, and biatrial pacing have been investigated using various methods. In an animal study, the features of myocardial activation during multisite pacing were assessed using multiple epicardial electrodes (128 bipoles). The activation time and local recovery intervals were minimized by triple-site stimulation, whereas four-site stimulation did not result in further shortening. Local refractory periods and their dispersion remained unaffected. The authors concluded that the shortening of local recovery

Mode of Pacing	Mechanism
AAI pacing	Eliminate pauses Overdrive supression
AAIR pacing	Overdrive with rate adapted pacing*
Continuous overdrive	AAI pacing, with special algorithm
Dual Site Right Atrial Pacing (Saksena) (DAP)	Resynchronisation
Biatrial Pacing (BAP) Daubert (splitting, anodal (+) CS pacing) Kutarski (inverted splitting, cathodal (-) CS pacing) Paralell lead connection dual cathodal (-) pacing and common anode (uni or bipolar configuration) AAD mode of DDD pacemaker for BAP (Biotronik Logos DS) cathodal (-) pacing (uni or bipolar pacing/sensing configuration)	Resynchronisation
Septal Biatrial Pacing (SBAP) Bachman's Bundle Pacing (Spencer) Koch triangle pacing (Padeletti)	Resynchronisation
Hybrid therapy	Pacing and drugs and/or RF abl.

*Table 2. Methods of pacing to prevent atrial fibrillation. *Not confirmed by a randomized study [15].*

intervals with an unaffected local refractory period might homogenize atrial repolarization and could play a role in the preventive effect of multisite pacing. [8,9].
To evaluate the efficacy of biatrial and multisite right atrial pacing, two multicenter, prospective, randomized trials have been initiated. SYNBIAPACE is a crossover trial comparing three pacing modes during three periods of 3 months each: biatrial pacing at a lower rate of 70 beats/min, single-site right atrial appendage stimulation at 70 beats/min, and inhibited DDD pacing at 40 beats/min (reference mode). Criteria for inclusion were long-lasting (≥ 1 year), recurrent, and drug resistant atrial fibrillation or atrial flutter (with at least two antiarrhythmic drugs tested, including amiodarone) associated with interatrial conduction block. The latter was defined by P-wave lengthening (> 120 ms) and interatrial conduction time equal or greater than 100 ms. The pacing devices used in the study were specially designed coronary sinus leads (Medtronic, USA) and a generator with a specific algorithm (ELA Medical, France). The primary endpoint of the study was to compare the time of the first atrial arrhythmia recurrence monitored by the Holter function of the pacemaker among the three pacing modes. 42 patients have been examined. Despite a tendency for a reduced incidence of atrial arrhythmia during biatrial pacing, no significant difference was found among the three pacing modes [10].
The Dual-site Right Atrial Pacing to Prevent Atrial Fibrillation (DAPPAF) trial is also a crossover study comparing the effects of dual-site pacing, single-site atrial pacing, and DDI mode at 50 beats/min in the prevention of AF. The study was limited to patients with a history of paroxysmal atrial fibrillation and a conventional indication for antibradycardia pacing. Inclusion criteria were at least two documented episodes of atrial fibrillation within 3 months prior to enrollment and constant antiarrhythmic therapy during the protocol. As primary endpoints, the time of the first symptomatic recurrence of atrial fibrillation with ECG verification and the quality of life were compared among the three pacing modes. The secondary endpoints include time to the first recurrence of atrial fibrillation as monitored by the implanted pacemaker, the measurement of echocardiographic parameters, and patient symptoms. After the implantation, the patients were treated by dual-site atrial pacing for the first 3 months and then by single-site pacing for another 3 months. Mode crossover was carried out at 6-month intervals thereafter [11].
In Hungary, the first biatrial pacing system was implanted in 1999. From September 1999 to March 2000, three biatrial pacing systems (Logos DS, Biotronik, Germany) were implanted in patients with symptomatic paroxysmal atrial fibrillation. Two of the three patients are still free of atrial fibrillation, and with a marked decrease in the number of left atrial premature beats. In the third patient, biatrial stimulation used in conjunction with a hybrid therapy has failed [12-14]. In our department, three biatrial implantations (Logos DS, Biotronik) were performed beginning in June 2000. All our patients have been symptom-free after a follow-up period ranging from 3 to 13 months.
Indications for left atrial pacing include the following:

- technical difficulty during lead positioning in the right atrial appendage or in the right atrium (e.g., stable lead fixation impossible after previous heart surgery), multiple lead dislodgment at conventional atrial sites, unacceptably high pacing threshold in the right atrium, poor quality of the sensed intracardiac signal from within the right atrium, etc.;

- hemodynamic reasons such as to prevent the DDD pacemaker syndrome in patients with dilative cardiomyopathy and interatrial conduction block, or to achieve a total right ventricular activation by means of very short atrioventricular delays in patients with hypertrophic obstructive cardiomyopathy;
- antiarrhythmic effect in order to prevent atrial arrhythmias from starting in patients with interatrial conduction block.

Recent indications for biatrial pacing:

- paroxysmal atrial fibrillation and/or atrial flutter;
- sick sinus syndrome and interatrial conduction block associated with a P-wave duration > 120 ms and interatrial conduction time > 100 ms;
- to reach an ultrashort atrioventricular delay in patients with hypertrophic obstructive cardiomyopathy;
- to accomplish atrial and ventricular resynchronization in patients with dilative cardiomyopathy.

Discussion

Having an understanding of the substrates, mechanisms, and triggers of atrial rhythm disturbances is essential for increasing the arrhythmia-free interval. There are different methods of cardiac pacing to prevent atrial rhythm disturbances. The dual-site atrial pacing requires a conventional J-shape lead positioned in the right atrial appendage and a lead with active fixation placed in the vicinity of the coronary sinus ostium. The septal atrial pacing uses one lead with active fixation. To find the appropriate pacing site, additional intraoperative examinations are necessary (i.e., electrophysiology, echocardiography).

Various forms of biatrial pacing differ from each other concerning the type of the left atrial lead, the sensing and pacing characteristics, the lead impedance dependency, the energy consumption, and the possibility of atrioventricular sequential stimulation. In patients without AV node disturbances, biatrial DDD stimulation (AAD mode of pacing) is probably the best choice. The septal atrial pacing provides biatrial stimulation via one atrial lead and conventional atrioventricular sequential pacing, respectively.

Saksena's method gives the ease of implantation and continuous dynamic overdrive after activation of the rate-adaptive pacing mode, but atrial asynchrony reappears immediately after an atrial extrasystole and even during sinus rhythm. For that reason, the hybrid dual-site atrial pacing therapy (pacemaker plus antiarrhythmic drug) is necessary to diminish atrial asynchrony. The preliminary results of ongoing, multicenter, randomized cross-over trials (SYNBIAPACE, DAPPAF) could justify evaluation of the efficacy of synchronous biatrial pacing for non-conventional indications, such as the prevention of common atrial flutter and paroxysmal atrial fibrillation with or without interatrial conduction block. The detailed data of finalized randomized trials will determine the modes of patient selection and indications for biatrial stimulation.

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