Septal atrial pacing for the prevention of atrial fibrillation

Nina Hakacova, Dusan Velimirovic, Peter Margitfalvi, Robert Hatala, and Thomas A. Buckingham

1Children’s Cardiac Centre, Bratislava, Slovak Republic; 2Institute for Cardiovascular Diseases, Clinical Center of Serbia, Belgrade, Serbia and Montenegro; and 3Slovak Cardiovascular Institute, Pod Krasnou Horkou 1, Bratislava 83348, Slovak Republic

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Aims Atrial fibrillation (AF) produces significant morbidity and mortality. The current method of permanent pacing of the right atrium (RA) may cause delayed interatrial conduction and predispose to AF. We hypothesized that atrial septal pacing would reduce AF compared with high RA pacing.

Methods and results The patients were randomized into two groups. After randomization, patients received a dual-chamber rate-responsive device capable of mode-switching with advanced telemetry features. Devices were programmed in a standardized manner. To be eligible, the patients were required to have a conventional indication for a permanent pacemaker and recurrent paroxysmal AF. Group 1 was paced from high RA and Group 2 was paced from the atrial septum. Analysis of 43 patients who have completed 6 months of follow-up and 22 patients who completed 12 months of follow-up showed no significant differences in the number of mode-switching episodes or in AF burden between groups (P = NS by Mann–Whitney) although there was a trend for less AF with septal pacing. There were no differences in thresholds, sensing, or lead impedance. Lead parameters remained stable over time and there were no displacements of the electrodes after implantation. No patient experienced lead-related complications. A significant variability in AF burden was noted in this patient population.

Conclusions Implantation of an atrial-active fixation lead on the atrial septum is safe and feasible. However, this study showed no significant difference between septal pacing and high atrial pacing, using the endpoints of AF duration and number of AF episodes.

Introduction

Atrial fibrillation (AF) is the most common cardiac rhythm disturbance and contributes substantially to cardiac morbidity and mortality. It carries a considerable risk of thromboembolism and sustained AF, with an uncontrolled ventricular response rate can cause congestive heart failure with an increased risk of death. Since AF initiates negative processes of remodelling within the atrial myocardium, it has tendency to perpetuate itself.

The occurrence of AF increases with age, with a prevalence rising from 0.5% of people in their 50s to nearly 10% of the octogenarian population. Treatments which prevent episodes of AF or which terminate it immediately after its onset are able to prevent or at least to delay its progression to chronic AF.

Potential therapies of atrial fibrillation

The possible mechanisms of the activation and perpetuation of AF have significant implications for potential therapies. Long-term antiarrhythmic drug therapy has been used for the maintenance of sinus rhythm in patients with paroxysmal AF (PAF). However, many patients with PAF experience AF recurrences over the long term. Non-pharmacological therapies have been investigated, including surgery, internal defibrillators, catheter ablation, pacemakers, or the combination of catheter ablation with atrial pacing and ventricular pacing.

Recently, techniques of multisite atrial pacing have been introduced. For example, bi-atrial and interatrial septal pacing showed promising preliminary results in AF prevention. Permanent single-chamber atrial pacing may seem obsolete. The prevention of AF may relate to the maintenance of atrioventricular synchrony, prevention of bradycardia, and/or an altered activation sequence in
the atria. We sought to compare standard high right atrial (RA) pacing with septal pacing in a randomized clinical trial.

Methods

Study population

To be eligible, a patient was required to have a conventional indication for a permanent pacemaker and recurrent PAF. The study population consisted of patients with an established Class 1 and 2 indications for a permanent pacemaker (American Heart Association). In addition, patients had one of the following risk factors for PAF:

Inclusion criteria:

(i) prior symptomatic episodes of PAF in the last 6 months were documented by ECG or Holter. Note that this includes patients who have undergone cardioversion in the last 6 months and have one of the following:

(a) mild-to-moderate mitral stenosis grade 1 or 2 (American Heart Association),
(b) left atrial (LA) enlargement >55 mm on echocardiogram,
(c) recurrent atrial flutter, or
(d) sick sinus syndrome.

Exclusion criteria:

(i) patent foramen ovale or atrial septal aneurysm;
(ii) prior surgery involving the RA (coronary bypass or valvular heart surgery) if performed <10 days before entry into the study;
(iii) severe mitral stenosis.

Study protocol

Patients who met the inclusion criteria for the study received a permanent pacemaker from October 2002 to December 2003. Patients were randomized into two groups. After randomization, they received a dual-chamber rate-responsive device (DDDR) capable of mode-switching and with advanced telemetry features. Group 1 received atrial pacing using a single-active fixation lead in the atrial septum above the bundle of His near the foramen ovale, and Group 2 received ‘standard’ RA pacing—a single-active fixation lead was placed in the high RA. Devices were programmed in a standardized manner.

After hospital discharge, patients were followed at 1 week, 1 month, 3 months, and every 3 months thereafter. They underwent clinical assessment, a standard 12-lead ECG, and interrogation of the pacemaker at every visit. We counted the number of mode switches (each mode switch was taken to represent a recurrence of AF) and the total duration of AF after 6 months of follow-up and after 12 months of follow-up. To examine the safety of septal and atrial pacing, we checked whether all parameters were stable and whether there was a displacement of the electrode.

Implantable devices

The devices were St Jude Medical Integrity DR, Affinity DR, or Trilogy DR models and were programmed in both groups in a standard manner, which was designed to overdrive the atria (DDDR mode).

The requirements of the pacemaker were:

(i) rate-responsive or sensor-based pacing;
(ii) mode switching with telemetry recording of mode switching episodes.

The atrial leads were St Jude Medical Tendril SDX-active fixation leads. The position of the septal atrial lead is shown in Figure 1a and b. The second lead was placed at the right ventricular apex. Figure 2 is a 12-lead ECG showing normal sinus rhythm and septal atrial activation (lead is placed above the bundle of His).

Programmed parameters

The lower rate was set to 70. Rate adaptive pacing was used with a maximum rate of 110 and mode switches were programmed to occur for atrial rates > 225 bpm. The distance between the electrodes was 13.8 mm.

The endpoints

The endpoints assessed in our study were:

(i) the number of AF episodes between septal and high atrial-paced patients;
(ii) the total duration of the AF episodes between septal vs. high atrial-paced patients;
(iii) the safety of septal pacing.

Statistics

Data are presented as mean ± SD. A value of $P < 0.05$ was considered statistically significant. We used non-parametric statistical methods, i.e. the Mann–Whitney test, to compare the two groups.

Results

Patient characteristics are shown in Tables 1 and 2. There were 43 patients who completed 6 months of follow-up and 22 patients who completed 12 months of follow-up. The success of atrial septal pacing was judged by pacemaker

Figure 1 (A) X-ray in AP projection. One lead is in high right atrium and the other is in the right ventricle. (B) X-ray in AP projection. The arrow points to the septal lead. The second lead is in the ventricle.
interrogation of the AF burden or the total duration of AF, and the number of mode switching episodes (number of AF episodes). The results are shown in Tables 3 and 4 and Figures 3 and 4. Table 3 shows the analysis of 43 patients who completed 6 months of follow-up and Table 4 shows the analysis of 22 patients who completed 12 months of follow up. The proportion of ventricular pacing was 89 ± 21% (median 98%) in patients paced at the standard RA location.
and 91 ± 22% (median 98%) in those paced in the atrial septum (NS by Mann–Whitney U-test). No significant differences were found in the number of total mode switching episodes between groups (P = NS by Mann–Whitney). Likewise, there was no significant difference in total AF burden (duration of AF) (P = NS). There were more mode switches and longer durations of AF in patients paced in the high RA than the atrial septum, but this did not reach statistical significance. This difference tended to become larger after 12 months of follow-up compared with 6 months of follow-up. Lead parameters remain stable over time and there were no lead-related complications.

**Discussion**

Atrial fibrillation is a common clinical arrhythmia, which is difficult to manage clinically. Consequently, there are an increasing number of therapies under investigation. Some clinical data suggest that atrial pacing might prevent PAF, and several clinical trials have shown that atrial or dual-chamber pacing in patients with bradycardia reduces the incidence of AF. In recent years, various types of atrial pacing that might reduce the occurrence of AF have been studied. One important factor predisposing to re-entry is an increased dispersion of atrial refractoriness. Dispersion of refractoriness can be reduced by shortening total atrial activation. Therefore, it may be desirable to find a location from which the stimulation of both atria is rapid and uniform. Septal pacing provides shorter atrial activation times, compared with high atrial activation and offers an attractive alternative to dual-site atrial pacing.

The majority of atrial leads are positioned in the RA appendage. It is possible that stimulation in this site results in delayed activation of areas of the atria that are important in the initiation of PAF. It is difficult to estimate the effect of high RA pacing alone on PAF from the literature because of conflicting data. In the Atrial Pacing Periablation for Paroxysmal Atrial Fibrillation (PA3) Study, high atrial pacing did not prevent PAF in patients without bradycardia over the short term. The patient population selected was different than ours and the follow-up was shorter by 3 months. In our study, 43 patients completed 6 months of follow-up and 22 patients completed 12 months of follow-up.

Several reports have suggested that site-specific atrial pacing, e.g. Bachmann’s bundle, LA, or dual-site atrial pacing, might be more effective by virtue of shortening the total interatrial activation times. Multisite pacing has generally positive results. However, the usual methods of bi-atrial stimulation require two leads: one placed in the RA and another in the LA, using the coronary sinus. The LA can be paced by placing a lead in the proximal coronary sinus. This approach has the disadvantage of requiring an extra lead, which increases costs and the difficulty of the implant procedure. Septal atrial pacing is a simple method, which may produce simultaneous bi-atrial stimulation, using a single lead. Prior clinical trials of atrial septal pacing have given mixed results. The study by Bailin of Bachmann’s bundle pacing (high interatrial septum) showed positive results with a longer survival free of AF in the group treated with septal pacing. A study by Padeletti et al. in 2001 showed benefit of septal pacing in 46 patients randomized to RA appendage pacing or septal pacing in the prevention of PAF. However, a larger, larger multicentre study of the combined effect of septal pacing and AF/atrial tachycardia pacing algorithms failed to show benefit of atrial septal pacing.

In our group of patients with drug refractory PAF, septal atrial pacing had a small incremental antifibrillatory effect.
compared with RA pacing, but this was not statistically significant. Another goal of our study was also to examine the safety and flexibility of septal pacing. We saw no electrode displacements, and lead parameters were stable all during the follow-up.

We did not find a significant difference in the number of AF episodes and the duration of AF between the septal vs. high atrial pacing group. This may be due to the limited number of patients relative to the high variability of the AF burden in this patient population.

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References