Safety and efficacy of AAIR pacing in selected patients with sick sinus syndrome

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Abstract

Background: The DANPACE study suggested implanting dual-pacing dual-sensing dual-response rate-adaptive (DDDR) pacemakers in patients with sick sinus syndrome, even though 90.7% of their atrial-pacing atrial-sensing inhibited-response rate-adaptive (AAIR) group did not require upgrade. Most centers implant DDDR pacemakers due to risk of future atrioventricular (AV) block. Given that AAIR pacemakers are less expensive, have one less lead with potentially one less point of complication, we question whether DDDR pacemakers are superior to AAIR pacemakers. We aim to describe long-term outcomes of AAIR implants.

Methods: Patients presenting to the Grey Nuns Hospital in Edmonton, Canada from 1990 to 2012 with sick sinus syndrome without AV block had AAIR pacemakers implanted. Outcomes that were measured over the follow-up time included need for ventricular lead reoperation, incidence of AV block and incidence of sudden cardiac death from AV block.

Results: During this period, 330 patients presented with sick sinus syndrome. Eighty-seven (26.4%) patients met criteria for and received AAIR pacemakers. Seventy-eight (91.8%) did not require upgrade over mean follow-up of 10.6±0.6 years. Amongst this group, 31 patients (99.7%) were alive, whereas 47 (60.3%) were deceased at end of follow-up due to other comorbidities. No sudden deaths were attributable to AV block. Only 7 patients (8.2%) required ventricular lead reoperation: 2 (2.4%) presented urgently with symptomatic AV block; 3 (3.5%) had atrial fibrillation requiring beta-blockade; 1 (1.2%) had atrial lead dislodgment; and 1 (1.2%) was electively upgraded at battery end-of-life.

Conclusions: This study looks at safety of AAIR pacemakers with only 2.4% of patients developing AV block requiring urgent upgrade. Approximately 91.8% of patients remained with their original AAIR pacemakers (mean follow-up 10.6 vs 5.4 years in DANPACE). Our findings are similar to the DANPACE study but our conclusions are different as we believe AAIR pacing should be considered for selected patients with sick sinus syndrome without AV block.

Abbreviations: AAIR = atrial-pacing atrial-sensing inhibited-response rate-adaptive, ACC/AHA = American College of Cardiology/American Heart Association, AV = atrioventricular, DDDR = dual-pacing dual-sensing dual-response rate-adaptive, ECG = electrocardiogram, SPSS = Statistical Package for Social Sciences, SS = sick sinus syndrome.

Keywords: atrial-pacing atrial-sensing inhibited-response rate-adaptive pacing, atrioventricular block, pacemaker, sick sinus syndrome

1. Introduction

Guidelines published by the American College of Cardiology/American Heart Association (ACC/AHA) regarding selection of appropriate pacing systems recommend single chamber atrial pacemakers as a viable method of pacing for patients with sick sinus syndrome (SSS) and normal atrioventricular (AV) conduction. However, despite these recommendations, atrial-pacing atrial-sensing inhibited-response rate-adaptive (AAIR) pacing is relatively rarely used by clinicians.[1]

Numerous studies have reported upon the merits of AAIR pacing in patients with SSS. However, daily clinical practice has seen a decrease in the use of AAIR pacing and a shift toward dual-pacing dual-sensing dual-response rate-adaptive (DDDR) pacing; in the United States, DDDR pacing increased from 62% to 82% between 1993 and 2009, whereas AAIR pacing remained stable at 1% during the same time period, mainly due to fears of the development of type II or III AV block.[2,3] The DANPACE study, for instance, followed 1413 patients randomized to either DDDR or AAIR pacing based on a diagnosis of SSS with no evidence for overt or latent AV block. Based on the results of the study, the authors suggested implanting DDDR pacemakers in patients with SSS even in the absence of AV block. However, only 9.3% of the patients who received an AAIR pacemaker required implantation of a ventricular lead over a mean follow-up of 5.4 years.[4] This recommendation was based on the fact that though there was no statistically significant difference in death between the 2 groups, the AAIR group was associated with a higher incidence of atrial fibrillation (28.4% vs 23.0%) and a...
2-fold increased risk of pacemaker reoperation during follow-up (22.1% vs 11.9%). The decision to implant AAIR versus DDDR for SSS is further affected by the lack of reliable markers for the risk of developing AV block, making the selection of an optimal pacing mode a difficult question for clinicians.

The aim of the present study was to establish the safety and efficacy of AAIR pacing. The primary outcome was need for ventricular lead reoperation. Secondary outcomes included incidence of AV block, incidence of atrial fibrillation, time to ventricular lead upgrade, and incidence of sudden cardiac death due to AV block.

2. Materials and methods

2.1. Patient selection and follow-up

All patients who underwent pacemaker implantation at the Grey Nuns Hospital in Edmonton, Alberta, Canada during the period of 1990 to 2012 were considered for AAIR pacing. The criteria for inclusion were patients older than 18 years, symptomatic sick sinus syndrome, lack of AV block at time of implantation, Wenckebach rates >120 bpm. Of these, only patients with sick sinus syndrome were included in the study as defined by the ACC/AHA guidelines for antibradycardia pacing. Patients having an indication for an implantable cardioverter defibrillator and/or cardiac resynchronization were excluded.

Implantation of an AAIR pacing system was done in patients with a diagnosis of sick sinus syndrome with no evidence of AV-nodal block. The latter was defined as the absence of a type 1 or type 2 second-degree AV block or any periods of third-degree AV block on 24-hour ambulatory electrocardiogram (ECG) recordings (where available) or on ECG strips or 12-lead ECGs. In addition, those with right bundle branch block with or without left anterior or posterior fascicular block and a PR interval >220 ms on a 12-lead ECG were not considered for AAIR pacing. Furthermore, at the time of implantation, atrial pacing was performed and those who demonstrated a Wenckebach block at atrial rates <120 bpm (500 ms interval) were also excluded from AAIR pacing. Patients with primary or secondary indications for implantable cardioverter defibrillator or cardiac resynchronization therapy implantation were excluded.

2.2. Surgical procedure

During the review period, all pacing system implantations were performed in a special pacemaker surgical suite. All patients provided written consent for the procedure. The team consisted of an implanting cardiologist, a pacemaker nurse, and a radiology technologist. In all patients, the implantation was done with local anesthesia using the transvenous approach via the subclavian vein. In some patients, midazolam and fentanyl were used intravenously for sedation and analgesia. Implantation of an atrial lead was done under fluoroscopic guidance. Passive or active leads were chosen at the discretion of the implantant. After evaluating the lead for adequate sensing and pacing thresholds, atrial pacing was initiated at a rate of 70 bpm then increased by increments of 10 beats/min to a rate of 140. Thirty seconds of continuous pacing was done at each rate. These pacing maneuvers were performed to document the maintenance of one to one AV conduction and the Wenckebach block point. Single-lead atrial pacing was selected at the time of system implantation when one to one AV node conduction was maintained up to an atrial pacing rate of 120 beats per minute. During generator replacement, incremental atrial pacing was repeated with a new ventricular lead implanted if the Wenckebach block was noted at a pacing rate <120 bpm.

2.3. Data collection

All clinical and pacing parameters were collected prospectively and entered into a database within the Statistical Package for Social Sciences data management system version 21 (SPSS, International Business Machines Corporation, Armonk, NY). Data collected included relevant demographic information, indications for pacing, implanted mode, investigational, and implantation data—including AV conduction characteristics during rapid atrial pacing. Where available, electrocardiographic findings obtained from the referring and implanting cardiologist were also included as discrete or continuous variables.

2.4. Follow-up

The visits were scheduled for 1 and 6 weeks after implantation. After this, the patients were followed every 3 to 6 months for the first year and every 6 months thereafter. All others were considered unscheduled visits if they were due to patient request due to symptoms or on the request of the attending physician or the patient’s own family physician. At each follow-up visit, lead impedance was checked and pacemakers were interrogated for atrial high rate episodes to ensure that atrial fibrillation was not missed.

2.5. Statistical analysis

Using SPSS, continuous variables were analyzed with a Student t test, whereas cross-tabulation analysis was conducted on discrete variables using a chi-square test. A 2-sided P value of <0.05 was deemed statistically significant. The primary outcome of interest over follow-up was need for ventricular lead upgrade. Secondary outcomes included need for urgent ventricular lead upgrade, need for elective ventricular lead upgrade, mortality, and sudden cardiac death. All deaths were adjudicated for cause.

2.6. Ethics

The present study received approval from the Health Research Ethics Board—Health Panel at the University of Alberta, Edmonton, Alberta Canada (Pro00082426).

3. Results

Between the years of 1990 and 2012, there were 2562 patients who underwent pacemaker implantation at our site. Of these, 330 patients (12.9%) had a primary indication of sick sinus syndrome. Amongst these 330 patients, 87 patients (26.4%) underwent AAIR pacemaker implantation, whereas 243 patients (73.6%) were implanted with alternative pacing systems based on the exclusion criteria (Fig. 1). The mean age of the 87 patients was 69.7 ± 1.4 [standard error of the mean (SEM)] years. There were 36 men (41.4%) and 51 women (58.6%). The baseline characteristics of the cohort included: 27 (31.0%) patients with hypertension; 11 (12.6%) with a previous history of myocardial infarction; 9 (10.3%) with paroxysmal atrial fibrillation; 7 (8.0%) with diabetes; 5 (5.7%) with previous coronary artery bypass grafting surgeries; and 4 (4.6%) with documented heart failure.
Of the 87 implantation procedures, 2 patients were lost to follow-up (1 was at 16 months, the other at 17 months) with no recorded incidents up until that point. The loss to follow-up was related to the patients moving out of the province. The remaining 85 patients were followed in clinic for a mean duration of 10.6 ± 0.6 years. Of these 85 patients, 78 (91.8%) did not require a lead upgrade during the follow-up period (Fig. 2). At the end of follow-up, 31 patients (39.7%) were alive (mean follow-up 14.3 ± 0.7 years) while 47 patients (60.3%) were deceased (mean follow-up 8.1 ± 0.7 years). The adjudicated causes of death were:
29 (61.7%) from frailty and old age after a change in their philosophy of care; 6 (12.8%) from miscellaneous cancers; 4 (8.5%) from pneumonia; 2 (4.3%) from renal failure; 2 (4.3%) from myocardial infarctions; 1 (2.1%) from stroke; and 1 (2.1%) from gastrointestinal bleeds (Table 1). There were no sudden cardiac deaths that could presumably be attributable to AV block. Of the patients that died from frailty with a change in philosophy of care, their mean age was 86.6 ± 1.4 years.

During the course of this study, 7 patients (8.2%) were upgraded with a new ventricular lead (primary endpoint) for the following reasons: 2 patients (2.4%) presented with presyncope/syncope with AV block at 1.8 years and 2.3 years after initial pacemaker implantation; 1 patient (1.2%) had recurrent atrial lead dislodgment 0.2 years after the initial implantation; 3 patients (3.5%) developed new onset symptomatic atrial fibrillation at 1.8, 3.3, and 18.3 years after initial implantation with a ventricular lead added electively due to slow ventricular responses while on beta-blockers for atrial fibrillation; 1 (1.2%) was electively upgraded at the time of generator replacement for Wenckebach block at pacing rates >120 bpm, at 13.5 years after initial pacemaker implantation. Figure 2 shows the breakdown of patients based on requiring urgent versus elective upgrade. These upgrades were done without adverse incidents. The mean time to upgrade was 5.9 years and the need for addition of a ventricular lead occurred at a rate of 7.8 per 1000 pacemaker-years.

Table 1
Causes of death for patients deceased at end of follow-up (n=47).

| Cause of death           | Number of patients | Percentage of patients, % |
|--------------------------|--------------------|---------------------------|
| Frailty                  | 29                 | 61.7                      |
| Cancer                   | 4                  | 8.5                       |
| Pneumonia                | 2                  | 4.3                       |
| Renal failure            | 2                  | 4.3                       |
| Myocardial infarction    | 2                  | 4.3                       |
| Stroke                   | 1                  | 2.1                       |
| Gastrointestinal bleed   | 1                  | 2.1                       |
| Urosepsis                | 1                  | 2.1                       |
| Atrioventricular block   | 0                  | 0.0                       |

*With a change in philosophy of care due to aging and frailty—mean age 86.6 ± 1.4 years.

4. Discussion

Despite ACC/AHA guidelines suggesting the use of AAIR pacemakers for SSS, this pacing system is highly underutilized by clinicians today often due to the worry about future AV block and thus prophylactic DDDR pacemakers are inserted instead.[1] However, the present study demonstrates that the vast majority of patients, 91.8%, remained programmed in their original AAIR pacing mode. Only 7 patients (8.2%) required lead upgrades after implantation, after a mean period of 5.9 years. Thus, the need for addition of a ventricular lead occurred at a rate of 7.8 per 1000 pacemaker-years. During the follow-up period, 30 patients (33.7% of total patients in study) had generator replacements with AAIR pacemakers.

Figure 2. Percentage of patients who received urgent and elective upgrades from AAIR to dual-pacing dual-sensing dual-response rate-adaptive (DDDR) pacing mode during follow-up. AAIR = atrial-pacing atrial-sensing inhibited-response rate-adaptive.

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our study. Furthermore, during the course of this study’s long follow-up, no sudden death was attributable to the development of AV block. As pacemaker technology progresses, a leadless pacemaker may even be an option in these patients obviating the need for as invasive a second procedure (which was not performed in the DANPACE study). Our findings are very similar to the DANPACE study in which only 9.3% of their patients required upgrade. [8]

Of the patients who did not require lead upgrade, our rate of 91.8% was very similar to the rate of 90.7% in the DANPACE study. [8] However, the authors of the DANPACE study conclude by suggesting implantation of DDDR pacemakers for SSS when 90.7% of their patients had 1 less lead. This may be associated with less cost and less risk of cardiac implantable electronic device infection, which is associated with the number of leads implanted for that portion of their cohort. There is also a lower risk of lead failure given that only 1 lead is implanted. [11,12] Several retrospective studies have called into question the use of dual chamber pacing by highlighting an increase in the risk of developing atrial fibrillation, thromboembolism, heart failure, and mortality when compared with atrial pacemakers. [5,12,13] Furthermore, randomized trials have demonstrated a significant link between patients paced in DDDR mode and increased rates of hospital admission for heart failure and atrial fibrillation. [14–16] In patients with normal AV conduction, right ventricular pacing leads to interventricular conduction delay and ventricular dyssynchrony. It may also lead to a potential reduction in pacemaker longevity due to additional voltage use for dual-chamber pacing. [12,17,18] Therefore, implantation of AAIR pacemakers over other pacing systems could lead to morbidity and economic savings in the long term for the portion of the cohort that did not require upgrade, especially when one considers that the need for further procedures due to the development of AV block is small. [19,20] A cost-effectiveness study of AAIR versus DDDR pacemakers by Clarke et al. [19] similarly concluded that even when considering the cost for upgrading the small portion of the AAIR cohort that needed upgrade, significant cost savings can be had by implanting significantly cheaper AAIR pacemakers. It should also be noted that many of the patients in our cohort had pacemakers that outlived them in that they often had concurrent medical problems that led to death. Once again, it would be more cost-effective in these patients to use the cheaper alternative of an AAIR pacemaker.

Despite its promising results, this study is limited on 2 fronts: the relatively small sample size and the lack of randomization to AAIR versus DDDR. A sample size of 87 patients poses questions about the generalizability of the study results to the general population. Unfortunately, given the fact that there is no incentive for pacemaker suppliers to complete a randomized trial comparing a cheaper alternative to DDDR pacemakers, it is unlikely that such a trial will be economically feasible. Although the sample size is small, it is worth noting that these patients were followed for an extended period of time, on average 10.6 years (which is almost twice the follow-up of the DANPACE trial). We would also like to mention 2 alternatives including newer mode-switching DDDR pacemakers that reduce the amount of time spent in RV pacing and RV His bundle pacing which is associated with less ventricular dyssynchrony. Although both are alternatives that deal with some of the issues with DDDR pacing, they still require the implantation of 2 leads that is associated with its own risks. The advent of leadless systems for reoperation may provide an opportunity of improving the costs/risks even more in those patients that do require upgrade.

5. Conclusions

The present study is a review of patients implanted with AAIR pacemakers for SSS. Only 2.3% of patients developed AV block requiring urgent upgrade; there were no recorded deaths due to the development of AV block. Approximately 91.8% of patients did not require an upgrade. Our results are very similar to the DANPACE study, but our conclusions are different as we believe AAIR pacing should be considered for selected patients with sick sinus syndrome without AV block given that in 91.8% of patients, it is associated with lower costs, fewer leads, and less RV pacing. This is especially true in our ever more elderly population where many of these pacemakers are being put in patients who have limited lifespans related to comorbidities.

Author contributions

Conceptualization: Janek Senaratne, Marleen Irwin, Sajad Gulamhusein, Manohara Piyasiri Senaratne.

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References

[1] Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the ACC/AHA Task Force on Practice Guidelines. Circulation 2008;117:e350–408.

[2] Greenspon AJ, Patel JD, Lau E, et al. Trends in pacemaker implantation in the United States from 1993 to 2009. J Am Coll Cardiol 2012; 60:1540–5.

[3] Bana G, Locatelli V, Piatti L, et al. AAI pacing in the bradycardia–tachycardia syndrome. Pacing Clin Electrophysiol 1990;13:254–70.

[4] Karrmos D, Camm AJ. AAI pacing mode: when is it indicated and how should it be achieved. Clin Cardiol 1993;16:339–43.

[5] Andersen HR, Nielsen JC, Thomsen PE, et al. Long-term follow-up of patients from a randomized trial of atrial versus ventricular pacing for sick-sinus syndrome. Lancet 1997;350:1210–6.

[6] Schaer B, Kindermann M, Schäfer-Klotz D, et al. AAR versus DDDR pacing in the bradycardia-tachycardia syndrome: a prospective, randomized, double-blind, crossover trial. Pacing Clin Electrophysiol 2001;24:1585–95.

[7] Brandt J, Andersen H, Faabroe T, et al. Natural history of sinus node disease treated with atrial pacing in 213 patients: implications for selection of stimulation mode. J Am Coll Cardiol 1992;20:633–9.

[8] Nielsen JC, Thomsen PE, Hoberg S, et al. A comparison of single-lead atrial pacing with dual-chamber pacing in sick sinus syndrome. Euro Heart J 2011;32:686–96.
[9] Andersen HR, Nielsen JC, Thomesen PE, et al. Atrioventricular conduction during long-term follow-up of patients with sick-sinus syndrome. Circulation 1998;98:1315–21.

[10] Tripp IG, Armstrong GP, Stewart JT, et al. Atrial pacing should be used more frequently in sinus node disease. Pacing Clin Electrophysiol 2005;28:291–314.

[11] Masumoto H, Ueda Y, Kato R, et al. Long-term clinical performance of AAI pacing in patients with sick sinus syndrome: a comparison with dual-chamber pacing. Europace 2004;6:444–50.

[12] Rosenqvist M, Brandt J, Schiller H. Long-term pacing in sinus node disease: effects of stimulation mode on cardiovascular morbidity and mortality. Am Heart J 1998;116:16–22.

[13] Sutton R, Kenny RA. The natural history of sick sinus syndrome. Pacing Clin Electrophysiol 1986;9:1110–4.

[14] Blanc JJ, De Roy L, Mansourati J, et al. Europace 2004;6:371–9.

[15] Nielsen JC, Kirstensen L, Andersen HR, et al. A randomized comparison of atrial and dual-chamber pacing in 177 consecutive patients with sick sinus syndrome: echocardiographic and clinical outcome. J Am Coll Cardiol 2003;42:614–23.

[16] Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. Circulation 2003;107:2932–7.

[17] Nielsen JC, Pedersen AK, Mortensen PT, et al. Programming a fixed long atrioventricular delay is not effective in preventing ventricular pacing in patients with sick sinus syndrome. Europace 1999;1:1113–20.

[18] Bellinder G, Nordlander R, Pehrsson SK, et al. Atrial pacing in the management of sick sinus syndrome: long-term observation for conduction disturbances and supra ventricular tachyarrhythmias. Eur Heart J 1986;7:105–9.

[19] Clarke KW, Connelly DT, Charles RG. Single chamber atrial pacing: an underused and cost-effective pacing modality in sinus node disease. Heart 1998;80:387–9.

[20] Castelnuovo E, Stein K, Pitt M, et al. The effectiveness and cost-effectiveness of dual-chamber pacemakers compared with single-chamber pacemakers for bradycardia due to atrioventricular block or sick sinus syndrome: systematic review and economic evaluation. Health Technol Assess 2003;7:1–246.