Cardiovascular Topics

A comparison of AAIR versus DDDR pacing for patients with sinus node dysfunction: a long-term follow-up study

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Abstract

Objectives: The aim of the study was to compare the clinical outcomes [atrial fibrillation (AF), atrio-ventricular (AV) block, device sepsis and lead revision] of patients with sinus node dysfunction (SND) between atrial-pacing atrial-sensing inhibited-response rate-adaptive (AAIR) versus dual-chamber rate-adaptive (DDDR) pacing. The choice of AAIR pacing versus DDDR pacing was determined by AV nodal functional testing at implant.

Methods: We conducted a retrospective review of consecutive patients who underwent AAIR and DDDR pacing over a 10-year period.

Results: One hundred and sixteen patients required pacing for symptomatic SND. Fifty-four (46.6%) patients received AAIR pacemakers and 62 (53.4%) received DDDR pacemakers based on AV nodal functional testing at implant. Patients who had AV Wenkebach with atrial pacing at 120 beats per minute received DDDR pacing. Overall the mean age of patients with SND was 65 years and 66.4% were females, 30% were diabetics and 71% were hypertensives. Pre-syncope/syncope (84%) and dizziness (69%) were the most common symptoms. Sinus pauses and sinus bradycardia were the most common ECG manifestations. Over a median follow up of five (IQR: 2–11) years, four patients (7.4%) developed AF in the AAIR group compared to three (4.8%) in the DDDR group (p = 0.70). AV block occurred in one patient in the AAIR group, who required an upgrade to a DDDR pacemaker. There was no difference in device sepsis or need for lead revision between the two groups.

Conclusion: We found that AV nodal functional testing with atrial pacing at the time of pacemaker implantation was a useful tool to help guide the implanter between AAIR or DDDR pacing. Patients who underwent AAIR pacing had a low risk of AF, AV block or lead revision. In resource-limited settings, AAIR pacing guided by AV nodal functional testing should be considered as an alternative to DDDR pacing.

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Symptomatic sinus node dysfunction (SND), also known as sick sinus syndrome, is usually due to age-related degeneration of the sinus node. SND can manifest on the ECG as a variety of ECG abnormalities, including sinus bradycardia, sinus arrest, sino-atrial block, chronotropic incompetence and the tachy–brady syndrome.[1] The most common symptoms of SND include syncope, dizzy spells, fatigue and exercise intolerance due to chronotropic incompetence.[2]

A diagnosis of symptomatic sinus node dysfunction requires correlation of symptoms with ECG findings. Secondary or reversible causes of SND may require specific treatment. The only treatment for primary symptomatic SND, usually due to age-related degeneration, is the insertion of a permanent pacemaker. SND is the second most common cause for cardiac pacing, accounting for approximately 30% of all pacemaker implantations.[3]

The indications and modes for pacemaker implantation for SND have been published. Both the European Society of Cardiology (ESC) guidelines[4] and the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines[5] recommend dual-chamber rate-adaptive (DDDR) pacing over atrial-pacing atrial-sensing inhibited-response rate-adaptive (AAIR) pacing. This recommendation is based on the subsequent risk of atrio-ventricular (AV) block, a higher risk of paroxysmal atrial fibrillation (AF) and the higher risk of complications with AAIR pacing in patients who require subsequent ventricular pacing.[6] However, the numbers of patients who develop these complications are low, and with the higher cost of DDDR pacing, the initial increased risks of the additional ventricular lead, together with the harmful effects of inappropriate ventricular pacing, AAIR pacing has remained a reasonable option for patients with SND, especially in resource-limited settings.[7] This is particular relevant for developing countries in Africa where pacemaker implanters implant mainly single-chamber pacemakers because of cost and expertise.[8]

The future development of AV block has been recognised as a potential problem with AAIR pacing. The incidence of AV block in patients with SND has been reported to range from < 1% to 4.5% per year.[9–13] In an observational study of AAIR and

DDDR pacing with long-term follow up, the annual incidence of AV block in the AAIR group was low (1.1%). Atrial pacing with an AV Wenckebach rate lower than 120 beats per minute (bpm) was found to be a predictor of high-grade AV block.[7] The DANPACE study, the largest randomised study of AAIR versus DDDR pacing, reported a higher incidence of paroxysmal AF with AAIR pacing compared to DDDR pacing, with a high risk of complications with subsequent pacemaker lead revisions.[6]

This study aimed to compare the outcomes (development of AF, AV block, lead revision and device sepsis) of AAIR versus DDDR pacing in patients with symptomatic SND using AV nodal functional testing at the time of implant (patients received DDDR pacing if there was evidence of AV Wenkebach or AV block with atrial pacing at 120 bpm).

The rationale for using AV nodal functional testing was based on a previous observational study that compared AAIR versus DDDR pacing with very long-term follow up. The authors reported that AV nodal functional testing using a Wenkebach block point lower than 120 bpm was found to be a predictor of later high-grade AV block.[7] Patients also received a DDDR pacemaker if there was evidence of bundle branch block (BBB) or AV block (except 1st degree AV block and fascicular blocks) at baseline. While the risk of development of AV block in patients with BBB remains unclear, the decision to implant a pacemaker is consistent with the DANPACE trial. A previous study reported an increase in cardiovascular death rate in patients with BBB, which may be related to the future development of AV block.[14,15]

Methods

A retrospective study was conducted on consecutive patients implanted with an AAIR or DDDR pacemaker for symptomatic SND at Groote Schuur Hospital (GSH) between 2007 and 2017. GSH is a large, government-funded teaching hospital in Cape Town, South Africa. GSH is a tertiary referral centre, based on a networking hub with secondary hospitals in the region, and therefore the recruited patients are representative of the general population.

Ethics approval was obtained from the Faculty of Health Sciences Human Research Ethics Committee of the University of Cape Town (UCT), HREC REF: 493/2017.

Clinical records were obtained from cardiologists' and cardiac technologists' implant records and patients' hospital files. All patients with a diagnosis of SND who received a pacemaker were included. Demographic and clinical variables were recorded on a clinical report form.

Socio-demographic variables including age, gender, presenting symptoms, co-morbidities, medications, ECG and echocardiographic findings were retrieved. Other parameters obtained were the mode of pacing and outcomes after pacing, including occurrence of complications such as the development of AF, AV block, lead revision and device sepsis.

Statistical analysis

The collected data were checked for quality and coding was done prior to entry. Two different people entered the data twice and checked to ensure no double or wrong entries. Continuous and discrete data are presented as mean ± SD and as counts (percentage), respectively. All mean ages reported were calculated at primary implantation. The Statistical Package for the Social Sciences 24.0 (SPSS, Inc, Chicago, IL, USA) for Windows was used. The chi-squared test was used to test for group differences at $p < 0.05$ significance level.

Results

A total of 211 patients received a permanent pacemaker between January 2007 and July 2017 at GSH. One hundred and sixteen patients (54.9%) received a pacemaker for symptomatic SND, 54 (46.6%) received an AAIR pacemaker and 62 (53.4%) a DDDR pacemaker based on BBB, AV block at baseline and AV nodal functional testing (Table 1).

A comparison of the baseline demographics, clinical presentation and co-morbidities of the patients who received AAIR and DDDR pacemakers is shown in Table 1. Overall, the majority (66.4%) of patients was female and symptomatic, with pre-syncope or syncope being the most common clinical presentation (84.4%). Patients in the DDDR group were also more likely to have experienced palpitations at presentation (22.6%, $p = 0.05$). There were no major differences in co-morbidities (hypertension, diabetes mellitus, renal disease, cerebrovascular disease, ischaemic heart disease) between the two groups.

Table 1. Baseline demographics and clinical presentation of patients who received AAIR versus DDDR pacing for sinus node dysfunction

Characteristic/parameter	*AAIR (n = 54)*	*DDDR (n = 62)*	p-*value*
Females, *n* (%)	38 (70.4)	39 (62.9)	0.396
Age at first implantation, mean ± SD (years)	65.8 ± 15.2	65.0 ± 15.4	0.766
Pre-syncope/syncope, *n* (%)			
Yes	45 (83.3)	53 (85.5)	0.750
No	9 (16.7)	9 (14.5)	
Tiredness, *n* (%)			
Yes	23 (42.6)	27 (43.5)	0.917
No	31 (57.4)	35 (56.5)	
Dizziness, *n* (%)			
Yes	44 (81.5)	54 (87.1)	0.405
No	10 (18.5)	8 (12.9)	
Palpitations, *n* (%)			
Yes	5 (9.3)	14 (22.6)	0.053
No	49 (90.7)	48 (77.4)	
Heart failure, *n* (%)			
Yes	2 (3.7)	4 (6.5)	0.684
No	52 (96.3)	58 (93.5)	
Hypertension, *n* (%)			
Yes	41 (75.9)	41 (66.1)	0.248
No	13 (24.1)	21 (33.9)	
Diabetes mellitus, *n* (%)			
Yes	18 (33.3)	17 (27.4)	0.489
No	36 (66.7)	45 (72.6)	
Renal disease, *n* (%)			
Yes	2 (3.7)	4 (6.5)	0.684
No	52 (96.3)	58 (93.5)	
Cerebrovascular events, *n* (%)			
Yes	5 (9.3)	4 (6.5)	0.732
No	49 (90.7)	58 (93.5)	
Ischemic heart disease, *n* (%)			
Yes	24 (44.4)	27 (43.5)	0.923
No	30 (55.6)	35 (56.5)	

AAIR: atrial-pacing atrial-sensing inhibited-response rate-adaptive; DDDR: dual-pacing dual-sensing dual-response rate-adaptive.

Table 2. Electrocardiographic diagnoses of patients who received AAIR versus DDDR pacing for sinus node dysfunction

ECG description	*AAIR* (n = *54*)	*DDDR* (n = *62*)	p-*value*
SND ECG diagnosis, *n* (%)			
SND only	44 (81.5)	32 (51.6)	
SND + BBB	1 (1.9)	4 (6.5)	
SND + AV block	0 (0.0)	15 (24.2)	< 0.001
SND + atrial tachyarrhythmia	9 (16.7)	11 (17.7)	
SND ECG categories, *n* (%)			
Sinus pauses/arrest	25 (46.3)	29 (46.8)	
Sinus bradycardia	20 (37.0)	20 (32.3)	0.700
Sino-atrial exit block	3 (5.6)	2 (3.2)	
Tachy–brady syndrome	6 (11.1)	11 (17.7)	

AAIR: atrial-pacing atrial-sensing inhibited-response rate-adaptive; DDDR: dual-pacing dual-sensing dual-response rate-adaptive; SND: sinus node disease; BBB: bundle branch block.

The ECG subgroups of sinus node dysfunction are shown in Table 2. Patients who received DDDR pacing had a higher likelihood of having BBB (6.5%) and evidence of AV block (24.2%) at baseline. There were no significant differences in ECG categories of SND (sinus bradycardia, sinus pauses/arrest, sino-atrial exit block, tachy–brady syndrome) between the AAIR and DDDR groups. Sinus pauses/arrest (47% overall in both groups) and sinus bradycardia (34% overall in both groups) were the most common ECG manifestations. Sino-atrial exit block and tachy–brady syndrome were less common.

A comparison of the development of AF, AV block, mortality, device sepsis and need for lead revision between AAIR and DDDR pacing is shown in Table 3. Over a median follow up of 5.0 (IQR: 2–11) years, four patients developed AF in the AAIR group (7.4%) compared to three (4.8%) who developed AF in the DDDR group (p = 0.70). One patient (1.9%) in the AAIR group developed AF and AV block and required an upgrade to DDDR pacing. Deaths occurred in 18 (33.3%) patients in the AAIR group and 14 (22.6%) in the DDDR group. Two (3.7%) and two (3.2%) patients were lost to follow up in the AAIR and DDDR groups, respectively. There were no significant differences between the AAIR and DDDR groups with regard to mortality, device sepsis or the need for subsequent lead revision.

Table 3. Comparison of mortality and the development of AF, AV block, device sepsis or lead revision between the AAIR and DDDR pacing groups

	Pacing mode		
Complication/procedures	*AAIR* (n = *54, 46.6%*)	*DDDR* (n = *62, 53.4%*)	p-*value*
Mortality, *n* (%)	18 (33.3)	14 (22.6)	0.196
AF, *n* (%)			
Yes	4 (7.4)	3 (4.8)	0.703
No	50 (92.6)	59 (95.2)	
AVB, *n* (%)			
Yes	1 (1.9)	1 (1.6)	1.000
No	53 (98.1)	61 (98.4)	
Sepsis, *n* (%)			
Yes	1 (1.9)	1 (1.6)	1.000
No	53 (98.1)	61 (98.4)	
Lead revision, *n* (%)			
Yes	4 (7.4)	2 (3.2)	0.415
No	50 (92.6)	60 (96.8)	

AAIR: atrial-pacing atrial-sensing inhibited-response rate-adaptive; DDDR: dual-pacing dual-sensing dual-response rate-adaptive; AF, atrial fibrillation; AVB: atrio-ventricular block.

Six patients needed lead revisions due to lead malposition or dislodgement (four right atrial and two right ventricular leads).

Discussion

The only effective treatment for symptomatic SND is the insertion of a permanent pacemaker. The choice of permanent pacemaker is either an AAIR pacemaker with an atrial lead or a DDDR pacemaker with atrial and ventricular leads. While most guidelines recommend DDDR pacing as the first choice of pacing, AAIR pacing remains an acceptable second choice, especially in resource-limited settings where the cost of DDDR pacing is prohibitive. The major disadvantage of AAIR pacing is the future development of AV block, which requires the addition of a ventricular lead.

In this study, we report only one case (1.9%) of AV block who required upgrade to DDDR pacing over a median follow up five years. The risk of development of AV block in patients with SND is reported to be between < 1% and 4.5% per year.[9–13] A possible reason for the low risk of AV block in our cohort is that routine functional AV block testing was used in all patients to decide on the choice of pacemaker. We used a standard pacing protocol of atrial pacing at the time of implant to determine the AV Wenkebach rate. All patients received a DDDR pacemaker if AV Wenkebach or higher-degree AV block was present with atrial pacing at 120 bpm.

An AV Wenkebach rate lower than 120 bpm was found to be a predictor of high-grade AV block in a previous retrospective study comparing AAIR with DDDR pacing and the authors reported an annual incidence of AV block to be 1.1%.[7] In the DANPACE trial, the risk of AV block or slow AF occurred in 54 out of 707 patients (7.6%) with an incidence of 1.5% per year. A lower Wenkebach rate of 100 bpm was used to determine the need for DDDR pacing in the DANPACE study, which could explain why the AAIR group had a higher risk of AV block compared to our study. We propose that AV functional testing be used to help guide implanters on the choice of pacemaker, especially in resource-limited environments where the cost of DDDR pacing is prohibitive.

To evaluate the cost saving of selective AAIR pacing versus routine DDDR pacing, we compared the total cost of AAIR and DDDR pacing in this study with a hypothetical scenario where all patients received DDDR pacing. Using data from South Africa from the PASCAR 2011–2016 survey,[8] the total procedural costs of AAIR (US$1 030 per pacemaker) and DDDR (US$1 380 per pacemaker) pacing for 116 patients (including one upgrade from AAIR to DDDR pacing) was estimated to have cost US$142 560. The procedural costs if all patients received DDDR pacing was estimated to have been US$160 080. The cost saving therefore amounted to US$17 520. This equates to a saving of 17 AAIR pacemakers or 12 DDDR pacemakers in this study.

The DANPACE randomised trial reported a higher rate of paroxysmal AF, but not chronic AF, in patients who received AAIR pacing compared to DDDR pacing (heart rate 1.27 with AAIR pacing, p = 0.02)[6] However, extended follow up of the DANPACE trial reported no differences in AF hospitalisation between AAIR and DDDR pacing, with an annual incidence of 1.4%.[15] We report a lower rate and no difference in the subsequent development of paroxysmal or persistent AF in

both pacing groups (7.4% in the AAIR group compared to 4.8% in the DDDR group, $p = 0.70$). These findings are similar to a prior study by Masumoto who also reported no difference in the development of AF between AAIR and DDDR pacing (6.4% in the AAIR group compared to 9.4% in the DDDR group at 10 years of follow up).[7] The above data suggest that the choice of pacemaker for SND should not be guided by the risk of subsequent AF alone.

This study showed no difference in the rate of device infection between the two groups (1.9% in the AAIR versus 1.6% in the DDDR group, $p = 1.00$). These findings are similar to those observed in the DANPACE trial, which showed no difference in device infection between AAIR and DDDR pacing (0.4% in both groups, $p = 0.98$).[6] This study also showed no difference in the need for lead/s revision (7.4% in AAIR versus 3.2% in DDDR group, $p = 0.42$). Similar findings were observed in the DANPACE trial where no differences in the need for lead revision were found between the two groups (5.2% in the AAIR versus 4.2% in the DDDR groups, $p = 0.42$).[6] The DANPACE trial reported that subsequent lead revision was associated with a high complication rate. This study had only six lead revisions and no complications were noted in any of these six patients.

Study limitations

This was a retrospective study from a single institution with a relatively small number of patients. The conclusions are therefore hypothesis generating. However, the results reflect real-world practice in a contemporary South African population. Larger randomised trials using AV nodal functional testing as required need to be adopted. The interpretation of ECGs showing AF was made by cardiac technologists who routinely perform pacemaker device interrogations in the device clinic. It is possible that the technologists may not have recognised AF and may have under-reported episodes of AF. This study has all the limitations of a retrospective study, including missing information. It is possible that patients in the AAIR group who developed AV block may have been lost to follow up or died. However, the numbers of deaths between the two groups were similar.

Conclusion

In this typical elderly population who presented with symptomatic SND, we found functional AV nodal testing with atrial pacing at the time of pacemaker implantation to be a useful tool to help guide the implanter about the choice of AAIR or DDDR pacing. Patients who underwent AAIR pacing had a low subsequent risk of AF, AV block or lead revision. In resource-limited settings, AAIR pacing should be considered as an alternative to DDDR pacing. Patients with AAIR pacemakers should be counselled regarding future symptoms of AV block, and device follow up may be required on a six-monthly basis to rule out the need for ventricular pacing. Randomised trials are required to further define the role of AV nodal functional testing.

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References

1. Rubenstein JJ, Schulman CL, Yurchak PM, Desanctis RW. Clinical spectrum of the sick sinus syndrome. *Circulation* 1972; **XLVI**(46): 5–13.
2. Nielsen JC. Pacing mode selection in patients with sick sinus syndrome. *Dan Med Bull* 2007; **54**(1): 1–17.
3. Mond HG, Irwin M, Morillo C, Ector H. The World Survey of Cardiac Pacing and Cardioverter Defibrillators: Calendar Year 2001. Vol. 27, PACE – Pacing and Clinical Electrophysiology. 2004: 955–964.
4. Brignole M, Auricchio A, Baron-Esquivias G, *et al*. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy. *Eur Heart J* 2013; **34**: 2281–2329.
5. Gregoratos G, Abrams J, Epstein AE, *et al.* ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE committee) *Circulation* 2002; **106**(16): 2145–2161.
6. Nielsen JC, Thomsen PEB, Højberg S, *et al*. A comparison of single-lead atrial pacing with dual-chamber pacing in sick sinus syndrome. *Eur Heart J* 2011; **32**(6): 686–696.
7. 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**(5): 444–450.
8. Bonny A, Ngantcha M, Jeilan M, Okello E, Kaviraj B, Talle MA, *et al*. Statistics on the use of cardiac electronic devices and interventional electrophysiological procedures in Africa from 2011 to 2016: Report of the Pan African Society of Cardiology (PASCAR) Cardiac Arrhythmias and Pacing Task Forces. *Europace* 2018; **20**(9): 1513–1526.
9. Brandt J, Anderson H, Fåhraeus T, Schüller H. 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**(3): 633–639.
10. Swiatecka G, Sielski S, Wilczek R, Jackowiak D, Kubica J, Raczak G. Atrioventricular conduction disturbances in patients with sinoatrial node disease and atrial pacing. *Pacing Clin Electrophysiol* 1992; **15**(11 II): 2074–2076.
11. Rosenqvist M, Obel IWP. Atrial pacing and the risk for AV block: is there a time for change in attitude? *Pacing Clin Electrophysiol* 1989; **12**(P1): 97–101.
12. Andersen HR, Nielsen JC, Thomsen PEB, Thuesen L, Vesterlund T, Pedersen AK, *et al*. Atrioventricular conduction during long-term follow-up of patients with sick sinus syndrome. *Circulation* 1998; **98**(13): 1315–1321.
13. Kristensen L, Nielsen JC, Pedersen AK, Mortensen PT, Andersen HR. AV block and changes in pacing mode during long-term follow-up of 399 consecutive patients with sick sinus syndrome treated with an AAI/AAIR pacemaker. *PACE – Pacing Clin Electrophysiol* 2001; **24**(3): 358–365.
14. Fahy G, Pinski S, Miller D, McCahe N, Pye C, Walsh M, *et al*. Natural history of isolated bundle branch block. *Am J Cardiol* 1996; **77**(14): 1185–1190.
15. Brandt NH, Kirkfeldt RE, Nielsen JC, *et al.* Single lead atrial vs. dual chamber pacing in sick sinus syndrome: Extended register-based follow-up in the DANPACE trial. *Europace* 2017; **19**(12): 1981–1987.