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Optimum pacing mode for patients with angina pectoris

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SUMMARY A within patient double blind prospective study of symptoms and exercise tolerance was designed to determine the preferred pacing mode in 10 patients with programmable dual chamber pacemakers who also had angina pectoris. Patients were randomly allocated to one month in each of the following modes: ventricular pacing at 70 beats/min (VVI) or atrioventricular synchronous upper rate 150 beats/min (DDD 150) or 100 beats/min (DDD 100). Medications were unchanged throughout the study; none was taking β blockers. At the end of each month patients underwent an exercise test. During each month patients recorded symptoms and their preferred pacing mode. DDD 100 was the preferred mode (seven patients). There was significantly less chest pain with this mode than with either of the other modes. There were significantly more episodes of dizziness in VVI, and two patients who developed pacemaker syndrome were unable to complete the pacing period. Three patients developed angina during exercise testing in DDD 150.

Atrial synchronous ventricular pacing is better than ventricular pacing for the control of symptoms in patients with angina pectoris provided that the upper atrial tracking rate is limited.

Ischaemic heart disease has been regarded as a contraindication to dual chamber pacing because of the risk of provoking angina at higher pacing rates.[1] Karlöf reported that some patients with angina have a better exercise tolerance on fixed rate pacing than on atrial synchronous ventricular pacing.[1] The pacing mode best suited to ischaemic heart disease has not been identified by appropriate clinical study; however, the potential advantage of maintaining atrioventricular synchrony in ischaemic patients has a strong physiological basis. Patients with coronary artery disease often have decreased myocardial compliance and should benefit from correctly timed atrial contraction. Furthermore, the capacity to increase stroke volume is often limited, necessitating higher heart rates to maintain cardiac output during exercise. The maintenance of atrioventricular synchrony and capability of rate increase should be of benefit in patients with ischaemic heart disease and angina pectoris, provided that the rate increase is limited to individual tolerance.

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A prospective within patient study was designed to compare symptoms of ischaemia and exercise capacity in dual chamber pacing (DDD) (at maximum and limited upper rates) with single ventricular chamber pacing (VVI). All tests were carried out one month after programmed mode change to allow for long term adaptation.

Patients

We studied 10 patients (6 female and 4 male; mean (SD) age 69·7 (10·4), range 52–83 years). All had multiprogrammable dual chamber pacemakers implanted (DDD) for a minimum of three months. The mean (SD) period since the implant was 17·9 (10·2) months. Each patient had angina pectoris. Three patients had had one or more myocardial infarction. Angina was defined according to Rose's questionnaire.[2] No patient was in cardiac failure or on β blockers. Other medications are listed in table 1 and were not altered during the study.

Pre-pacing investigations included measurement of the His bundle electrogram, estimation of sinus node recovery times for atrial pacing rates between 90 and 220 beats/min, assessment of atrioventricular conduction for ventricular pacing rates of 50–160 beats/min, and observation of the effects of carotid sinus massage on sinoatrial activity and atrioventricular conduction. Five patients had atrioventricular block alone, two had sick sinus syndrome alone, two had atrioventricular block and sick sinus syndrome, and one had atrioventricular block and carotid sinus syndrome. Table 1 shows their clinical and electrophysiological details.

TRIAL PROTOCOL

The trial was designed as a within patient double blind prospective study of symptoms and exercise tolerance on VVI mode at 70 beats/min (VVI), DDD mode with upper synchronous rate at 100 beats/min (DDD 100), and DDD mode with upper synchronous rate at 150 beats/min (DDD 150).

Patients were investigated as outpatients in three consecutive one month periods during which patients were asked to keep diary cards of their symptoms. A maximal exercise test was performed at the end of each monthly study period.

During the first month the pacemaker was randomly programmed to VVI or DDD 100 or DDD 150; for the second month one of the two remaining modes was chosen, and during the last month patients were programmed to the remaining mode.

EXERCISE STRESS TESTS

At the end of each study month, patients underwent a symptom limited maximum stress test on an electrically braked bicycle ergometer (Siemens-Elema). Before entry to the trial patients also had two exercise stress tests to familiarise them with the bicycle ergometer and to eliminate training effects. Exercise was started at 120 kpm for 1 min and increased to 180 kpm for 3 min, then to 420 kpm for 3 min, and then by 180 kpm every 3 min. Total work load achieved (expressed in kpm (1 kpm = 9·8 J)) was recorded. Blood pressure was monitored by conventional mercury sphygmomanometer and heart rate was recorded on a three lead surface electrocardiograph. Blood pressure and heart rate readings were taken before exercise, at the end of every 3 min stage, and every 2 min for 10 min after exercise.

DIARY CARDS

Patients recorded the daily frequency of symptoms of chest pain, dizziness, palpitation, and syncope. At the end of each month they were asked to give a subjective score to compare the following symptoms with those in the previous month: chest pain, dizziness, palpitation, and general wellbeing. The scores were: 1, much worse; 2, a little worse; 3, no change; 4, a little improved; and 5, much improved.

PROGRAMMED PACEMAKER VARIABLES

In VVI mode the rate was set at 70 beats/min. In DDD mode the back up rate was 60 beats/min and the upper P synchronous rate was 100 beats/min (DDD 100) or 150 beats/min (DDD 150) with an atrioventricular interval of 150 ms. At the upper rate the pacemaker was programmed to an atrioventricular blocking response similar to the Wenckebach phenomenon.

The programmed mode and the results of the exercise test were not known by the patient and the medical observer assisting in exercise testing. Pacemaker programming and electrocardiographic monitoring during exercise testing were performed by a pacing technician (AI) who was not subsequently involved in the analysis. The observer also performed statistical analyses while still blind to the pacemaker mode.

STATISTICAL ANALYSES

Student's paired *t* test was used to compare maxi-

Table 1 *Clinical and electrophysiological data in the ten patients with angina pectoris*

Case no	*Sex*	*Age*	*Medication*	*Year of previous myocardial infarction*	*Other diagnoses*	*Electrophysiological study*
1	F	79	Nifedipine, isosorbide, sublingual GTN	—	Hypertension	IAVB
2	M	73	Nifedipine, sublingual GTN	1961	—	AVB, SSS
3	M	65	Bendrofluazide, isosorbide, sublingual GTN	1961, 1976	Hypertension	AVB, CSS
4	F	78	Transiderm nitro patch, sublingual GTN	—	Hiatus hernia	SSS
5	M	54	Frusemide, amiodarone, amiloride, sublingual GTN	1983	Mild left ventricular failure	IAVB
6	F	67	Isosorbide, sodium valproate, chlorazepam, sublingual GTN	—	Epilepsy	SSS, 2:1 AVB
7	M	76	Nifedipine, sublingual GTN	—	Hypertension	AVB
8	F	52	Amiodarone, sublingual GTN	—	—	SSS
9	F	70	Sublingual GTN	—	—	AVB
10	F	83	Diazepam, triazolam, sublingual GTN	—	—	IAVB

AVB, atrioventricular block; IAVB, intermittent atrioventricular block; SSS, sick sinus syndrome; CSS, carotid sinus syndrome; GTN, glyceryl trinitrate.

mum effort tolerance and heart rate at rest and peak exercise. To compare these variables in different pacing modes we used Friedman's analysis of variance and an unpaired *t* test. Symptoms were expressed as number of attacks per week for each month and symptom scores were compared by Wilcoxon's ranked pairs test. Symptom variance between pacing modes was assessed by the Mann-Whitney U test. Results are expressed as mean (SD) except maximum exercise capacity which is expressed as mean (SE).

Results

Ten patients entered the study; eight completed three one month study periods; in two severe symptoms developed in the VVI mode and they were unable to tolerate pacing in this mode and complete the study month. They were therefore reprogrammed to DDD mode at 3 and 14 days respectively after exercise testing in VVI mode. One had sick sinus syndrome and the other had atrioventricular block. Both had retrograde atrioventricular conduction and complained of palpitation, shortness of breath, and non-anginal chest pain which lasted for seconds to over one hour.

Three patients were in sinus conducted rhythm with ventricular pacing inhibition at rest in the VVI mode: two had intermittent atrioventricular block and one had sick sinus syndrome (cases 1, 8, 10) (table 1). Three patients developed sinus rhythm at peak exercise in the VVI mode (cases 1, 5, 8). One patient with intermittent atrioventricular block (case 5) developed sinus rhythm at peak exercise in DDD 100 and DDD 150; otherwise patients showed atrial synchronous ventricular pacing or ventricular pacing at rest and at peak exercise according to the programmed mode.

Resting heart rates were 75 (9) beats/min (VVI), 78 (12) beats/min (DDD 100), and 82 (17) (DDD 150) (NS). Maximum heart rates achieved at peak exercise were 81 (22) beats/min (VVI), 91 (19) beats/min (DDD 100) (NS), and 124 (18) beats/min (DDD 150) ($p < 0.01$ for DDD 100 *vs* DDD 150 and $p < 0.01$ for VVI *vs* DDD 150 (fig 1).

Maximum exercise capacity was highest for DDD 100 but this did not reach statistical significance. Maximum workload for VVI was 2246 (1321) kpm, for DDD 100 it was 2312 (1035) kpm, and for DDD 150 it was 1194 (1178) kpm. In the VVI mode all patients stopped stress tests because of fatigue and one patient was also dyspnoeic. In DDD 100 one patient who was in sinus rhythm stopped exercise because of angina. The remainder stopped because of fatigue. In DDD 150 three patients developed chest pain during exercise and the remainder stopped because of fatigue; one also complained of shortness of breath. Resting systolic blood pressure was 122 (23) mm Hg (VVI), 136 (21) mm Hg (DDD 100), and 138 (26) mm Hg (DDD 150) (NS). Systolic blood pressure during peak exercise was 148 (11) mm Hg (VVI), 169 (31) mm Hg (DDD 100), and 169 (24) mm Hg (DDD 150) (NS; fig 2).

Figure 3 shows the number of episodes of palpitation, dizziness, and chest pain each week for the three pacing programs. The frequency of palpitation in each mode did not differ significantly. Chest pain occurred more frequently in VVI ($p < 0.02$) and DDD 150 ($p < 0.01$) than in DDD 100. Dizziness was more frequent in VVI than DDD 100 ($p < 0.01$) or DDD 150 ($p < 0.01$).

In seven patients the preferred pacing mode for chest pain control was DDD 100. Two patients preferred both DDD 100 and VVI and one preferred DDD 150. Table 2 shows the overall symptom scores at the end of each month.

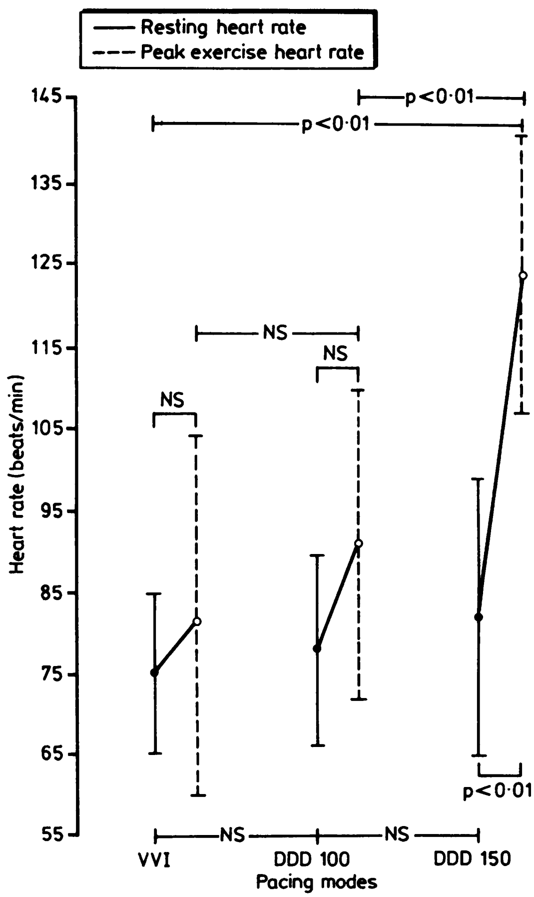

Fig 1 *Heart rate at rest and peak exercise in VVI, DDD 100, and DDD 150 pacing modes.*

Table 2 *Overall symptom scores at the end of each month*

	No of patients with the following scores				
	1 *Much worse*	*2* *Little worse*	*3* *Unchanged*	*4* *Better*	*5* *Much better*
VVI (n = 10)	3	2	3	0	2
DDD 100 (n = 10)	—	1	1	4	4
DDD 150 (n = 10)	2	1	3	1	3

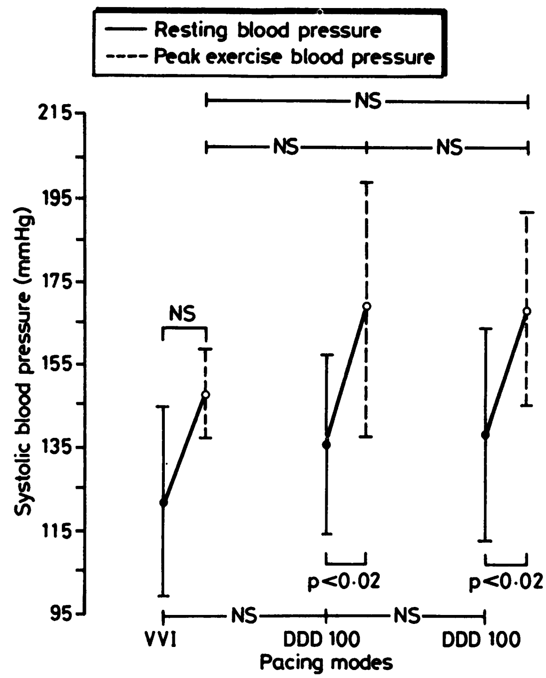

Fig 2 *Systolic blood pressure at rest and at peak exercise in VVI, DDD 100, and DDD 150 pacing modes.*

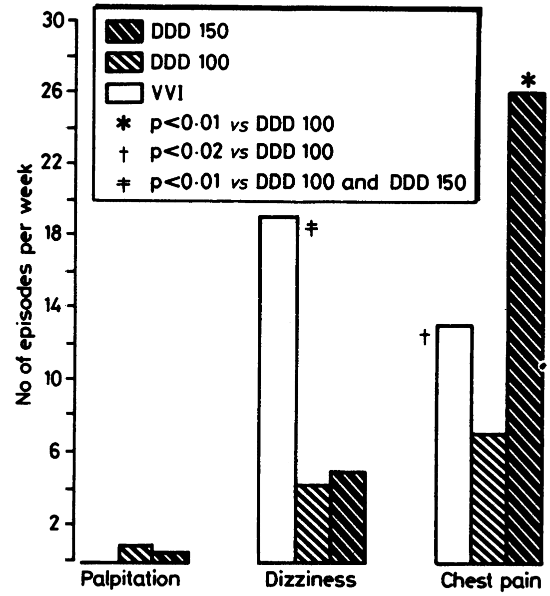

Fig 3 *Number of episodes of palpitation, dizziness, and chest pain each week for each pacing mode.*

Discussion

Atrial synchronous ventricular pacing produces better haemodynamic function than single chamber ventricular pacing: the normal temporal relation between atrial and ventricular contraction and the capacity of the heart rate to increase during exercise is restored by the dual chamber mode of pacing available in a DDD pacemaker.[3-5] The improved haemodynamic capacity afforded by atrial synchronous ventricular pacing is not a short term effect that diminishes with time because of adaptive mechanisms as suggested by Sowton *et al*,[6] but rather it is maintained with no evidence of long term fall off in performance.[4 7 8] Advances in pacing systems and the ability to program pacing units means that complications previously associated with dual chamber systems may be corrected by appropriate mode selection and alteration of programmable variables.[3]

In patients with ischaemic heart disease reduced myocardial function may be expected, if not at rest, on exercise. When these patients require pacing, pacemakers that permit both rate responsiveness and atrioventricular synchrony are likely to produce the best symptomatic results and optimum haemodynamic function. This applies in atrioventricular block,[9] where the atria remain normal in their rate responsiveness and an artificial sinus rhythm can be created throughout the rate range of the pacemaker. It also applies where sick sinus syndrome occurs with atrioventricular block, despite the fact that rate responsiveness of the atria may be attenuated.[10 11] In pure sick sinus syndrome with extreme attenuation of the rate response, the best result will be achieved with a sensor driven atrial pacemaker. Dual chamber versions of these pacemakers are not yet available. Since 1979 we have not implanted atrial pacemakers at this centre because of the risk of later development of atrioventricular block.[12 13] Thus the two patients in this study with sick sinus syndrome (one of whom returned to sinus rhythm on exercise in VVI mode but showed atrial synchronous ventricular pacing in DDD mode) were given DDD pacemakers.

Haemodynamic studies at rest and on exercise in non-ischaemic patients with atrioventricular block and with sick sinus syndrome show a benefit of up to 30% in cardiac output when a physiological mode of stimulation is used instead of VVI.[4 9 14] Thus the provision of rate responsiveness or atrioventricular synchrony or both is expected to confer some benefit in ischaemic patients. Rate responsiveness, however, means that the patient can more easily reach the anginal threshold rate and for this reason some have reservations about using dual chamber pacing in anginal patients. Kristensson *et al* showed how important appropriate pacing modes were in ischaemic heart disease when they found that symptom limited maximal exercise capacity was better in the VDD (atrial synchronous ventricular pacing) than in the VVI mode.[14] When angina developed in two patients during exercise, reduction of the maximum synchronous rates to below the rate at which angina developed retained the haemodynamic benefit of VDD and avoided chest pain. This study included patients with known ischaemic heart disease who were not necessarily symptomatic, and all studies were done by acute programming and without double blind technique. Thus long term adaptive changes were not considered and the possibility of observer bias was not eliminated. Furthermore, only exercise capacity was examined and symptoms were not assessed over a longer period. In the present study exercise tests were performed one month after mode change. This is more representative of the haemodynamic adaptive changes that occur with program change.[15] We also chose patients with a history of angina rather than symptom free patients with previous myocardial infarction, so that we could analyse symptom frequency as well as the maximum heart rate and workload achieved during exercise. Despite these points our overall conclusions are similar to those of Kristensson *et al*.

A double blind prospective protocol was used to eliminate bias. Some patients, however, did recognise that the pacing mode had been changed (to VVI) when their heart rate failed to increase with exertion or when symptoms developed. It is impossible to keep patients completely unaware of the pacemaker mode in all cases. One of us (AI) knew the programmed mode and monitored the electrocardiograph during exercise testing, but took no part in the subsequent data analysis which was carried out blindly by RAK.

A uniformly reduced maximum tracking rate of 100 beats/min was chosen for the purpose of the study and was significantly better for symptom control than the maximum upper tracking rate in DDD 150 or VVI pacing. Seventy per cent preferred dual chamber pacing when upper rates were set at 100 beats/min, and control of chest pain was significantly better for DDD 100 than for either DDD 150 or VVI. Exercise capacity was also highest for DDD pacing at an upper rate limit of 100 beats/min, although this did not reach statistical significance. The failure to reach statistical significance may be explained by the development of sinus rhythm in three patients during VVI pacing. Exercise capacity was lowest in DDD 150. This may be because three patients stopped exercise when chest pain developed.

Despite significant increases in heart rate during exercise for the three pacing modes, maximum blood pressure was not significantly different. The findings indicate that any increase in myocardial oxygen consumption, as assessed by rate pressure products during exercise, is essentially attributable to an increase in rate rather than a change in systolic blood pressure. In no case did heart rate or systolic blood pressure fall during exercise.

In keeping with previous reports comparing symptoms in subjects randomly programmed to VVI or DDD,[7 15] two patients were unable to tolerate VVI mode and required reprogramming to DDD before the end of the one month study period. Both patients complained of neck pulsations, shortness of breath, dizziness, and chest pain that was not anginal in character and lasted for minutes to over one hour, and both had preserved retrograde atrioventricular conduction. Symptoms were in keeping with a diagnosis of pacemaker syndrome.

Dizziness was significantly more common during VVI pacing than DDD pacing. This may be attributed to varying degrees of severity of pacemaker syndrome in the VVI mode. Alternatively, the frequency of dizziness in VVI mode in this group of medically treated angina pectoris patients may be the result of an inability to increase heart rate and cardiac output in response to postural hypotension induced by vasodilator medication.

In conclusion, in patients with angina pectoris a programmed reduction in the maximum atrial tracking rate is preferable to either the VVI mode or DDD pacing at high upper tracking rates.

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