Comparison of physical work capacity and systolic time intervals with ventricular inhibited and atrial synchronous ventricular inhibited pacing

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SUMMARY Sixteen patients with a non-invasively programmable pacemaker (Medtronic 2409) were examined with the unit in ventricular inhibited (VVI) and atrial synchronous ventricular inhibited (VDT/I) mode, respectively. Maximal exercise capacity was determined by means of bicycle ergometry. Work load was increased in steps of 10 watts each minute. Atrial and ventricular rates, brachial artery pressure, and respiratory rate were studied at rest and during exercise while systolic time intervals were determined at rest. There was an important increase in maximal exercise capacity when changing from VVI to VDT/I pacing. The extent of improvement was the same for patients above and below the age of 65 years. At comparable work loads VDT/I pacing resulted in significantly lower atrial rates than VVI pacing. Systolic time intervals did not differ between VVI and VDT/I pacing apart from an increase in left ventricular ejection time index with VDT/I pacing. Systolic time intervals and maximal exercise capacity with VVI pacing did not correlate with the increase in exercise capacity induced by VDT/I pacing. Physical performance can be significantly improved by VDT/I pacing in both young and old patients. Exercise capacity on VVI pacing cannot predict the possible benefit of change to VDT/I pacing.

During recent years there have been many reports on the successful clinical use of electrodes for transvenous atrial pacing and sensing.¹⁻³ Thus, one of the main obstacles to the more widespread use of physiological pacing has been overcome.⁴ For many patients with complete heart block and intact sinus node function, the most effective mode of pacing should be the atrial synchronous, and beneficial haemodynamic effects of this type of pacing have been described.^{5,6}

To our knowledge, systematic studies comparing the physical work capacity during ventricular inhibited (VVI)⁷ and atrial synchronous pacing (VAT; VDT/I) have not been published. One explanation may be that the use of the latter mode of pacing is, as yet, limited.^{4,8} Another comes from the difficulties that exist in comparing two different types of pacemakers when this either necessitates investigation with the pacemaker exteriorised or before and after the exchange of an implanted pacemaker. Recently, however, we described an atrial synchronous ventricular inhibited pacemaker offering unique investigational opportunities,

being non-invasively programmable to either VVI or atrial synchronous ventricular inhibited (VDT/I) pacing⁹ and the aim of the present study was to compare the maximal physical work capacity with these two modes of pacing. The results have been used to study factors which could predict a possible beneficial effect of VDT/I pacing in a particular patient. The determination of systolic time intervals is a convenient method of non-invasive evaluation of cardiac performance¹⁰ and a secondary aim was to investigate whether these could be used to predict the possible beneficial effects of a change from VVI to VDT/I pacing.

Subjects and methods

PATIENTS

There were 16 patients (Table 1). The current pacemaker was implanted at least one week before the investigation. Some patients had previously been paced with another VDT/I pacemaker, explaining the varying duration of this mode of pacing. At the time of study none of the patients showed clinical signs of myocardial dysfunction apart from the arrhythmia.

Table 1 Clinical characteristics of patients

Case no.	Age (y)	Sex	Heart disease	Duration of VDT/I pacing before test (mth)	Pacing mode first exercise test	Drugs
1	64	M	AVCD 3°	32	VVI	—
2	66	F	AVCD 3°	31	VDT/I	Quinidine 1.2 g, digoxin 0.25 mg
3	61	F	AVCD 3°	30	VVI	—
4	67	F	AVCD 3°	29	VVI	—
5	60	M	AVCD 2-3°, ventricular arrhythmia	24	VDT/I	Quinidine 1.2 g, digoxin 0.25 mg
6	59	F	AVCD 3°	16	VVI	—
7	50	M	AVCD 3°	1.5	VVI	—
8	59	M	AVCD 3°	2	VVI	—
9	57	M	AVCD 3°	0.25	VDT/I	—
10	65	M	AVCD 3°	0.25	VDT/I	—
11	79	F	AVCD 3°, hypertension	0.75	VDT/I	Digoxin 0.25 mg, frusemide 40 mg
12	65	M	AVCD 2-3°, aortic stenosis	0.5	VDT/I	Digoxin 0.25 mg
13	65	F	AVCD 3°	1	VDT/I	—
14	71	M	AVCD 3°, hypertension	1	VDT/I	Hydrochlorthiazide 50 mg, amiloride 5 mg, digoxin 0.25 mg
15	60	M	Sarcoidosis with AVCD 3°	1	VVI	Digoxin 0.25 mg, frusemide 40 mg, prednisolone 10 mg
16	81	F	AVCD 3°	1.5	VVI	Levothyroxine 0.1 mg
Mean 64				Mean 10.7		

AVCD, atrioventricular conduction defect; 2-3°, second to third degree.

THE PACEMAKER

The pacemaker (Medtronic 2409) has previously been described in detail.⁹ Briefly, it is an atrial synchronous ventricular inhibited unit with ventricular escape rates of 50, 60, 70, or 80/minute and a maximum atrial synchronous rate of 100, 125, 150, or 175/minute (in the first units the maximal programmable rate was 150/minute: cases 7 and 8).

The rates can be non-invasively programmed. When the back-up rate is programmed, the mode is also programmed to VVI at the selected rate. Programming the upper rate limit simultaneously programs the mode to VDT/I without changing the previously programmed back-up rate. The pacemaker provides a constant PQ delay of 120 milliseconds when in the atrial synchronous mode. When the atrial rate of the patient reaches the programmed upper rate limit of the pacemaker blocking of conducted impulses occurs occasionally. With increasing atrial rate the frequency of blocked impulses increases and the stimulation interval is constrained so as to maintain it within the programmed upper rate limit.

EXERCISE TESTS

Exercise tests were performed on a calibrated electrically braked bicycle ergometer (Siemens-Elema,

Sweden). A 12 lead electrocardiogram, brachial artery cuff pressure, and respiration rate were recorded in the supine position before exercise. Thereafter the patient was seated on the bicycle and, after an electrocardiogram at rest, exercise was started at a load of 30 watts for the women and 50 watts for the men. The load was increased stepwise each minute by 10 watts until the patient could not continue because of exhaustion, severe angina, or ventricular tachycardia. This procedure is a sensitive way of determining the exercise tolerance of cardiac patients.^{11,12} The patient then resumed the supine position. Systolic brachial artery cuff pressure and respiration rate were recorded during every second work load, during the final load, and four minutes after exercise. Electrocardiograms were obtained during the last 10 seconds on each work load, and directly after, and four minutes after exercise. In addition, the electrocardiogram was continuously monitored on an oscilloscope during the procedure. Ventricular and atrial rates were calculated from the electrocardiograms. All exercise tests were performed during strictly standardised conditions by the same investigator. To rule out bias induced by noncomparable reasons for stopping exercise, such an investigation should preferably be performed with the investigator unaware of the pacing mode. Since this was impossible the patients performed

Fig. 1 Definition of systolic time intervals used in the present study. Electromechanical systole (QS_2) represents the time from the point on the electrocardiogram when the upstroke after the pacemaker artefact intersects the isoelectric line to the aortic component of the second heart sound. LVET, left ventricular ejection time; PEP, pre-ejection period.

a maximal work load rather than stopping at a predetermined submaximal level of effort or because of slight discomfort such as tiredness or dyspnoea.

SYSTOLIC TIME INTERVALS

Systolic time intervals were determined in 11 of the cases as outlined by Weissler and Garrard.^{13 14} The carotid artery pulse curve was recorded on a Mingo-graph 82 at a paper speed of 100 mm/s by means of a pressure transducer, EMT 510 C (Siemens-Elema, Sweden). A phonocardiogram was simultaneously recorded from the third intercostal space at the left sternal edge. Electromechanical systole, left ventricular ejection time, and pre-ejection period were measured in ms as outlined in Fig. 1. Thus, electromechanical systole represents the time on the electrocardiogram from the intersection between the upstroke after the pacemaker artefact and the isoelectric line to the first high frequency vibrations of the aortic component of the second heart sound. The values given are the mean of 10 consecutive beats. For electromechanical systole, left ventricular ejection time, and pre-ejection period, the formulae given by Weissler and Garrard^{13 14} have been used to correct for heart rate.

PROCEDURE

The patients were investigated as outpatients. A light meal was permitted in the morning. The patients were randomised to start with either VVI or VDT/I pacing (Table 1). For those starting with VVI pacing the re-programming to this mode was performed upon arrival at the laboratory. The investigation started two hours later. After the determination of systolic time intervals the patient was exercised. Thereafter the pacemaker was reprogrammed and two hours later the investigation was repeated. When programming to VDT/I mode the highest obtainable atrial synchronous setting was

used except in cases 9, 13, and 14. These cases were programmed to 150 beats per minute. The patients could have a light meal but no coffee or tea between the first and second investigation. Any prescribed drugs were taken normally. Cases 2, 9, and 10 had their two tests on consecutive mornings but followed the same schedule (that is two hours between reprogramming and investigation). In case 12 the repeated exercise tests were performed with the maximal synchronous rate and drug treatment was adjusted between tests.

Student's *t* test for paired differences was used for the statistical calculations, accepting $p < 0.05$ as statistically significant.

Results

PHYSICAL WORK CAPACITY

The maximal exercise capacity with the VVI and VDT/I mode of pacing is shown in Fig. 2 and Table 2. There was a 20% mean increase in exercise capacity from 94 ± 26 watts (mean $\pm$ SD) on VVI pacing, to 113 ± 33 watts on VDT/I pacing ($p < 0.001$). All patients except two (cases 12 and 16) improved. When separating the patients into two groups according to age (> 65 years, $n = 5$, mean age 73 years; ≤ 65 years, $n = 11$, mean age 61 years) both groups showed the same mean increase in exercise capacity of 20%. The highest individual increase was found, however, among the younger patients.

Case 16, an 81-year-old woman, showed unaltered exercise capacity. The limiting factor was leg weariness and it was not felt that the patient reached her circulatory limit during either VVI or VDT/I pacing. Case 12 performed less work at the first exercise test during VDT/I compared with VVI pacing but later improved on VDT/I pacing. This patient is described in detail.

Case report (case 12)

A 65-year-old man had had VVI pacemaker since 1974 because of intermittent second degree atrioventricular block. In 1977 the patient experienced palpitation, dyspnoea, and fatigue. A non-invasive investigation disclosed mild aortic stenosis with moderately enlarged heart. From 1978 he had moderate exercise-induced angina. In February 1979 he complained increasingly of dyspnoea, angina, and fatigue. The atrioventricular conduction defect had deteriorated from intermittent second degree to complete heart block with continuous paced rhythm. Since the atrial rate was normal, a VDT/I pacemaker was implanted. The back-up rate was 50/minute and the maximal synchronous rate 150/minute. One month later the patient felt less tired and dyspnoeic but complained of increasing angina. Exercise tests performed with the pacemaker in the VVI and VDT/I modes are shown in Fig. 3. Exercise performed with the pacemaker in VDT/I mode had to be stopped earlier (80 watts) than with VVI pacing (100 watts) because of severe angina beginning at a ventricular rate of about 135 bpm. With VVI pacing there was frequent retrograde atrial emptying owing to atrial contraction against closed atrioventricular valves, with resulting variation in the arterial pressure. It was still considered probable that the patient would benefit from

VDT/I pacing. The pacemaker was therefore reprogrammed to a maximal synchronous rate of 125/minute so that the ventricular rate on exercise could not exceed the point at which angina started. The patient was also given metoprolol 50 mg daily but because of sinus bradycardia at a rate below the back-up rate of the pacemaker, verapamil 160 mg daily was substituted for it two months later. The patient improved and reported less dyspnoea, fatigue, and angina. On exercise testing (Fig. 3) he had an unchanged maximal exercise capacity with VVI pacing (100 watts) but on VDT/I pacing he reached 120 watts. This time he stopped exercise because of tiredness and dyspnoea, but not angina.

During VVI pacing exercise was stopped in three cases for reasons other than exhaustion (Table 2). Case 2 became pale and showed a fall in blood pressure at a work load of 80 watts, but on VDT/I pacing managed 100 watts with a normally increasing blood pressure. Case 16 has already been mentioned. Exercise had to be stopped in case 9 because of ventricular tachycardia. The case report on this patient follows.

Case report (case 9)

A 57-year-old man with complete heart block since

Table 2 Results of exercise test with VVI and VDT/I pacing

Case no.	Ventricular rate at rest (bpm)		Systolic BP at rest (mmHg)		Pulse pressure at rest (mmHg)		Maximal work load (W)		Atrial rate at max work load (bpm)		Ventricular rate at max work load (bpm)	
	VVI	VDT/I	VVI	VDT/I	VVI	VDT/I	VVI	VDT/I	VVI	VDT/I	VVI	VDT/I
1	72	76	155	155	75	75	110	150	156	162	72	162
2	70	67	140	155	65	80	80	100	99	112	70	112
3	71	109	185	160	95	70	80	110	172	178	71	178
4	71	85	175	165	80	75	70	90	170	175	71	175
5	70	57	140	148	40	56	130	170	180	148	70	148
6	70	80	115	120	25	40	80	110	172	174	70	174
7	71	80	130	125	45	40	110	130	185	185	71	144
8	71	100	130	120	50	30	130	150	172	172	88	135
9	71	76	135	125	45	35	130	150	165	155	135	135
10	69	72	160	165	65	75	120	140	174	174	69	174
11	69	52	170	180	90	100	50	60	133	130	69	130
12	70	60	130	135	30	40	100	80	165	150	70	150
13	71	82	185	185	110	80	80	100	170	165	71	130
14	71	75	170	205	80	105	80	100	168	170	71	130
15	71	89	130	135	50	65	100	110	170	175	71	175
16	71	105	215	200	130	100	60	60	165	172	71	172
Mean	71	79	154	155	67	67	94	113	164	162	76	152
SD	0.8	16	27	28	29	24	26	33	21	19	16	22
p	<0.05		NS		NS		<0.001		NS		<0.001	

BP, blood pressure; E, exhaustion; PVC, premature ventricular contraction; VT, ventricular tachycardia.

October 1978 had had Adams-Stokes attacks. Despite a VVI pacemaker he continued to have attacks of giddiness and also complained of exertional dyspnoea. Apart from the conduction defect there were no signs of cardiac disease. Retrograde atrial emptying and loss of the capability of an increase in heart rate during exercise were considered the probable causes of his symptoms. In May 1979 a VDT/I pacemaker with a back-up rate of 50/minute and a maximal synchronous rate of 150/minute was substituted for the VVI pacemaker. After this the symptoms vanished and the patient remained well. An exercise test was performed with the pacemaker in the VVI and VDT/I mode, respectively. As can be seen from Fig. 4 an alternative explanation for the remaining attacks of dizziness during VVI pacing is possible. When exercising with the pacemaker in the VVI mode, he developed ventricular ectopic beats at a work load of 110 watts. The exercise test was stopped because of runs of ventricular tachycardia with severe dyspnoea and fatigue at a work load of 130 watts. When performing exercise with the pacemaker in the VDT/I mode there was no ventricular tachyarrhythmia despite the higher work load (150 watts).

Only one patient stopped exercise during VDT/I pacing because of symptoms other than exhaustion—case 12, described in detail above.

Fig. 2 Maximal work capacity with VVI and VDT/I pacing. Individual data together with mean $\pm$ SD for the group (thick line).

The respiration rates and systolic pressures during maximal work in the two pacing modes differed significantly ($p < 0.01$) at the end of exercise, the difference in absolute figures being small.

The atrial rates during all work levels were significantly higher with VVI than with VDT/I pacing (Fig. 5). Comparing the two modes of pacing, there was no statistically significant difference in systolic and diastolic pressure at rest or in systolic pressure and respiration rate at maximal work load (Table 2). The working capacity during VVI pacing and the difference on changing to the VDT/I mode showed no correlation.

SYSTOLIC TIME INTERVALS

Systolic time interval indices and pre-ejection period divided by left ventricular ejection time during VVI and VDT/I pacing are shown in Fig. 6 and 7. The only statistically significant difference was an increase in left ventricular ejection time index from 381 ± 25 ms to 400 ± 22 ms ($p < 0.01$) with the institution of VDT/I pacing. Indices for electromechanical systole, pre-ejection period, and pre-ejection period divided by left ventricular ejection time did not show any uniform changes. No correlation could be shown between the different systolic time intervals during VVI pacing and

Programmed max atrial synchronous rate (bpm)	Systolic BP at maximal work load (mmHg)		Respiration at max work load (rate/min)		Reason for terminating work	
	VVI	VDT/I	VVI	VDT/I	VVI	VDT/I
VDT/I						
175	200	215	32	36	E	E
175	130	195	32	32	BP drop, E pallor	E
175	180	190	30	30	E	E
175	205	190	28	32	E	E
175	180	185	30	32	E	E
175	165	175	32	34	E	E
150	155	160	44	44	E E	E
150	210	215	32	34	E+PVC	E
150	195	190	36	44	VT	E
175	215	200	34	32	E	E
175	190	185	36	44	E	E
175	175	130	36	40	E	Severe angina pectoris
150	215	245	28	28	E	E
150	210	230	28	36	E	E
175	150	175	32	32	E	E
175	220	—	28	30	Fatigue in legs	
—	183	192	32	35		
—	24	28	4	5		
—	NS		<0.01

Fig. 3 Results of repeated exercise tests in case 12. See text for details. x, ventricular rate with VVI pacing June 79 and February 80; ▲, atrial and ventricular rate with VDT/I pacing June 79; ■, ventricular rate with VDT/I pacing February 80; ●, atrial rate with VDT/I pacing when exceeding ventricular rate February 80; dotted line indicates the gap between atrial and ventricular rate resulting from blocking in the pacemaker; 1 and 2, supine and sitting at rest; 3 and 4, directly after and four minutes after exercise.

Fig. 4 Results of exercise tests in case 16. See text for details. x, ventricular rate with VVI pacing; ○, atrial rate with VVI pacing; ■, ventricular rate with VDT/I pacing; ▲, atrial rate with VDT/I pacing when exceeding ventricular rate. Dotted line indicates the gap between atrial and ventricular rate due to blocking in the pacemaker.

Fig. 5 Mean ($\pm$ SD) atrial rate with VVI (○) and VDT/I (●) pacing at rest, 50%, 75%, and 100% (W_3) of the maximal workload obtained with VVI pacing. W_4 represents the maximal workload with VDT/I pacing. The differences are all significant: (W_1 : $p < 0.001$; W_2 : $p < 0.01$; W_3 : $p < 0.05$).

the resulting relative or absolute change in exercise capacity after reprogramming to the VDT/I mode.

Discussion

Changing from fixed rate to atrial synchronous pacing improves the haemodynamic response to physical work in patients with complete heart block because of the restoration of a normal temporal relation between atrial and ventricular contraction and of the capacity to increase heart rate during exercise,^{6,15} though to what extent this haemodynamic improvement results in an increased exercise capacity is not certain.

The present data show that physical working ability is better with VDT/I than with VVI pacing. Though a higher degree of exhaustion was produced with VDT/I than with VVI pacing at the end of exercise it still seems reasonable to conclude that the main reason for the differences in physical working capacity was the change in pacing mode. The improvement varied in different patients but was substantial in most of them. Our results suggest that older patients may be expected to derive the same benefit from VDT/I pacing as younger ones.

The time before the exercise tests was considerably longer with VDT/I than with VVI pacing in our patients. It can be questioned whether equally long periods on the two pacing modes would result in less

Fig. 6 Pre-ejection period index (PEPI) and electromechanical systole index (QS_2I) with VVI and VDT/I pacing. Individual data together with mean $\pm$ SD for the group (thick line).

difference in exercise capacity. Adaptation, however, to different pacing modes occurs rapidly.^{6,16} Furthermore, patients paced in the VVI mode for longer periods before being changed to the VDT/I mode showed even greater improvement in exercise capacity (Kruse and Rydén, to be published).

The improvement in cardiac output produced by VDT/I pacing is dependent principally on heart rate increase at rates below 100/minute, while at higher rates the atrial contribution to ventricular filling becomes more important.¹⁷⁻¹⁹ The value of atrial transport is greater in patients with poor myocardial function and valvular heart disease.²⁰ But our results indicate that atrioventricular synchronous pacing may substantially improve even patients without signs of myocardial dysfunction.

Most patients do not seem to need a higher syn-

Fig. 7 Left ventricular ejection time index (LVETI) and pre-ejection period divided by left ventricular ejection time (PEP/LVET) with VVI and VDT/I pacing. Individual data and mean $\pm$ SD for the group (thick line).

chronous rate than 150/minute (Table 2, Fig. 5). Paced patients are often old and the maximal effective heart rate in a corresponding age group has been claimed to be 150 to 160/minute.²¹ Some of our patients reached higher heart rates than 150 and seemed to benefit. This occurred during maximal exercise and in daily life such high levels of exercise and heart rate are unusual. The higher atrial rates during exercise with VVI pacing than with VDT/I pacing during corresponding work loads (Fig. 4) are probably caused by a higher sympathetic tone needed to maintain cardiac output during the former. Similar findings have been reported in patients with intermittent complete heart block when comparing exercise during sinus rhythm and periods of block.²² A practical implication is that the final syn-

chronous rate setting of the pacemaker should not be based on the atrial rate reached in the exercise test during pacing in the VVI mode. Coronary heart disease has been considered a contraindication to atrial synchronous pacing because of the risk of provoking angina with high heart rates.⁶ But patients with coronary disease often have decreased myocardial compliance and should benefit from a correctly timed atrial contraction. Furthermore, their capacity to increase stroke volume is often limited, necessitating higher heart rates to maintain cardiac output during exercise. Angina usually does not occur below a critical heart rate. If the highest synchronous rate of the pacemaker can be adjusted to a level below this, the beneficial effects of VDT/I pacing can be made available for such patients also as shown in case 12.

The elimination of exercise-induced ventricular tachycardia after the initiation of VDT/I pacing in case 9 is interesting. Case 8 also had ventricular premature contractions while exercised in the VVI but not in the VDT/I mode. When considering candidates for VDT/I pacing it is important to note that exercise tolerance with VVI pacing does not seem to predict the magnitude of possible improvement after the change of pacing mode, nor do systolic time intervals. Digital pulse plethysmography has been suggested as a method for selecting patients suitable for various modes of physiological pacing.²³ Such convenient non-invasive methods could be of great clinical importance and the lack of correlation between systolic time intervals and changes in working capacity in the two pacing modes is disappointing. After the change to VDT/I pacing the only consistent difference, an increase in the left ventricular ejection time index, probably reflected an increased stroke volume. Different pacing modes may simultaneously produce several alterations in cardiac performance. Some of these, such as increased stroke volume or decreased sympathetic tone, may vary in extent from one patient to another with inconsistent effects on particular systolic time intervals.^{13 14}

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