Optimal atrioventricular delay at rest and during exercise in patients with dual chamber pacemakers: a non-invasive assessment by continuous wave Doppler

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SUMMARY The optimal atrioventricular delay at rest and during exercise was investigated in nine patients with heart block and implanted dual chamber pacemakers. All patients studied had normal left ventricular function and a normal sinus node rate response to exercise. Cardiac output was measured by continuous wave Doppler and was calculated as the product of stroke distance measured by Doppler at the left ventricular outflow, aortic root area measured by M mode echocardiography, and heart rate. Pacemakers were programmed in the DDD mode. Cardiac output was measured with the patient at rest while supine and while erect and at the peak of submaximal exercise (the end of stage 1 of the Bruce protocol) with the pacemakers programmed to the following atrioventricular intervals: 75–80 ms, 100–110 ms, 140–150 ms, and 200 ms. During exercise the basic pacing rate was programmed to 70 beats/min. Cardiac output at rest while supine and erect was greatest with an atrioventricular delay of 140–150 ms and it was significantly higher than that with an atrioventricular delay of 75–80 ms. On average there was a 31% decrease in cardiac output when patients stood up. During treadmill exercise, however, cardiac output was greatest when the atrioventricular delay was 75–80 ms, and this was significantly higher than the cardiac output with atrioventricular delays of 150 and 200 ms. During exercise 1:1 atrioventricular relations were maintained in all patients at all atrioventricular intervals.

In patients with atrioventricular sequential pacemakers cardiac output at rest is greatest with an atrioventricular delay of 140–150 ms but during exercise the optimal atrioventricular delay is shorter. Rate modulation of the atrioventricular interval may improve the haemodynamic response and possibly exercise tolerance in patients with dual chamber pacemakers.

The importance of an appropriately timed atrial contraction in maintaining optimal cardiac output is now well established in patients with normal and abnormal ventricular function.¹⁻⁴ The temporal relation between atrial and ventricular systole is a determinant of ventricular performance because this interval influences both ventricular filling⁵ and closure of the atrioventricular valve.^{6,7} Several invasive⁸ and non-invasive⁹⁻¹² studies have reported that an atrioventricular interval of 150–200 ms is associated with maximal cardiac output at rest. We

evaluated the optimal atrioventricular delay on exercise in patients with normal left ventricular function. Cardiac output was measured non-invasively by continuous wave Doppler techniques.

Patients and methods

Thirteen patients with dual chamber pacemakers and complete heart block were considered for the study. All had normal left ventricular function (mean ejection fraction 63.8 (7.9)%) and no evidence of valvar heart disease on M mode echocardiography. To assess their suitability for inclusion patients underwent a three minute treadmill exercise test (treadmill speed = 2.7 km/h and gradient = 10%). Doppler signals from the aorta were recorded at rest

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Table 1 Clinical and pacemaker data of the patients

Patient	Age (yr)	Sex	Pacemaker	Duration of implantation (yr)	EF %
1	40	M	Telectronics(Autima II)*	5	53.3
2	58	M	Telectronics(Autima II)	2	44.6
3	66	M	Cordis(Sequicor III)†	3	71.0
4	59	F	Telectronics(Autima II)	2	75.5
5	22	F	Medtronic (Symbios 7005C)‡	1	67.9
6	70	M	Medtronic (Symbios 7005C)	1	62
7	53	M	Telectronics(Autima II)	1	59
8	43	M	Medtronic (Symbios 7005C)	1	56.8
9	46	M	Cordis(Sequicor III)	4	62

*Telectronics, Sydney, Australia, †Cordis Corporation, Miami, Florida, USA, ‡Medtronic, Inc., Minneapolis, USA.
EF, left ventricular ejection fraction measured by M mode echocardiography.

and during exercise. Four patients were excluded from the study—two with unsatisfactory Doppler signals, one with an inadequate sinus node rate response to exercise (atrial rate of <85 beats/minute at end of three minutes exercise) and one because 1:1 atrioventricular conduction developed on exercise. Table 1 shows selected clinical and pacemaker data of the nine patients (average age 53) included in the complete study.

CARDIAC OUTPUTS MEASURED BY DOPPLER

Cardiac output was measured by a continuous wave Doppler system (Quinton Exerdop). This "stand alone" continuous wave Doppler equipment transmits a 3 MHz signal through a 10 mm diameter crystal. A proprietary circuit uses frequency analysis to process the reflected signal. The signal is sampled every 5 ms. Only signals coming towards the transducer and at least 10 decibels above the background noise are processed. A dedicated computer calculates the flow velocity by integrating the area under the curve (systolic velocity integral) using a modified rectangular algorithm. An average of at least 10 consecutive beats was used to calculate the cardiac output at any stage of the experiment. Cardiac output was calculated as the systolic velocity integral $\times$ aortic root area $\times$ heart rate. The aortic root area was calculated from the diameter of the root of the ascending aorta measured by M mode echocardiography. The measurement was taken just above the level of the aortic cusps. The heart rate used for the calculation of cardiac output was averaged from 10 beats recorded simultaneously with the Doppler recordings. In previous studies cardiac output measured in this way has been shown to correlate well with measurement of cardiac output by the Fick¹³ and thermodilution methods¹⁴ (correlation coefficient 0.80–0.96).

The feasibility of Doppler techniques for measuring cardiac haemodynamic function during exercise is now established.^{15,16} The transducer used is small and the probe sufficiently angled so that the ultrasound signal can be easily directed parallel or nearly parallel to the blood flow in the ascending aorta. Because the transducer is small it can easily be maintained in a stable recording position during exercise and has been previously used satisfactorily at our centre to assess the haemodynamic function of post-infarction patients during exercise.¹⁵ Because it is non-invasive, this technique of measuring cardiac output is well suited for repeated assessment of patients with implanted devices.

PACEMAKER SETTINGS

During the study the pacemakers were programmed to the DDD mode. Cardiac output was measured at rest at four atrioventricular intervals with the basic pacing rate programmed to 70 beats/minute and 90 beats/minute. At each rate the atrioventricular interval was randomly programmed to 75, 100, 150 and 200 ms. Telectronics pacemakers have a different range of programmable atrioventricular delays—the corresponding atrioventricular delays in patients with these pacemakers were 80, 110, 140, and 200 ms. For uniformity, hereafter, these are also referred to as 75, 100, 150, and 200 ms. After each reprogramming the atrioventricular interval was confirmed by electrocardiography.

During exercise the basic pacing rate was programmed to 70 beats/minute. At each setting of the atrioventricular interval Doppler measurements were made five minutes after standing and at the peak of treadmill exercises. The operator making the Doppler recordings was unaware of the pacemaker settings.

EXERCISE PROTOCOL

Patients were exercised on a treadmill for three minutes at settings identical to Bruce protocol stage 1 (gradient = 10%, speed = 2.7 km/h.¹⁷ Doppler measurements were made during the last 15 s of exercise. Faster treadmill walking speed was not used because it caused unacceptable background noise on Doppler recordings.

Table 2 Mean (SD) heart rate (beats/minute) at different stages of the protocol

Atrioventricular interval	Supine	Standing	Peak exercise
75 ms	70.8 (2)	70.9 (3)	102 (9)
100 ms	70.6 (2)	70.6 (2)	101.6 (10)
150 ms	70.6 (2)	71.2 (2)	101.5 (9)
200 ms	70.6 (2)	71.4 (3)	101.6 (7.9)

Fig 1 Comparison of mean (SD) cardiac output at the four atrioventricular delays with basic pacing rates programmed at 70 and 90 beats/minutes in resting supine patients. Cardiac output was significantly higher at an AV interval of 150 ms compared with an interval of 75 ms. This result was true at both pacing rates.

STATISTICAL METHOD

All values were expressed as group mean (SD). Paired *t* tests were used to measure statistical differences between heart rates and between cardiac outputs at various atrioventricular intervals. A *p* value of <0.05 was regarded as significant.

Results

At rest, with the basic pacing rate programmed to 70 beats/minute, four patients were pacing in both the atrium and ventricle, while five were tracking the P waves and pacing in the ventricle. Table 2 shows the mean pacing rates (SD) of the group at different stages of the protocol. The pacing rates at rest and during exercise at each of the four atrioventricular intervals were not significantly different. With the pacing rate programmed to 90 beats/minute, cardiac outputs at atrioventricular delays of 75, 100, 150, and 200 ms were 5.55 (1.5), 6.29 (1.7), 6.42 (1.8), and 5.88 (1.6) l/min respectively (fig 1). Cardiac output was significantly greater ($p < 0.05$) with an atrioventricular interval of 150 ms than with one of 75 ms¹⁸. No other difference was significant. Before exercise when the patient was supine with the basic

Fig 2 Changes in mean (SD) cardiac output at rest when the patient stood up. With all four atrioventricular delays there was a similar fall in cardiac output (mean 31%).

pacing rate programmed to 70 beats/minute cardiac output was again greatest with an atrioventricular interval of 150 ms (5.81 (1.5) l/min) (fig 2), and it was significantly lower at atrioventricular intervals of 75 (5.20 (1.3) l/min, $p < 0.01$) and 200 ms (5.51 (1.5) l/min, $p < 0.05$). Whatever the atrioventricular delay, there was a 31% decrease in cardiac output on standing (fig 2). Cardiac output on standing was again greatest with an atrioventricular delay of 150 ms (4.13 (1.4) l/min), and this was significantly higher than the cardiac output with an atrioventricular delay of 75 ms (3.40 (1.02) l/min, $p < 0.01$).

The greatest cardiac output during exercise was seen with an atrioventricular delay of 75 ms (8.26 (1.1) l/min); this was significantly higher than cardiac outputs at atrioventricular intervals of 150 and 200 ms (7.46 (0.9) l/min ($p < 0.05$) and 7.85 (1.1) l/min ($p < 0.05$) respectively). Thus with the mild exercise used in our protocol the greatest increase in cardiac output was seen with an atrioventricular delay of 75 ms (fig 3). These changes in cardiac output between atrioventricular intervals are unrelated to changes in pacing rate because the increase in heart rate on exercise at all four atrioventricular intervals was virtually identical (table 2).

Discussion

OPTIMAL ATRIOVENTRICULAR INTERVAL

The benefits of atrioventricular sequential pacing in

Fig 3 Mean (SD) increase in cardiac output on exercise showing an average 110% increase in cardiac output at all four atrioventricular intervals compared with values at rest (standing). The increase in cardiac output (from 3.4 (1.0) l/min to 8.19 (3.1) l/min) was greatest with a short atrioventricular delay (75 ms).

patients with complete heart block have been shown by invasive,^{3,8} Doppler^{19,20} and radionuclide^{9,10,21} methods. During atrioventricular sequential pacing cardiac output was significantly affected by changes in atrioventricular interval. In our patients, all of whom had normal left ventricular function, an atrioventricular interval of 150 ms at rest was associated with maximum cardiac output. In previous studies, however, the optimal atrioventricular delay at rest varied between 150 ms and 200 ms.⁸⁻¹² This variability may be because the results for patients with normal and abnormal left ventricular function were grouped together. Videen *et al* used radionuclide ventriculography to show that patients with low ejection fraction functioned better at a longer atrioventricular interval,²¹ whereas a shorter atrioventricular interval gave the highest cardiac output in patients with heart block complicating acute myocardial infarction. Leinbach *et al* and Chamberlain *et al* found that the optimal atrioventricular interval was 150 ms in patients with chronic complete heart block and 100 ms or less in patients with heart block complicating acute myocardial infarction.^{8,22} Hartzler *et al* also showed that a comparatively short atrioventricular interval was associated with a higher cardiac output during the

period immediately after operation in patients in whom heart block developed at operation.²³ Thus in patients with normal left ventricular function who are at rest an atrioventricular delay of around 150 ms is optimal. In patients with impaired left ventricular function a longer delay is optimal. In situations of acute stress like myocardial infarction and post-operative states, where the heart rate is expected to be faster, a relatively short atrioventricular delay was found to be optimal.

Although others showed that an atrioventricular delay of 150–200 ms was associated with maximal cardiac output at rest, we found that this delay is not optimal during exercise. Our results confirm the observations of Leman and Kartz who found that on exercise a shorter atrioventricular interval was associated with a larger stroke volume.¹⁰ In their study, however, left ventricular function was assessed only at atrioventricular intervals of 100 and 150 ms and cardiac output was not measured. The results of our study accord with the observation that exercise and its catecholamine response is associated with a shortening of the PR interval in subjects with normal atrioventricular conduction.²⁴

EFFECT OF ATRIOVENTRICULAR INTERVAL ON CARDIAC EVENTS

The benefits of atrioventricular sequential pacing are related to the timing of atrial contraction, which if appropriate leads to an increment in ventricular filling and thereby to a ventricular contractile force (according to Starling's law).²⁵ To contribute most to left ventricular filling, atrial contraction must coincide with late diastole so as to cause maximum filling of the ventricle before onset of systole. In a recent study that used Doppler assessment of mitral flow, Iwase *et al* reported maximal left ventricular filling with an atrioventricular interval of 150 ms in patients at rest.⁵ When they measured mitral flows during early and late diastole they found that decreased left ventricular filling with a suboptimal atrioventricular interval was mainly caused by a decreased atrial (late diastolic) component. Both very short and long atrioventricular intervals reduced left ventricular filling.

With a physiological atrioventricular delay, atrial systole causes a surge of blood into the ventricle at the end of diastole. When the atrium relaxes, inertia causes this blood to continue flowing into the ventricle, producing a region of reduced pressure between the valve cusps, which are therefore pulled into apposition (the so called atrigenic theory of valve closure).^{26,27} If the atrial contraction is late in diastole (as with a short atrioventricular interval), ventricular systole starts when the atrioventricular valves are still wide open and this leads to mild mitral

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or tricuspid regurgitation.²⁸ Furthermore, because ventricular systole starts before atrial emptying is complete the atrial contribution to left ventricular volume is less.⁷ Thus the cardiac output would be expected to decrease.

An atrioventricular interval that is longer than the physiological atrioventricular delay also leads to a decrease in left ventricular performance. Dean, as early as 1916, in isolated heart preparations, showed that longer intervals between atrial and ventricular systole (> 270 ms) allowed the atrioventricular valves to move into apposition and separate again before ventricular contraction started.²⁷ Subsequent studies have shown that an inappropriately long atrioventricular delay is associated with some mitral regurgitation at the onset of systole.^{29,30} Premature atrial systole also reduces the time available for atrial filling from the pulmonary veins; thus it would be less effective than atrial systole in end diastole, when atrial filling would be maximum. Furthermore, atrial systole too early in diastole leads to premature closure of the atrioventricular valves thereby shortening the duration of left ventricular filling.⁶ Studies by Iwase *et al* did show a decreased left ventricular filling volume with long atrioventricular intervals.⁵

A decrease in PR interval with physiological exercise is well known. This decrease is caused by an improvement in nodal conduction under the effect of sympathetic stimulation and the decrease in vagal tone. In healthy subjects Daubert *et al* showed a linear shortening of the atrioventricular interval during exercise with an increase in heart rate.²⁴ An increase in heart rate produces a disproportionate shortening of diastole compared with systole. If the atrioventricular interval were to remain constant, atrial systole would occur relatively early in diastole—a situation similar to that seen with unphysiologically long atrioventricular intervals at rest.

PROBLEMS ASSOCIATED WITH UNIFORM PROGRAMMING OF ATRIOVENTRICULAR INTERVAL

The major difficulty in programming the atrioventricular interval in patients with complete heart block and atrioventricular sequential pacemakers is the difference in the atrioventricular delay between atrioventricular sequential pacing and ventricular pacing with atrial tracking. In the case of atrioventricular pacing the atrioventricular interval begins with a paced event while with atrial tracking the atrioventricular interval begins with a sensed atrial event. Because there is a delay of 35–40 ms before atrial sensing, the mechanical atrioventricular delay is relatively longer despite a similar program-

med atrioventricular interval.^{6,31} This makes uniform programming of the atrioventricular interval during atrial and ventricular pacing and atrial tracking difficult. Most of the present generation of dual chamber pacemakers do not distinguish between the paced and sensed atrial activity. In five of our nine patients there was tracking at the atrium at rest. This is an expected problem because of the inherent variation in sinus rate at rest from one patient to another. In previous studies, including ours, where the basic pacing rates at rest have been programmed up to 80 or 90 beats/minute so that atrioventricular pacing is established, an atrioventricular interval of 150–200 ms has still been found to be optimal.^{11,12,18} However, during exercise in all our patients there was tracking of the atrium. This means that the relative changes in cardiac output on exercise are more relevant and indicate the benefit of a relatively short atrioventricular delay on exercise.

CLINICAL IMPLICATIONS

In patients with complete heart block and atrioventricular sequential pacemakers, rate modulation of the atrioventricular delay may improve cardiac haemodynamic function. The degree of exertion used in our study was quite mild but it is likely that the haemodynamic advantage of a shorter atrioventricular interval would also be seen with moderate to severe exertion. Further studies are needed to assess the effect on the exercise capacity of rate modulation of the atrioventricular interval.

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