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Chronotropic Responses to Exercise on Treadmill by Patients with Implanted Rate Responsive Pacemaker

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Summary. **The rate-responsive ventricular pacing (VVIR) was evaluated by the comparison of responses of the sinus rate during exercise on a treadmill, between the VVIR mode and rate-fixed (VVI) mode as well as by the comparison of hemodynamic responses. The duration of exercise was increased with the VVIR pacing, and at low to moderate levels of exercise the sinus rate was significantly lower in the VVIR mode than in the VVI mode ($p<0.01$-0.05). Blood pressure remaind at a lower level and pulse pressure was smaller in the VVIR mode. The beneficial effects of the chronotropic responses of the VVIR mode were reflected in hemodynamic responses and response of the sinus rate.**

INTRODUCTION

Many pacing modalities have been invented and used for the treatment of patients with bradyarrhythmias, and guidelines for the implantation of pacemaker have been established.[1]

If patients have a normal sinus node, atrioventricular sequential pacing can be employed for physiological pacing and augmentation of cardiac output, and a working capacity can be achieved.[2-6]

However, the use of AV sequential pacing is limited to those patients who have a normal sinus node function.When patients have dysfunction in the sinus node.[7] or supraventricular arrhythmias, such pacing modality is not available. However, as it was confirmed that the rate-responsiveness is more important than the atrio-ventricular synchrony to increase cardiac output and working capacity during exercise,[4-6] other types of rate-responsive pacemakers have been invented. Physiological demand can be monitored using parameters other than the sinus rate. They include blood temperature,[8] arterial oxygen saturation,[9] stroke volume or cardiac volume,[10] right ventricular pressure,[11] QT interval,[12] respiration rate,[13] and mechanical activity.[14] However, there is no golden standard which allows us to judge whether the chronotropic response of the rate-responsive pacemaker is adequate or not.

In the present paper, the appropriateness of one of the rate-responsive ventricular pacing was assessed by comparison of the responses of the sinus rate during exercise on a treadmill between the rate-responsive and the rate-fixed pacing.

The sinus rate was assumed to be an ideal sensor which would reflect the physiological demands,[15] and if the chronotropic response of the ventricular pacing is poor, the reflex increase in the sinus rate would be larger. The working capacities between the two pacing modes were also compared.

SUBJECTS AND METHODS

Subjects comprised 18 patients who underwent pacemaker implantation for chronic A-V block. Five males and thirteen females were included, with age ranging between 30-80 years.

Fourteen patients had been admitted because of Stokes-Adams syndrome and received emergency pacing. Four other patients had no neurological symptoms but complained of the easy fatigability and dyspnea upon exertion.

On admission, there were no abnormal findings in the serum electrolytes, blood cell counts and serological tests in all patients. No inflammatory sign was detected.

Elecerocardigram showed a complete AV block and the R-rate was 35 ± 7/min. The P-wave showed normal configuration, and was diagnosed to be of sinus origin. The P-rate was 80 ± 12/min. In 14 patients, QRS was as narrow as less than 0.10 sec, and in 4 patients it was as wide as more than 0.12 sec. Two dimensional echocardiography revealed normal dimensions for the heart chambers and normal valve motions.

Electrocardiogram (ECG) monitoring, performed continuously after admission for 2 to 7 days, showed no evidence of sinus node dysfunction such as inappropriate sinus bradycardia, sinoatrial block or sinus arrest.[7]

Eight patients underwent electrophysiologic study before the implantation, but the overdrive suppression test[7] showed normal findings.

Implantation of pacemaker

In 9 patients, VVI pacemaker (Medtronic Co. Model 8420 Minneapolis, U.S.A.) was implanted and in the other 9 patients, a rate responsive pacemaker (Medtronic Co. Model 8412 Activitrax II, Minneapolis, U.S.A.) was implanted. The latter pacemaker acts as a rate-responsive pacemaker which senses the mechanical activity and transforms the signal to an electric one.[14] The generator then determines the increment of the pacing rate depending on the magnitude of the mechanical signal.

The increment for a given mechanical activity can be adjusted in three steps, and the increment and the maximal pacing rate can also be selected in 10 steps. The surgical procedure of the implantation was performed in the standard manner.

Exercise on treadmill

Exercise on a treadmill (Fukuda Denshi Co. MAT-2000) was performed using the Bruce protocol, and the 12-lead ECG was recorded in one-minute intervals during the exercise and recovery phases.

Blood pressure was also measured automatically, with ECG also taken automatically (Nihon Korin Co. STBP-680)

It is well known that the chronotropic and hemodynamic responses are different between the first and the second exercise tests but not between the second and the third ones,[16] so patients underwent a preliminary exercise test within one month before commencing the comparative study after the implantation of the pacemaker.

All patients underwent the exercise test on a treadmill at the fixed pacing rate of 70 pacing/min: the VVI study.

In nine patients who were implanted with a rate-responsive pacemaker, the second exercise testing was performed in the same manner, except that this time, the pacemaker was set to a rate-responsive mode (the VVIR study). Between the two studies, a 30 min or longer rest was interposed and it was confirmed that sinus rate and blood pressure to the control levels.

Termination points of the exercise

The exercise testing was terminated on the request of patients because of dyspnea, or fatigue. When ventricular tachyarrhythmias developed, or blood pressure fell by 10 mmHg or more, the study was terminated immediately. After the termination of the exercise, ECG recordings and measurements of blood pressure were continued for 5 min.

Evaluation of the chronotropic response

In the VVI study (n=18), the sinus rate was obtained at each stage of exercise. The author hypothesized that the ideal chronotropic response means the state in which the ventricular rate becomes identical with the sinus rate during the exercise. Therefore, sinus rate was used as an indicator of physiological demand.[15,16] If the chronotropic response of the rate-responsive pacemaker is inadequate, the increase in cardiac output would be limited and a lower cardiac output during exercise would reflexly increase the sinus rate to a greater degree. In order to determine the beneficial effect of the rate-responsive pacing, we performed comparative studies between the fixed and rate-responsive pacing mode in 9 patients.

During two exercise testings, sinus rates were obtained from a P wave and compared with the ventricular rates (pacing rates), the difference between the sinus rate and ventricular rate (pacing rate) was compared.

In the VVI study, the ventricular rate was fixed at 70/min. In the VVIR study, the pacing rate at rest was set 70/min and 120/min for the maximal pacing rate in 7 patients and at 150/min in 2 patients. The pacemaker was set at a moderate sensitivity for sensing of the mechanical activity.

Hemodynamic changes and working capacity

Responses in blood pressure and pulse pressure were obtained every one minute and compared in the testings. The working capacity was determined as the duration of exercise on the treadmill.

A fall in blood pressure, ECG changes such as an ST-T abnormality or the development of arrhythmias were carefully monitored and compared in the two studies.

Values of the data were presented as mean±S.D. and statistical analysis was performed by the t-test.

If the p value was less than 0.05, the difference was considered as statistically significant.

RESULTS

Sinus rate during exercise on treadmill

The control sinus rate was 89±14 beats/min when the pacing rate was fixed at 70 beats/min. At peak exercise, it rose to 137±19 beats/min ($p<0.001$). The exercise was terminated at 6.4±2.1 min because of fatigue in 18 patients.

Comparative studies between the VVI and VVIR pacings

Duration of exercise: In seven patients, a prologation in the duration of exercise was observed when the pacing mode was changed from the VVI mode to VVIR mode, but two patients showed no prolongation. During the VVI study, patients achieved Bruce's protocol for 5.1±1.1 min. When the pacing mode was changed to the VVIR mode, the duration of exercise was prolonged to 6.3±1.9 min, which was significantly longer than that of the VVI study ($p<0.01$).

Ventricular rate: In the VVI study, the ventricular rate was kept at 70/min during the study. No ventricular arrhythmias developed during the study (Fig. 1). In the VVIR study, the ventricular rate increased from 70/min to 108±8/min at 6 min. After the termination of the exercise, the rate returned to the control rate in 2 min (Fig. 2).

Sinus rate (P-rate): In the VVI study, sinus rate increased from 92±13 beats/min to 135±15 beats/min. It then, fell gradually toward the control level during the recovery stage (Fig. 1 and Table 2).

In the VVIR-study, the sinus rate was 92±12 beats/min in the resting state and increased more gradually than that of the VVI study. The sinus rate remained at significantly lower levels than that of the VVI study during the initial 2 through 5 min ($p<0.01$-0.05) (Fig. 2, Table 2). At 6 min of exercise, the P-rate

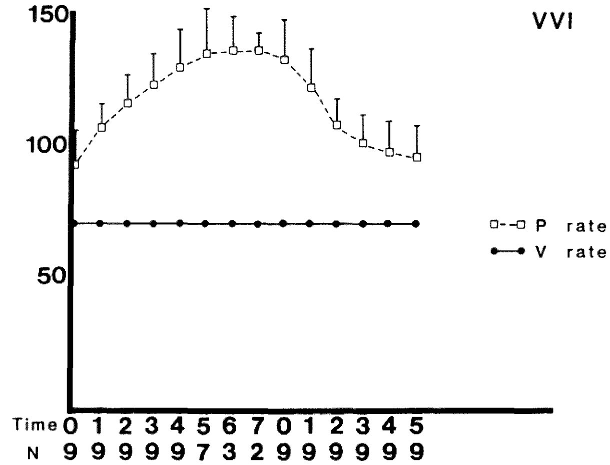

Fig. 1. Changes in sinus rate (P rate) and ventricular rate (V rate) during and after treadmill exercise in 9 of VVI pacing patients. V rate was fixed at 70/min. P rate increased during exercise and decreased gradually toward the control level.

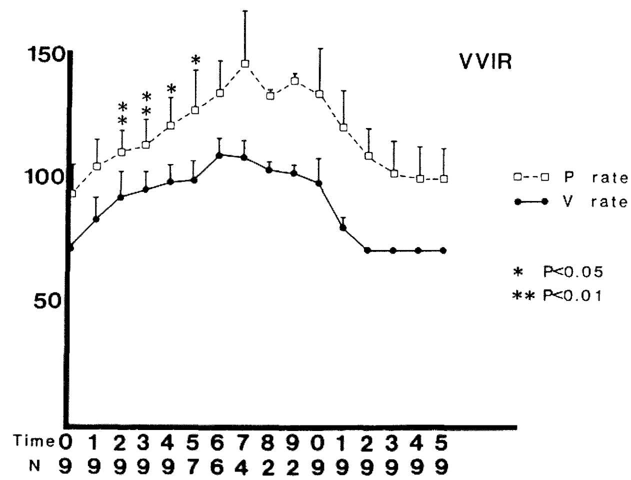

Fig. 2. Changes in sinus rate (P rate) and ventricular rate (V rate) during and after treadmill exercise in 9 of VVIR pacing patients. V rate increased from 70/min to 108±8/min at 6 min. P rate was lower than that of VVI study during the initial 2-5 min ($p<0.01$-0.05).

Table 1. Summary of changes before and during peak exercise on the treadmill during VVI and VVIR pacing.

	P rate		P-Vgap		SBP		DBP		PP		EX. Time
	Before	Peak	Before	Peak	Before	Peak	Before	Peak	Before	Peak	
VVI	92±13	137±15	19±14	66±18	125±16	165±30	69±11	65±23	55±17	100±27	5.1±1.1
VVIR	92±12	128±12**	22±22	37±9***	125±20	162±29	68±13	73±20	57±19	88±27	6.3±1.9**

P rate=sinus rate P-V gap=gap of sinus rate and ventricular rate
SBP=systolic blood pressure DBP=diatolic blood pressure
PP=pulse pressure EX. Time=exercise time
**p<0.01 ***p<0.001

Table 2. Changes in sinus rate and ventricular rate during treadmill exercise compared between VVI and VVIR

	Exercise 0	1	2	3	4	5	6	7	8	9
P rate										
VVI	92±13	106± 9	115±11	122±12	129±12	134±17	135±13	135± 7		
VVIR	92±12 NS	103±90 NS	109± 9 **	112±10 **	120±11 *	126±16 *	133±13 NS	145±21 NS	132± 2	138± 3
V rate										
VVI	70	70	70	70	70	70	70	70		
VVIR	70	82± 9 *	91±10 ***	94± 7 ***	97± 7 ***	98± 9 ***	108± 8 ***	107± 7 ***	102± 3	101± 3

* P<0.05 ** P<0.01 *** P<0.00 NS no significant

Table 3 Hemodynamic changes occurring in treadmill exercise during VVI and VVIR pacing in 9 patients.

		Exercise 0	1	2	3	4	5	6	7
VVI	SBP	125±16	147±24	148±24	157±29	164±27	173±23	165±25	165±33
	DBP	69±11	68±19	68±18	65±20	66±23	64±23	62±27	71±34
	RPP	8734±1134	10313±17	10392±1683	10798±1983	11472±1863	12080±1614	11643±1760	12740±594
	PP	55±17	80±22	84±24	93±26	97±28	109±26	105±21	111±25
VVIR	SBP	125±20	134±22 *	140±24	140±20 *	154±31 *	162±28 *	154±30 *	162±32
	DBP	68±13	73±20	71±26	77±19 *	72±16	75±18	80±16	82±18
	RPP	8742±1383	11052±2763	12197±2890 *	13273±2105 ***	14907±3127 ***	15958±3104 ***	15769±3196	17337±2786 *
	PP	57±19	62±24 ***	68±20 *	62±26 ***	83±33 ***	87±34 *	75±33 **	80±40

SBP=systolic blood pressure DBP=diastolic blood pressure RPP=rate pressure product PP=pulse pressure

increased to the same level of the peak level (136±18 beats/min) and stayed at the level. When compared at the time of peak exercise, the VVIR study showed a significantly lower P-rate than the VVIR-study: 128±12/min vs. 137±15/min ($p<0.01$).

Hemodynamic changes

The control blood pressure was 125±16 mmHg and 125±20 mmHg systolic, and 69±11 mmHg and 68±13 mmHg diastolic, for the VVI and VVIR studies, respectively. At 4 min, blood pressure was 164±27/66±23 mmHg (systolic/diastolic) in the VVI study (n=9) and 154±31/72±16 mmHg in the VVIR study, and the rise in blood pressure was significantly higher in the VVI study. At the same time, pulse pressure was also significantly larger in the VVI study than in the VVIR study: 97±28 mmH vs 83±33 ($p<0.05$). The difference in pulse pressure during the initial 1-6 min was significantly smaller in the VVIR study than the rate-fixed study ($p<0.05$). Two patients achieved exercise for 7 min, and blood pressure reached simipacing.

Recovery					
0	1	2	3	4	5
132±15	121±15	107±10	100±12	97±12	95±12
133±18 NS	119±15 NS	108±11 NS	101±13 NS	99±13 NS	92±12 *
70	70	70	70	70	70
97±10 ***	79±4 *	70	70	70	70

8	9	0	1	2	3	4	5
		165±34	162±16	160±25	153±18	144±18	136±23
		63±18	67±18	71±11	71±12	72±15	69±12
		11542±2353	11270±1100	11146±1737	10694±1254	10111±1226	9528±1620
		102±27	95±22	89±24	82±21	72±18	67±22
187±19	200±15	151±27	161±21	159±17	151±18	148±13	139±18
85±29	87±27	67±21	67±15	70±12	72±14	66±13	70±11
22050±6718	20139±1218	14606±2863 ***	12803±2009 **	1114±1205	10578±1286	10383±920	9769±1266
102±48	113±12	84±26 *	94±20	88±22	77±19	82±13	70±16

* P<0.05 ** P<0.02 *** P<0.01

lar levels: 165±33/71±34 mmHg vs. 162±32/82±18 mmHg in the VVI and VVIR studies, respectively. Pulse pressure at this time was larger in VVI study than VVIR study: 111±25 mmHg vs. 80±40 mmHg (Table 3).

On cessation of exercise, blood pressure fell from 165±34/63±18 mmHg to 136±23/69±12 mmHg in the VVI study and from 151±27/67±21 mmHg to 139±18/70±11 mmHg in the VVIR study.

The rate pressure product was significantly larger in the VVIR-study during 2-5 min than in the VVI study. The difference was due to a larger increase in the ventricular rate in the VVIR study (Table 3).

Complications (Table 3)

Two patients showed a duration in hypertensive response at 189/68 mmHg and 210/106 mmHg, respectively, at the time of peak exercise during the VVIR study. However, blood pressure returned to the control level during the recovery stage. No other complication was found.

DISCUSSION

The cardiac output and the working capacity were confirmed to increase with a rate-responsive pacing.[2-7] In the study by Kristensson et al., cardiac output was found to increase by 3.8*l*/min[6] during the rate-responsive pacing. A decrease in the difference of the arterio-venous oxygen saturation, and a decrease in the serum lactate level during exercise were considered to reflect improved hemodynamics induced by a rate-responsive pacemaker.[6] The beneficial effect of a rate-responsive pacing has been confirmed in a recent double blind cross-over study,[17] and in a long-term study.[18]

For the beneficial hemodynamic effects of the VDD pacemaker, two factors are responsible: atrio-ventricular (A-V) synchrony and rate-variability. In the study by Kristensson et al.,[6] responses at rest and during exercise in pacing with A-V synchrony and one without A-V synchrony but ventricular pacings at the same rates were characterized in comparable tasks. When exercise was carried out at 50% and 80% of the maximal aerobic tolerance, atrial synchrony and asynchronous ventricular pacing showed no significant difference in cardiac output and stroke volume. Therefore, it is now believed that the rate variability is more important than the A-V synchrony.[17,19] This fact means that, if we use a rate-responsive pacemaker, we will be able to improve hemodynamic response on exertion, and the rate-responsive ventricular pacing alone would be able to achieve this goal. Only in limited cases might ventricular pacing result in a hemodynamic deterioration because of a loss of A-V synchrony and a possible vasodepressor reflex.[20] However, assessment is still required to ascertain the adequacy of the rate responsiveness in the rate-responsive pacemaker therapy, but only a few studies have been so far performed.

Baig et al.[21] studied the appropriateness of the rate responsive pacemaker by comparing the pacing rate with the atrial rate, and obtained an improved correlation between the atrial and the pacing rates during exercise when they had modified the response pattern of the QT interval sensing pacemaker. The sinus rate was used as the indicator of the physiologic demands.

In this paper, the author studied the adequacy of the rate responsive pacemaker by comparing the pacing rate with the sinus rate (atrial rate). Patients underwent exercise on a treadmill, both in the rate-responsive pacing (VVIR), and in the rate-fixed pacing (VVI).

In the VVIR pacing, the sinus rate increased with each step up in exercise, and remained at significantly lower levels than in the VVI mode at low to moderate levels of exercise (Table 2).

For the higher atrial rate in a rate-fixed pacing (VVI study), the enhanced sympathetic nervous activity can be said to be responsible because it is considered to be activated to a greater degree because of the limited increase in the cardiac output during exercise,[15] and the lack of chronotropic response is responsible for the limited increase in cardiac output.[2-6,17,18]

In this study, blood pressure also remained at significantly higher levels in the VVI study than that in the VVIR study, and pulse pressure was larger in the VVI study. These changes may be due to the absence of the chronotropic response in the VVI study, in which the increase of cardiac output might be brought about by increasing stroke volume.

However, it is noted that even in the VVIR pacing, the pacing rate remained at significantly lower levels than the sinus rate, and this fact could mean that the chronotropic response in the VVIR study is still inadequate. We might be able to improve the chronotropic response by changing the rate-responsiveness of the pacemaker during bodily movements, but in such instances, the pacing rate might increase inappropriately on moderate activity and result in palpitation.

In conclusion, the present study confirmed beneficial hemodynamic effects of the rate-responsive pacemaker. The exercise-induced reflex increase in the sinus rate remained at lower levels during the rate-responsive pacing than in the rate-fixed pacing. Since the pacing rate was significantly lower than the atrial rate even in the rate-responsive pacing, the pacing modality seems incomplete.

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