Cardiovascular Response to Exercise in Pacemaker Implanted Patients with Fixed Heart Rate

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SUMMARY

Cardiovascular response to supine exercise was studied in 11 patients with chronic ventricular pacing for complete atrioventricular block whose heart rate was fixed during exercise, and compared with 11 age- and sex-matched normal subjects. Oxygen uptake increased linearly with increasing work rate, and attained maximum values of 15.7 ± 0.7 and 29.5 ± 1.1 ml/min·kg, respectively. In both groups, cardiac output increased in association with oxygen uptake, although the maximum value in the patients was less than one half that in the controls (6.8 ± 0.5 and 15.1 ± 0.3 l/min). Stroke volume, however, could change in patients, as in the controls under similarly increased afterloads (maximum values were 96 ± 7 and 93 ± 3 ml/beat, respectively). During exercise, the systolic arterial pressure elevated to a similar extent in both groups (221 ± 14 and 235 ± 12 mmHg, respectively). The increase in stroke volume in the patients was achieved by complete systolic emptying and the Frank-Starling mechanism. It is considered that in patients with ventricular pacing, exercise can produce an increase in stroke volume when myocardial function is not impaired.

Additional Indexing Words:

Pacemaker implantation Dynamic exercise Maximum work
capacity Cardiac pump function Ventricular asynchrony

PACEMAKER implantation is now widely used as an effective procedure for the treatment of complete heart block. Among many pacing modes, a ventricular inhibited (VVI) pacemaker is commonly used, although other types of pacemaker provide a more physiologic mode of pacing. In spite of numerous reports on the optimal stimulation rate at rest, there have been little definitive data on the hemodynamic response to exercise in patients with ven-

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tricular pacing whose heart rate remains constant during exercise.^{1),2)} This study was undertaken to evaluate the exercise capacity in patients with complete heart block, in whom the ventricular rate was fixed during exercise testing and to discuss the effect of ventricular asynchrony on stroke volume.

SUBJECTS AND METHODS

Eleven patients treated with a VVI pacemaker were selected for this study. The study was performed in out-patients in whom at least 10 months had elapsed after pacemaker implantation. Clinical details of the patients are given in Table I. The heart block was considered to be acquired in all the patients. They consisted of 3 males and 8 females aged from 46 to 67 years with a mean of 59.5 ± 2.5 (SEM) years. Of these patients, 7 had suspected ischemic heart disease and 4 had hypertension. All the patients were in NYHA functional class I or II. One patient was taking propranolol and diltiazem, 2 were on antiarrhythmic medication and 8 had no medication at the time of the study.

Eleven healthy control subjects matched for age (57.0 ± 1.0 years, range 53 to 63 years) and sex (male 3, female 8) were studied for comparison. These subjects had no history of cardiovascular disease and showed normal physical and laboratory findings, including chest x ray, respiratory function, hematologic and biochemical examinations. They had normal ECGs at rest and during exercise.

Exercise was carried out with the subjects in the supine position, using an electrically braked bicycle ergometer (Siemens-Elema, 380 B). A 21 G polyethylene tube was fixed percutaneously in the right brachial artery for pressure tracing, and an 18 G teflon tube was placed in the subclavian vein through the right cubital vein for indocyanine green dye injection. After measurements of resting arterial pressure, cardiac output and left ventricular

Table I. Clinical Remarks

	Patients (n=11)	Controls (n=11)	P value
Age (yr)	59.5 ± 2.5	57.0 ± 1.0	NS
Male	3	3	
Female	8	8	
Height (cm)	151 ± 3	156 ± 2	NS
Weight (kg)	55.3 ± 3.1	53.0 ± 1.7	NS
BSA (m ²)	1.52 ± 0.05	1.51 ± 0.03	NS
CTR (%)	55.5 ± 1.7	48.5 ± 1.3	<0.01

BSA=body surface area; CTR=cardiothoracic ratio.

dimension, leg exercise was started at 15 or 25 W and increased by 15 or 25 W every third minute until the subjects were exhausted.

Electrocardiogram and arterial pressure were monitored continuously throughout the study. Phasic and mean arterial pressures were measured with strain gauge transducers. Cardiac output and left ventricular dimension were measured during the last 30 sec of each step of exercise. Cardiac output was determined by the dye dilution technique with an earpiece densitometer (Nihon-Kohden, MLC-4100 S). As reported previously,³⁾ this technique causes no systematic error of cardiac output measured during rest and exercise as compared with the values simultaneously obtained from a cuvette densitometer. Stroke volume was calculated as the ratio of cardiac output to heart rate.

Expired gas analysis and oxygen uptake measurement were performed through a closed circuit respiratory gas analyzer (Anima, R 1500 S). The arterio-venous oxygen difference (avO_2D) was calculated by the Fick principle.

Left ventricular dimension was obtained from M-mode echocardiograms (Toshiba, SSH-60 A) taken from the third or fourth intercostal space along the left sternal border. End-diastolic dimension was measured at the peak of the R wave of the ECG. End-systolic dimension was determined at the most anterior ascent of the posterior wall motion.

Hemodynamic measurements at rest and during exercise were compared using the paired t-test. Intergroup comparisons were performed by the unpaired t-test. The values are expressed in terms of $\text{mean} \pm \text{SEM}$.

RESULTS

Hemodynamic data at rest and during maximum exercise of the study groups are presented in Table II. At rest, there was no significant difference in oxygen uptake ($\dot{\text{V}}\text{O}_2$) or cardiac output (CO) between the 2 groups, while stroke volume (SV) was smaller and heart rate (HR), systolic (SAP), mean (MAP) and diastolic arterial pressures (DAP) were larger in the patient group than those in the control group.

All subjects exercised to exhaustion and the limiting symptom was leg fatigue or dyspnea. During and after exercise, no subject developed anginal pain. Exercise level completed was 65 ± 7 W in the patients and 113 ± 6 W in the controls ($p < 0.001$). Oxygen uptake increased linearly with increasing work rate, and attained maximum values of 15.7 ± 0.7 and 29.5 ± 1.1 ml/min·kg, respectively ($p < 0.001$).

During exercise, the control group had a progressive increase in SAP

Table II. Hemodynamic Changes during Maximum Exercise

	Patients		Controls	
	Rest	Exercise	Rest	Exercise
$\dot{V}O_2$ (l/min)	0.19 ± 0.01	$0.87 \pm 0.07^{***}$	0.20 ± 0.01	$1.55 \pm 0.08^{***\dagger\dagger\dagger}$
CO (l/min)	4.0 ± 0.4	$6.8 \pm 0.5^{***}$	4.9 ± 0.2	$15.1 \pm 0.3^{***\dagger\dagger\dagger}$
avO ₂ D (vol%)	4.9 ± 0.4	$13.0 \pm 0.7^{***}$	4.1 ± 0.2	$10.3 \pm 0.6^{***\dagger\dagger}$
SAP (mmHg)	169 ± 10	$221 \pm 14^{***}$	$146 \pm 6^\dagger$	$235 \pm 12^{***}$
DAP (mmHg)	94 ± 4	93 ± 5	$77 \pm 3^{\dagger\dagger}$	$104 \pm 3^{***}$
MAP (mmHg)	123 ± 6	$135 \pm 7^{***}$	$103 \pm 4^\dagger$	$151 \pm 5^{***}$
SV (ml/beat)	58 ± 5	$96 \pm 7^{***}$	$77 \pm 3^{\dagger\dagger}$	$93 \pm 3^{**}$
HR (beats/min)	69 ± 1	69 ± 1	63 ± 3	$164 \pm 4^{***\dagger\dagger\dagger}$
Dd (mm)	49.5 ± 1.5	$51.5 \pm 1.5^{**}$	48.7 ± 0.8	48.6 ± 0.8
Ds (mm)	34.1 ± 1.3	$29.0 \pm 1.4^{***}$	$30.0 \pm 0.7^{\dagger\dagger}$	$25.5 \pm 1.0^{***\dagger}$

$\dot{V}O_2$ =O₂ uptake; CO=cardiac output; avO₂D=arteriovenous O₂ difference; SAP=systolic arterial pressure; DAP=diastolic arterial pressure; MAP=mean arterial pressure; SV=stroke volume; HR=heart rate; Dd=left ventricular end-diastolic dimension; Ds=left ventricular end-systolic dimension.

** p<0.01, *** p<0.001 Rest vs. Exercise.

† p<0.05, †† p<0.01, ††† p<0.001 Patients vs. Controls.

and DAP, whereas in the patient group there was little change in DAP despite a progressive increase in SAP. Although 1 patient was receiving propranolol, hemodynamic response to exercise was similar to the other patients who were not receiving this drug. The maximum SAP and DAP attained were 221 ± 14 and 93 ± 5 mmHg in the patient group, and 235 ± 12 and 104 ± 3 mmHg in the control group, respectively.

Figure 1 demonstrates the relationships between CO, avO₂D and $\dot{V}O_2$ at rest and during exercise. For the same $\dot{V}O_2$, CO was smaller and avO₂D was larger in the patients than in the controls. At the maximum exercise level, CO was 6.8 ± 0.5 and 15.1 ± 0.3 l/min, and avO₂D was 13.0 ± 0.7 and 10.3 ± 0.6 vol%, respectively.

Figure 2 shows the changes in HR and SV for percent of maximum oxygen uptake (% $\dot{V}O_2$ max). During exercise, HR remained constant (69 ± 1 beats/min) in the patient group, while in the control group it rose linearly from 63 ± 3 to 164 ± 4 beats/min at the maximum level. Stroke volume, although smaller in the patient group at rest, increased from rest to exercise in both groups, and no significant difference was observed between the 2 groups at the maximum level of exercise (96 ± 7 and 93 ± 3 ml/beat, respectively).

The dimensional changes from rest to maximum exercise are shown in Table II. At rest, there was no significant difference in left ventricular end-diastolic dimension (Dd) between the patients and controls, but end-systolic dimension (Ds) was larger in the former. With exercise, Ds decreased signifi-

Fig. 1. Relationships between cardiac output (CO), arterio-venous oxygen difference (avO_2D) and oxygen uptake ($\dot{\text{V}}\text{O}_2$) at rest and during exercise. Each point from rest to maximum exercise (MAX) indicates 40, 60 and 80% of maximum oxygen uptake ($\dot{\text{V}}\text{O}_2 \text{ max}$), respectively.

Fig. 2. Heart rate (HR) and stroke volume (SV) plotted vs. percent of maximum oxygen uptake (% $\dot{\text{V}}\text{O}_2 \text{ max}$).

cantly in both groups ($p < 0.001$). Dd remained unchanged in the controls, whereas it increased in the patients ($p < 0.01$).

DISCUSSION

The maximum work rate and the maximum oxygen uptake in the patients were lower than those in the controls. Energy expenditure is often

represented by METS, multiples of resting oxygen requirement equivalent to 3.5 ml/min·kg. It is generally known that daily physical work consists of less than 4 METS. In 9 of 11 patients, functional capacity was more than 4 METS. It is considered that although the results of the supine study are not directly applicable to upright exercise, most patients can enjoy their daily activities without requiring prolonged or vigorous effort.

The maximum oxygen uptake is determined by maximum cardiac output and by maximum oxygen extraction. In both groups, cardiac output increased in association with work rate, although the maximum value in the patients was less than one half that in the controls. For the same oxygen uptake level, the patients had a smaller cardiac output and larger arterio-venous oxygen difference. Arterio-venous oxygen difference at the maximum exercise level was much larger in the patients, suggesting that the oxygen extraction in the working muscle was not impaired in the patients.

The increase in cardiac output during exercise is a result of the increases in both heart rate and stroke volume in the controls. In contrast, it is entirely dependent on increased stroke volume in the patients. As is well known, stroke volume is not only influenced by myocardial contractile function, but also related to cardiac loading conditions. In the normal human heart, however, there are conflicting data regarding the validity of the Frank-Starling mechanism during exercise.⁴⁾⁻¹⁰⁾ An increment in heart rate during exercise would decrease the left ventricular end-diastolic volume by a shortened diastolic filling period. Despite the tachycardia, stroke volume in the control group increased significantly during exercise. Echocardiography demonstrated that in the control group, end-diastolic dimension did not change significantly and end-systolic dimension decreased progressively with graded exercise. Unchanged end-diastolic dimension under extreme tachycardia indicates that the working muscle contraction promotes venous return. On the other hand, the patient group showed an increase in end-diastolic dimension from rest to exercise and a progressive decrease in end-systolic dimension. In both groups, systolic arterial pressure was equally elevated in association with graded exercise. A decrease in end-systolic dimension against an increase in afterload signifies an augmentation of the myocardial contraction. These results indicate that in the controls the increase in stroke volume during exercise was achieved by an increase in myocardial contractility, while the primary cardiac response of the patients was both enhanced myocardial contractility and utilization of the Frank-Starling mechanism.

We have already reported that in the open-chest dog, ventricular pacing resulted in a diminution of stroke volume and arterial pressure as compared with atrial pacing at the same stimulation rate.¹¹⁾ Ventricular pacing alters

the normal left ventricular contraction pattern and produces dyssynchronous contraction with interaction between the early and late activated areas. Namely, the early activated areas of the left ventricle relax in late systole, and blood would displace into these regions.¹²⁾⁻¹⁷⁾ Thus, ventricular pacing itself would have an unfavorable effect on left ventricular performance. In this study, the patients showed an increase in stroke volume in the presence of the elevated systolic pressure, increased preload and ventricular asynchrony during exercise. It is considered that the increases in myocardial contractility and preload may have compensated for higher afterload and ventricular asynchrony, both of which oppose the increase in stroke volume.

In summary, we demonstrated that in patients with fixed rate right ventricular pacing, oxygen uptake increased 4.5 fold and maximal stroke output attained a level 1.7 fold that of the resting state. The increase in stroke output was achieved by enhanced myocardial contractility and preload reserve. Exercise testing is an important method of evaluating objectively exercise capacity and cardiovascular reserve of patients.

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