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Anaerobic Metabolism in Hypertensive Patients During Exercise Stress Test

Pietro Amedeo Modesti, Giuseppe Olivo, Franceso Pestelli, Vincenzo Guarnaccia, Gian Franco Gensini, Pier Luigi Malfanti, and Gian Gastone Neri Serneri

An impaired maximal vasodilating capacity has been reported in hypertensives. This study aimed to assess whether mild hypertensives depend on anaerobic metabolism more than do normal subjects during the exercise stress test. The oxygen uptake (V_{O_2}) and carbon dioxide output (V_{CO_2}) were measured at the anaerobic threshold (AT) and at peak exercise ($V_{O_2}p$ and $V_{CO_2}p$) during the cardiopulmonary exercise test by breath-by-breath expiratory gas analysis in 21 mild hypertensives and 19 age-matched normotensives. AT was reached earlier in hypertensives than in normotensives, but with similar V_{O_2} uptake, V_{CO_2} output, and V_{CO_2}/V_{O_2} ratio. At peak exercise, however, hypertensives showed lower $V_{O_2}p$ than controls (29 ± 5 *v* 33 ± 5 mL V_{O_2}/kg/min, ($P < .03$) but similar $V_{CO_2}p$ (36 ± 6 *v* 39 ± 6 mL V_{CO_2}/kg/min, $P = .19$). As a result, the slope of carbon dioxide output increase versus oxygen uptake after anaerobic threshold was steeper in hypertensives than in controls ($P < .002$). The higher CO_2 production per unit of O_2 in hypertensives as compared with controls seems to reflect a greater involvement of the anaerobic metabolism to supplement energy output. Am J Hypertens 1994:7:469–473

KEY WORDS: **Hypertension, exercise stress test, oxygen consumption, pulmonary ventilation.**

A reduction in both maximal oxygen consumption during the cardiopulmonary exercise test[1,2] and in coronary reserve[3] has been reported in hypertensives. More recently, a reduction in maximal O_2 consumption during the exercise test has also been reported in mild uncomplicated hypertensives.[2,4]

The reduced vascular relaxation[5–8] might impair muscle oxygen supply during the exercise stress test and make hypertensives more dependent on anaerobic metabolism than normotensives during physical exercise. For the same level of exercise more carbon dioxide (CO_2) would be generated in hypertensives than in controls. During exercise, CO_2 production increases linearly in relation to O_2 uptake. The metabolism is mainly aerobic until the anaerobic threshold is reached when V_{CO_2}/V_{O_2} approximates to 1. Thereafter if exercise is continued, anaerobic glycolysis complements the aerobic metabolism and the slope of the V_{CO_2}/V_{O_2} relationship becomes steeper.

The aim of this study was to assess in hypertensives the relationship between aerobic and anaerobic metabolism during exercise by measuring the relationship between CO_2 production and O_2 uptake at different steps of an exercise stress test.

METHODS

Subjects Twenty-one (n = 21) consecutive male subjects aged 42.5 ± 8.8 years (body weight 82.7 ± 11.9 kg, height 174 ± 8 cm), affected with essential mild hypertension (stage I according to WHO), were recruited from the hypertension unit of our department. All the hypertensives were newly diagnosed patients who had not previously received antihypertensive medication. Arterial blood pressure (BP) was

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From the Clinica Medica 1, University of Florence, Florence, Italy.

Address correspondence and reprint requests to Dr. Pietro Amedeo Modesti, Clinica Medica 1, Viale Morgagni 85, 50134 Florence, Italy.

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determined with a conventional sphygmomanometric technique at each of four separate clinical examinations. At each examination patients were allowed 3 min of rest in the seated position before three measurements were performed using first- and fifth-phase Korotkoff sounds. Blood pressures from the four examinations were averaged and patients were considered for enrollment if mean diastolic BP was higher than 90 mm Hg. Exclusion criteria included angina pectoris, recent myocardial infarction (within 6 months), heart failure, cerebrovascular accidents, clinically important renal, hepatic, or hematologic disorders, secondary hypertension, hyperkalemia or hypokalemia, and obstructive lung disease.

Nineteen normotensive males, matched for age (43.2 ± 8.6 years), body weight (76.7 ± 9.1 kg), and height (175 ± 8 cm), formed the control group.

All subjects gave informed consent. None of the investigated subjects had participated in an exercise training program.

Mono- and two-dimensional echocardiography were performed with an annular array transducer (2.5–3.5 MHz). Left ventricular internal dimensions, volumes, and wall thicknesses were measured, and ventricular mass was calculated according to the recommendations of the American Society of Echocardiography.[9] All measurements were indexed for body surface area.

Cardiopulmonary Exercise Stress Test All subjects underwent a symptom-limited treadmill test using the Bruce protocol as modified by the addition of two initial steps at low workload.

Twelve standard electrocardiographic leads were monitored with a computerized analysis of the ST segment (CASE 12, Marquette, Milwaukee, WI). Expired air was collected with a facemask for breath-by-breath quantification of ventilatory volumes and gas exchanges (Sensormedics 4400 unit, Anaheim, CA). Blood pressure was measured using a manometer cuff against mercury during the final 30 sec of each 3 min stage. Exercise duration was defined as the time (to the nearest tenth of a minute) from the onset of stage 0 to the point of test termination. In all subjects but two, the test was terminated because of fatigue and dyspnea.

The anaerobic threshold (AT) was identified as the value of O_2 consumption (Vo_2) at which the linear relation between ventilation (VE) and Vo_2 was lost, whereas the relation between VE and CO_2 consumption (Vco_2) remained steady.[10] The determination was validated by the analysis of VE/Vo_2 versus time, Vco_2 versus Vo_2, and end-tidal Po_2 versus time.[10] Oxygen consumption at peak exercise was identified as the Vo_2 value that remained unchanged during the final 30 sec of the last stage of the exercise test.

AT was independently assessed by three operators who were unaware of the test results. Interobserver variability and reproducibility of ventilatory AT and Vo_2 at peak exercise had been previously assessed in our laboratory in nine healthy normotensive control subjects and seven hypertensive patients. The variability of Vo_2 was 0.8 ± 0.7 mL/kg/min (4%) in the controls and 0.9 ± 0.8 mL/kg/min (7%) in hypertensives. Day-to-day reproducibility was satisfactorily high (r = 0.93 in normotensives v 0.87 in hypertensives).

Carbon dioxide output (Vco_2) and oxygen consumption (Vo_2) were recorded at the anaerobic threshold (AT), at 80% and 90% of the total exercise duration, and at exercise peak. The relation between Vco_2 and Vo_2 before and after AT was plotted and the slope of the line was calculated by linear regression. In addition, the slope of the increase in CO_2 output versus oxygen uptake ($\Delta Vco_2/\Delta Vo_2$) was calculated below and above the AT as follows: $\Delta Vco_2/\Delta Vo_2$ below AT = (Vco_2 at AT − Vco_2 at rest)/(Vo_2 at AT − Vo_2 at rest), $\Delta Vco_2/\Delta Vo_2$ above AT = (peak Vco_2 − Vco_2 at AT)/(peak Vo_2 − Vo_2 at AT).

Statistical Analysis Results are expressed as mean ± standard deviation. Comparisons were performed using the two-way analysis of variance and the analysis of variance for repeated measures. The interfering effects of age and the body mass index were excluded in all statistical comparisons by considering age and body mass index as covariates. All tests were performed with BMDP (BMDP Statistical Software, Los Angeles, CA).

RESULTS

Maximum workload and total exercise duration were not significantly different between hypertensives (250 ± 50 W and 953 ± 117 sec) and controls (247 ± 50 W, P = NS, and 1013 ± 67 sec, P = NS). The maximum rate–pressure product was 37461 ± 3431 in hypertensives and 34802 ± 4098 in controls ($P < .04$). All data are reported in Table 1.

Hypertensives reached the AT before normotensives (648 ± 76 sec v 744 ± 102 sec, $P < .006$) but with similar Vo_2 uptake (21.7 ± 3.3 v 22.4 ± 3.8 mL Vo_2/kg/min; P = .42). However, at AT no differences were found in the Vco_2 output between the two groups (20.8 ± 2.7 mL Vco_2/kg/min and 22.2 ± 5.1 mL Vco_2/kg/min, in hypertensives and in controls respectively, P = .14).

Instead, although the overall duration of the exercise was similar in the two groups (Table 1), Vo_2p was significantly reduced in hypertensives (29.1 ± 4.6 v 33.0 ± 5.1 mL Vo_2/kg/min; $P < .03$). The Vco_2 output was not significantly different (35.7 ± 5.9 mL Vco_2/kg/min in hypertensives v 39.0 ± 6.5 mL Vco_2/kg/min

TABLE 1. VENTILATORY AND ERGOMETRIC PARAMETERS ACHIEVED BY CONTROLS AND HYPERTENSIVES DURING THE EXERCISE TEST (AGE AND BODY MASS INDEX ARE CONSIDERED AS COVARIATES)

	Controls (n = 19)	Hypertensives (n = 21)	F	P	Age Effect F	Age Effect P	BMI Effect F	BMI Effect P
Time (sec)								
AT	744 ± 102	648 ± 76	8.37	0.006	0.00	0.95	0.01	0.91
Peak	1,013 ± 67	953 ± 117	0.70	0.30	0.58	0.44	7.74	0.008
Systolic pressure (mm Hg)								
Baseline	127 ± 17	148 ± 14	14.58	0.0005	2.30	0.14	3.12	0.08
Peak	197 ± 24	211 ± 22	3.05	0.08	4.05	0.06	0.94	0.34
Diastolic pressure (mm Hg)								
Baseline	82 ± 8	97 ± 9	28.97	0.0001	0.66	0.42	0.46	0.50
Peak	89 ± 15	101 ± 16	5.87	0.02	3.35	0.07	0.18	0.67
Heart rate (beats/min)								
Baseline	88 ± 10	93 ± 13	1.81	0.18	0.14	0.71	0.95	0.33
Peak	177 ± 12	178 ± 12	0.60	0.44	2.33	0.13	3.00	0.09
Rate-pressure product								
Baseline	11,359 ± 2,347	13,796 ± 2,640	8.19	0.007	1.10	0.30	0.13	0.72
AT	22,871 ± 3,914	23,888 ± 3,999	0.50	0.48	0.07	0.79	0.04	0.84
Peak	34,802 ± 4,098	37,461 ± 3,431	4.81	0.04	1.43	0.24	0.00	0.98
Workload (W)								
AT	159 ± 29	140 ± 40	5.39	0.03	0.03	0.87	4.26	0.04
Peak	247 ± 50	250 ± 50	0.00	0.98	2.10	0.15	0.01	0.93
Vo_2 (mL/kg/min)								
Basal	4.1 ± 1.0	5.3 ± 2.7	4.29	0.05	0.07	0.78	1.08	0.30
AT	22.4 ± 3.8	21.7 ± 3.3	0.68	0.42	0.67	0.41	0.36	0.54
Peak	33.0 ± 5.1	29.1 ± 4.6	5.08	0.03	3.09	0.08	1.91	0.17
Vco_2 (mL/kg/min)								
Basal	3.4 ± 0.8	4.4 ± 2.1	4.27	0.05	0.27	0.61	2.07	0.16
AT	22.2 ± 3.8	20.8 ± 2.7	2.23	0.14	0.06	0.81	0.89	0.35
Peak	39.0 ± 6.5	35.7 ± 5.9	1.80	0.19	2.01	0.16	2.30	0.14
$\Delta Vco_2/\Delta Vo_2$								
Below AT	1.02 ± 0.07	1.01 ± 0.11	0.14	0.71	1.04	0.31	0.25	0.60
Above AT	1.61 ± 0.27	2.01 ± 0.33	15.18	0.0004	0.88	0.35	0.02	0.88
Slope of the Vco_2/Vo_2 relationship after AT	1.60 ± 0.28	1.99 ± 0.37	11.99	0.0014	0.61	0.44	0.09	0.76

in controls; $P = .18$). As a result the $\Delta Vco_2/\Delta Vo_2$ below the AT was similar in the two groups (Table 1), whereas after AT the slope of the relationship between Vco_2 and Vo_2 was steeper in hypertensives (1.99 ± 0.37 in hypertensives *v* 1.60 ± 0.28 in controls; $P < .0014$) (Fig. 1).

DISCUSSION

A reduced Vo_2 at peak exercise, with a steeper slope of the Vco_2/Vo_2 ratio, was detectable in mild hypertensives. The increased CO_2 output per unit of consumed O_2 indicates the prevalence of the anaerobic metabolism in hypertensives.

A reduction in maximal oxygen uptake was previously reported in mild to moderate hypertensive patients both with and without left ventricular hypertrophy.[2,4] In hypertensives with left ventricular hypertrophy a lower heart rate increase was also reported, so that the occurrence of a blunted hemodynamic response to maximal treadmill exercise was suggested.[2] On the other hand, the mild uncomplicated hypertensives investigated in our study showed a reduced Vo_2p, but no differences in heart rate and systolic blood pressure responses or maximum workload attained, as compared to controls. The calculation of the Vco_2/Vo_2 ratio, an objective and reliable measurement of anaerobic metabolism unaffected by the patient's motivation, revealed a prevalent role of the anaerobic metabolism.

Hypertensives reached the anaerobic threshold earlier with a normal cardiac response and performed the largest portion of the exercise test in anaerobiosis. Various evidence indicates that cardiovascular response to exercise in hypertensives is influenced by abnormalities of the peripheral circulation rather than by central mechanisms. The underlying hypothesis is

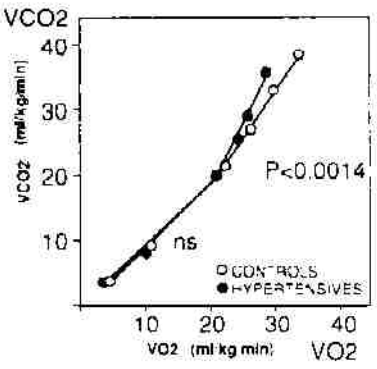

FIGURE 1. *Relation between carbon dioxide output (V_{CO_2}) and oxygen uptake (V_{O_2}) at rest and at different steps of exercise test (baseline, after 3 min of exercise, at anaerobic threshold, and at 80%, 90%, and 100% of $V_{O_2}p$) in normotensives (n = 19) and hypertensives (n = 21).*

that in hypertension the increase in blood flow to the exercising muscle is reduced, resulting in the observed reduction in O_2 consumption. Hypertensives experience a lower blood perfusion of the exercising muscle than controls despite an increased systemic blood pressure response. This pattern is mainly due to abnormalities of the vasomotor tone, with lower response to vasodilatory stimuli[8] and a relatively higher increase in peripheral vascular resistance than in controls.

The increased V_{CO_2} production per unit of consumed O_2 in hypertensives was detectable only after the anaerobic threshold, during the advanced phase of physical exercise when the exercise became strenuous and metabolic muscle requirements were maximal.[11] No differences were detectable during the early phase of physical exercise. Several sequential phases characterize the peripheral vascular response to physical exercise. The first vascular response of the exercising muscle to physical exercise is a pH- and endothelium-mediated vasodilation. The endothelium mediated component of vasodilation is reduced in hypertensives[8] and this peculiarity might be the main reason for the metabolic impairment observed in this study. However the role of endothelium-mediated vasodilation seems to be maximal during the early phases of exercise, whereas the impaired aerobic metabolism observed here seems to occur in the latter phases of physical exercise. After the initial vasodilation of the exercising muscle, two separate reflex systems increase the sympathetic outflow and play a vasoconstrictory role. The first is activated parallel to α-motor neuron unit recruitment[12] and plays an important role in heart-rate control but only a minor role in sympathetic constrictor activity to peripheral vascular beds.[13] On the other side, there is the skeletal muscle metaboreflex whose activation, operated by changes in metabolite concentrations in the interstitium of the exercising muscles,[14] increases the sympathetic outflow to skeletal muscles with only a minor influence on heart rate.[14] The latter reflex is particularly important in hypertensives, where it induces a marked reduction in blood flow to exercising muscles and might contribute to the prevalence of anaerobic metabolism.

A second important aspect to consider is the different skeletal muscle fiber composition reported in hypertension. The relative preponderance of glycolytic fast-twitch (type IIB) over oxidative fast-twitch (type IIA) or slow-twitch (type I) might lead to an impaired aerobic metabolism, resulting in the exercise response pattern described here.

However, whatever the mechanism responsible, the impaired aerobic metabolism might be an important factor in conditioning hypertensives' response to exercise. In fact, the reduced aerobic metabolism implies an increased activation of the muscle metaboreflex system,[15] with further activation in the sympathetic nervous system and further increase of peripheral vascular resistance during exercise.

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