Pediatr Cardiol 17:7–14, 1996

Pediatric Cardiology

Measurement and Validity of the Ventilatory Threshold in Patients with Congenital Heart Disease

H. Ohuchi,[1] **T. Nakajima,**[1] **M. Kawade,**[2] **M. Matsuda,**[3] **T. Kamiya**[1]

[1]Department of Pediatrics, National Cardiovascular Center, 5-7-1, Fujishiro-dai, Suita, Osaka 565, Japan
[2]Department of Pediatrics, University of Gifu, Japan
[3]Department of Pediatrics, Medical College of Fukui, Japan

Abstract. The purpose of the present study was to measure oxygen uptake ($\dot{V}O_2$) at the ventilatory threshold (VT) in patients with congenital heart disease using a progressive exercise protocol on a treadmill and to evaluate the validity and feasibility of this procedure. Eight control subjects and seventeen patients performed a maximal exercise test with breath-by-breath measurement of ventilation and gas exchange variables. VT(VE) was determined by the change in the ventilatory equivalent for $\dot{V}O_2$ and carbon dioxide output, VT(V-sl) by the V-slope method, and the lactate threshold (LT) by the change in blood lactate concentration; these parameters were determined in 100%, 88%, and 96% of subjects, respectively. The interobserver error among three evaluators was not significant, and LT was correlated with each VT ($r = 0.97$, 0.92; $p = 0.0001$) and with peak $\dot{V}O_2$ ($r = 0.91$; $p = 0.0001$). The VTs were correlated with each other when expressed as milliliter per minute and milliliters per kilogram per minute. It was concluded that a progressive exercise protocol on a treadmill was a feasible procedure for determining the VTs in most individuals and that VTs were valid, useful parameters for evaluating submaximal exercise tolerance in patients with congenital heart disease.

Key words: Lactate threshold — Ventilatory threshold — Treadmill — Congenital heart disease — Exercise tolerance

The anaerobic threshold (AT), defined as the highest oxygen uptake ($\dot{V}O_2$) above which lactic acidosis occurs, is used to predict the ability of a subject to sustain a given work rate for a prolonged period without metabolic (lactic) acidosis [21]. Because the blood lactate concentration rises at this exercise level, its increase during exercise is thought to cause a nonlinear increase in ventilation as a result of bicarbonate buffering of the excess H^+ ions of lactate in the blood and consequent production of carbon dioxide. Thus the AT can be determined noninvasively by continuous measurement of ventilatory and gas exchange variables [20–22]. In pediatric patients or healthy children, the AT has been widely applied clinically as an index of the functional state of patients with cardiac disease and to evaluate the effects of training [5, 12, 14, 17]. In adult subjects, the noninvasive ventilatory and gas exchange indices used in previous studies correlated closely with a nonlinear increase in blood lactate concentration. It has been reported that the $\dot{V}O_2$ at AT varies considerably depending on the detection method, exercise protocol, and evaluators [4, 7, 8, 13, 18]. However, few studies of this matter have been reported in pediatric patients, especially those with congenital heart disease (CHD). The purpose of the present study was to measure $\dot{V}O_2$ at the ventilatory threshold (VT) in patients with CHD using a progressive exercise protocol on a treadmill and to evaluate the validity and feasibility of the VT and exercise procedure on a treadmill.

Methods

Subjects

The subjects included 8 patients aged 8–21 years who had a history of Kawasaki disease and served as controls and 17 patients aged 7–17 years with complex CHD. The latter group consisted of patients who had undergone the following procedures: right ventricular outflow tract reconstruction for tetralogy of Fallot with pulmonary atresia ($n = 6$), modified Fontan procedure ($n = 7$), septation for a single ventricle ($n = 1$), and Mustard operation for transposition of the great arteries ($n =$

Correspondence to: H. Ohuchi

Table 1. Clinical characteristics of the subjects

Patient no.	Sex	Diagnosis	Age (years)	Height (cm)	Weight (kg)	Definitive repair	CPX	
							Protocol ramp[a]	Duration (min)[b]
1	M	History of Kawasaki disease	8	139	35	—	B	8.0
2	M	History of Kawasaki disease	9	130	29	—	B	9.0
3	M	History of Kawasaki disease	9	140	38	—	B	9.0
4	M	History of Kawasaki disease	9	138	32	—	B	9.0
5	M	History of Kawasaki disease	11	144	35	—	B	9.0
6	M	History of Kawasaki disease	12	168	58	—	B	9.0
7	M	History of Kawasaki disease	20	171	57	—	B	9.0
8	M	History of Kawasaki disease	21	174	56	—	B	9.0
9	M	TOF, PA, MAPCAS	7	114	20	RVOTR	A	8.0
10	F	TOF, PA	10	145	36	RVOTR	A	6.0
11	M	TOF, PA	11	142	41	RVOTR	B	7.8
12	M	TOF, PA	12	137	27	RVOTR	B	7.0
13	M	TOF, VT	13	151	36	RVOTR	B	9.0
14	M	TOF, PA, MAPCAS	15	167	39	RVOTR	A	8.0
15	M	UVH(RV-type), CAVC, PS, Bil-SVC	9	123	23	Fontan	A	7.0
16	F	UVH(RV-type), CAVC, PS, Bil-SVC	9	126	24	Fontan	B	5.0
17	M	UVH(RV-type), CAVC, PS, Bil-SVC	9	132	27	Fontan	B	6.0
18	M	UVH(RV-type), CAVC, PS, Bil-SVC	10	134	28	Fontan	B	7.8
19	M	UVH(DILV), TS, PS	10	131	31	Fontan	A	6.5
20	M	UVH(RV), CAVC, PA, PDA	12	135	26	Fontan	A	7.0
21	M	TA(Ia)	17	165	60	Fontan	B	9.0
22	M	UVH(LV)	10	137	30	Septation	A	5.0
23	M	TGA (I)	12	155	40	Mustard	B	7.0
24	M	UVH(RV)	13	143	35	—	A	11.0
25	M	UVH(RV)	14	166	45	TCPS	B	7.5

M, male; F, female; CPX, cardiopulmonary exercise testing; TOF, tetralogy of Fallot; PA, pulmonary atresia; MAPCAS, major aortopulmonary artery collaterals; UVH, univentricular heart; RV, right ventricle; CAVC, common atrioventricular canal; PS, pulmonary stenosis; Bil-SVC, bilateral superior vena cava; DILV, double inlet left ventricle; TS, tricuspid stenosis; PDA, patent ductus arteriosus; TA, tricuspid atresia; LV, left ventricle; TGA, transposition of the great arteries; RVOTR, reconstruction of the right ventricular outflow tract; TCPS, total cavopulmonary shunt.
[a] CPX protocol A is selected for patients who have relatively low exercise tolerance and B for patients who have relatively high exercise tolerance.
[b] Time it takes after a 3-min warm-up to walking to exhaustion.

1). Two patients with cyanotic complex CHD did not undergo definitive surgery (Table 1).

Exercise Protocol

Because of complex mechanical factors, such as the subject's varying center of gravity as the angle of the treadmill is changed and the variable length of the stride as the speed or angle is altered, it has been suggested that predicting $\dot{V}O_2$ adjustment for body weight may not be possible [23]. Walking and running are more strenuous physiologic forms of exertion than ergometric exercise and do not require special skills; this point is particularly important for children with CHD. The following equation, reported by Itoh and Taniguchi [10], predicts oxygen uptake ($\dot{V}O_2$):

$$\dot{V}O_2 \text{ (ml/kg/min)} = 0.067V^2 + 0.289VG + 7.37 \quad (1)$$

where V and G are the velocity (km/h) of the belt and its grade (%), respectively [10].

We employed a ramp-like progressive exercise test on a treadmill to demonstrate the clinical usefulness and validity of measurements of VT as well as those of peak $\dot{V}O_2$, particularly in pediatric patients with CHD. We formulated two 30-second incremental protocols on a treadmill, which we called ramp A and ramp B. In both, the incremental part of the exercise test was terminated within about 10 minutes. With the ramp A protocol, for patients who had a lower exercise capacity, exercise intensity was increased stepwise every 30 seconds by 0.5 metabolic unit (MET). With the ramp B protocol, for patients who had a relatively higher exercise capacity the increment was 0.7 MET. When determining the slope of $\dot{V}O_2$ as a function of work rate according to Eq. (1), we employed a value of 3.5 ml/kg per minute (= 1.0 MET), as reported in adults. It was derived from the resting $\dot{V}O_2$ for a 70-kg, 40-year-old man because of the difficulty determining an actual MET in children. According to equation 1 the predicted oxygen uptake at 10 minutes from the start of the progressive exercise is 42 ml/kg per minute in ramp A and 56 ml/kg per minute in ramp B in young adults.

The more suitable protocol, ramp A or ramp B, was chosen on the basis of an individual patient's daily activity, and the progressive exercise stress tests were performed on the treadmill (Q-5000 System, Quinton). Each test was begun with a 4-minute rest, after which the patient performed a 3-minute warm-up walk at 1.5 km/h (grade 0), exercising progressively until exhaustion. Before any invasive study was undertaken, each subject first performed the treadmill exercise test at least once to become accustomed to the protocol and to set a baseline for exercise tolerance (Table 2, Fig. 1).

Table 2. Progressive exercise protocol on a treadmill

Stage no.[a]	Speed (km/h)		Grade (%)		Predicted $\dot{V}O_2$ (ml/kg/min)		Predicted METS	
	A	B	A	B	A	B	A	B
Warm-up								
1	1.5	1.5	0.0	0.0	7.5	7.5	2.1	2.1
Progressive exercise								
2	1.7	1.8	2.9	4.3	8.7	9.4	2.5	2.7
3	1.9	2.1	6.4	8.4	10.5	11.9	3.0	3.4
4	2.1	2.4	9.1	11.5	12.2	14.4	3.5	4.1
5	2.3	2.7	11.4	13.8	14.0	16.8	4.0	4.8
6	2.5	3.0	13.3	15.7	15.7	19.2	4.5	5.5
7	2.7	3.3	14.9	17.3	17.5	21.7	5.0	6.2
8	2.9	3.6	16.3	18.5	19.2	24.2	5.5	6.9
9	3.1	3.9	17.5	19.5	21.0	26.6	6.0	7.6
10	3.3	4.2	18.6	20.4	22.8	29.0	6.5	8.3
11	3.5	4.5	19.5	21.2	24.5	31.5	7.0	9.0
12	3.7	4.8	20.3	21.8	26.2	33.9	7.5	9.7
13	3.9	5.1	21.0	22.3	28.0	36.3	8.0	10.4
14	4.1	5.4	21.7	22.9	29.8	38.9	8.5	11.1
15	4.3	5.7	22.3	23.3	31.5	41.3	9.0	11.8
16	4.5	6.0	22.8	23.7	33.2	43.8	9.5	12.5
17	4.7	6.3	23.3	24.0	35.0	46.2	10.0	13.2
18	4.9	6.6	23.7	24.3	36.7	48.6	10.5	13.9
19	5.1	6.9	24.1	24.6	38.5	51.1	11.0	14.6
20	5.3	7.2	24.5	24.8	40.3	53.5	11.5	15.3
21	5.5	7.5	24.8	25.0	42.0	56.0	12.0	16.0
22	5.7	7.8	25.0	25.0	43.6	58.1	12.5	16.7
23	6.0	8.2	25.0	25.0	45.6	60.9	13.0	17.4
24	6.2	8.5	25.0	25.0	47.0	63.0	13.5	18.1
25	6.5	8.9	25.0	25.0	49.0	65.9	14.0	18.8

$\dot{V}O_2$, oxygen uptake; METS, metabolic units (predicted $\dot{V}O_2$/3.5 in this protocol); A and B, ramp A and ramp B protocols using a treadmill.
[a] The warm-up lasted 3 minutes and every other exercise segment lasted 0.5 minute.

Informed consent was obtained from each subject and his or her parents. This protocol was in agreement with the guidelines of the Ethics Committee of the National Cardiovascular Center.

Gas Exchange Measurements

Ventilation and gas exchange variables were measured on a breath-by-breath basis. Subjects breathed through a mask connected to a hot-wire anemometer (Minato Medical Science, Riko AS500) for continuous measurement of inspired and expired volumes and to a mass spectrometer (Perkin Elmer, MG-300) for continuous measurement of oxygen and carbon dioxide partial pressures (PO_2, PCO_2). We used two mask sizes: one with a deadspace of 80 ml for children shorter than 150 cm, and the other with a deadspace of 100 ml for children taller than 150 cm. Derived respiratory parameters, including minute ventilation ($\dot{V}E$; BTPS), ventilatory equivalents for oxygen ($\dot{V}E/\dot{V}O_2$) and carbon dioxide ($\dot{V}E/\dot{V}CO_2$), and respiratory gas exchange ratio (R), were computed in real-time and displayed with heart rate and $\dot{V}O_2$ (STPD) on a monitor during exercise testing, using a PC-9801 NEC personal computer. Breath-by-breath data points were transformed by interpolation into plots constructed using a 30-second moving average; these data were used for analysis.

Calibration of the Gas Analyzer System

The delay times and response characteristics of the O_2 and CO_2 analyzers were checked carefully before each testing session by sampling the square-wave changes in the O_2 and CO_2 concentrations between gas calibrations.

Arterial Blood Gas Analyses

Arterial blood samples were obtained from an indwelling 22-gauge angiocath in a radial or brachial artery while the patient was at rest, 2 and 3 minutes after the warm-up walking began, and every minute during progressive exercise until exhaustion. Samples were held on ice until they were analyzed for pH, PO_2, PCO_2, and base excess (BE) (ABL3 blood gas analyzer; Radiometer, Copenhagen, Denmark) within 20 minutes of sampling. Arterial blood lactate concentration (La) was measured by an enzyme electrode.

Determinations of the Lactate Threshold and Ventilatory Thresholds

VT(VE) was defined as the $\dot{V}O_2$ at which there was an increase in $\dot{V}E/\dot{V}O_2$ without an increase in $\dot{V}E/\dot{V}CO_2$, as described by Wasserman

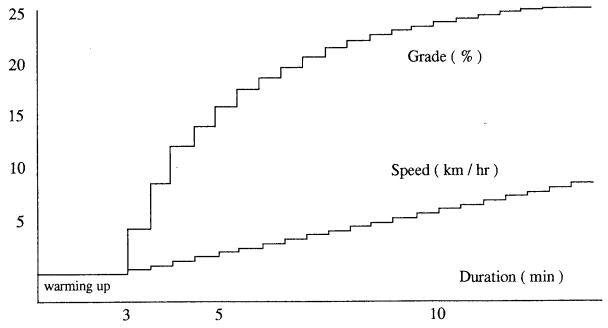

Fig. 1. Exercise protocol for ''ramp B'' on a treadmill. After 3–4 minutes of rest, each patient walked for 3 minutes and then performed progressive exercise to exhaustion. Exercise intensity was increased every 30 seconds by 0.5 metabolic units (METS) (1 MET = 3.5 ml/kg/min in this protocol) in ramp A and 0.7 METS in ramp B. The speed of the belt was increased every 30 seconds by 0.2 km/h in ramp A and by 0.3 km/h in ramp B. The grade in each protocol increased according to Itoh and Taniguchi [10]. According to this equation, the predicted oxygen uptake at 10 minutes from the beginning of the progressive exercise is 42 ml/kg/min in ramp A and 56 ml/kg/min in ramp B in young adults. See text for further explanation.

et al. [22]. VT(V-sl) was determined by the V-slope method, as reported by Beaver et al. [2], and lactate threshold (LT) was determined by regression analysis of the two-segment model plot of log[La] versus log[$\dot{V}O_2$], as described by Beaver et al. [1]. To measure interobserver variability in VT(VE) determinations, three experienced evaluators (two pediatricians and one medical practitioner) were asked to determine VT(VE) independently of each other for 13 subjects (6 controls, 7 patients with CHD). Figure 2 shows the LT, VT(V-sl), and VT(VE) determinations for one patient. The percent predicted peak $\dot{V}O_2$ (%peak $\dot{V}O_2$) as an index of individual exercise tolerance was determined from control values obtained from 117 gender- and age-matched children.

Statistical Analysis

Linear regression analysis was used to assess the correlations among the threshold values determined by the three methods and evaluators, those between the threshold values and %peak$\dot{V}O_2$, those between %peak$\dot{V}O_2$ and the ratio LT/peak$\dot{V}O_2$, and the magnitude of the change in BE from LT to peak exercise. Student's *t*-test was used to compare the measured variables of control subjects and patients with CHD, and one-factor analysis of variance was used to compare the three measured variables where appropriate. Any p value < 0.05 was taken as statistically significant, and the data are expressed as the mean ± 1 SD.

Results

Determination of the Thresholds

The LT was determined in 24 of 25 subjects (96%), VT(VE) was determined in all subjects (100%), and VT(V-sl) was determined in 22 subjects (88%).

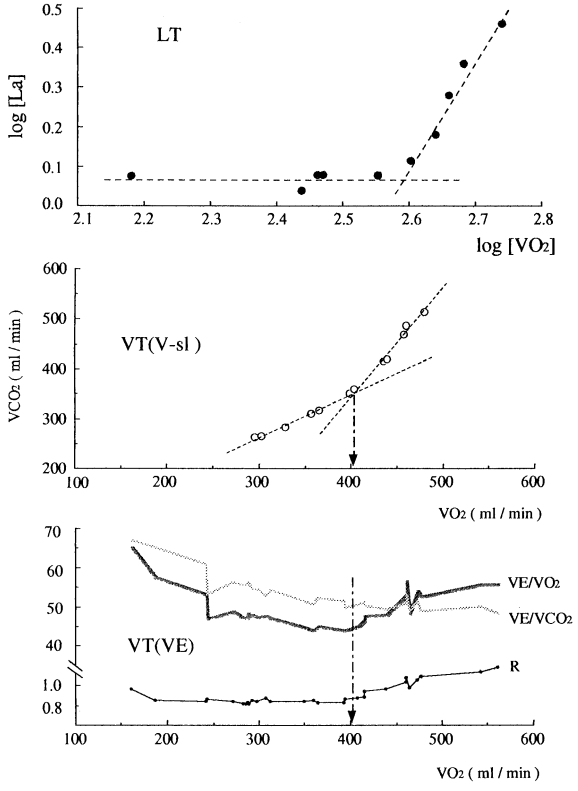

Fig. 2. Determination of lactate threshold (LT) and ventilatory threshold [VT(V-sl) and VT(VE)].

Differences Among the Threshold Values

No significant differences were observed on average between the values of LT, VT(V-sl), and VT(VE) when expressed as milliliters per minute and those expressed as milliliters per kilogram per minute (Table 3). VT(V-sl) and VT(VE) were correlated with LT (r = 0.80, p = 0.0001 and r = 0.91, p = 0.0001, respectively), and VT(VE) was correlated with VT(V-sl) (r = 0.93, p = 0.0001) (Table 4).

Differences Among the Three Evaluators (Interobserver Error)

No significant difference in $\dot{V}O_2$ at VT(VE) was observed between the determinations of three experienced evaluators (Table 3), and no significant differences from zero were observed on average. Each value determined by the three evaluators correlated well with LT, VT(V-sl), and each other (each p = 0.0001) (Table 4).

Table 3. Variability in VO_2 at threshold as a result of disease, method of evaluation and evaluator

Variable	No.	VO_2 at threshold				Threshold/peak VO_2 ratio	
		(ml/min)	Significance	(ml/kg/min)	Significance	(%)	Significance
Disease							
LT							
Control	8	966 ± 276	$p < 0.001$	22.9 ± 2.8	$p < 0.03$	49.4 ± 8.7	$p < 0.0005$
CHD	16	609 ± 179		18.5 ± 4.5		66.5 ± 9.8	
VT(V-sl)							
Control	8	859 ± 199	$p < 0.02$	20.7 ± 3.8	NS	44.6 ± 9.5	$p = 0.0001$
CHD	14	612 ± 207		18.3 ± 5.0		67.6 ± 9.0	
VT (VE)							
Control	8	946 ± 267	$p < 0.003$	22.5 ± 3.2	NS	48.4 ± 9.0	$p = 0.0001$
CHD	17	620 ± 207		19.2 ± 5.1		68.5 ± 8.1	
Method							
LT	24	728 ± 272		20.0 ± 4.5		60.8 ± 12.3	
VT(V-sl)	22	701 ± 233	NS	19.2 ± 4.6	NS	59.2 ± 14.4	NS
VT (VE)	25	724 ± 271		20.2 ± 4.8		62.1 ± 12.6	
Evaluator							
A	13	801 ± 272		20.7 ± 4.8		60.8 ± 14.2	
B	13	816 ± 262	NS	21.1 ± 4.3	NS	62.5 ± 15.4	NS
C	13	799 ± 282		20.7 ± 5.0		60.1 ± 12.9	

Values are the mean ± SD.
VO_2, oxygen uptake; LT, lactate threshold; CHD, congenital heart disease; VT(VE), ventilatory threshold determined by the criteria of ventilatory equivalents for O_2 uptake and CO_2 output; VT(V-sl), VT determined by the V-slope method.

Table 4. Correlations among VO_2 values at threshold according to method and evaluator

Variable	No.	LT	VT(V-sl)	Evaluator		
				A	B	C
Method						
LT	24	—				
VT(V-sl)	22	0.80 (0.90)	—			
VT(VE)	25	0.91 (0.96)	0.93 (0.96)			
Evaluator						
A	13	0.89 (0.96)	0.90 (0.94)	—		
B	13	0.77 (0.90)	0.87 (0.93)	0.91 (0.95)	—	
C	13	0.85 (0.95)	0.85 (0.91)	0.97 (0.99)	0.88 (0.94)	—

Numbers in parentheses are the correlation coefficient (r) when values (VO_2) are expressed as milliliters per minute.
VO_2, oxygen uptake; LT, lactate threshold. VT(VE), ventilatory threshold determined by the criteria of ventilatory equivalents for O_2 uptake and CO_2 output; VT(V-sl), VT determined by the V-slope method.

Comparison of the Three Thresholds in Control Subjects Versus Patients with Congenital Heart Disease

Each mean value of LT, VT(V-sl), and VT(VE) in patients with CHD was significantly lower than that in control subjects ($p < 0.02 \sim 0.001$) when expressed as milliliters per minute. On the other hand, only the mean LT was significantly lower than that of control subjects ($p < 0.03$) when expressed as milliliters per kilogram per minute (Table 3).

Relation Between LT and Exercise Tolerance

Lactate threshold (ml/kg/min) was significantly correlated with peak $\dot{V}O_2$ (ml/kg/min) ($r = 0.75$, $p = 0.0001$), as illustrated in Figure 3. The correlation was

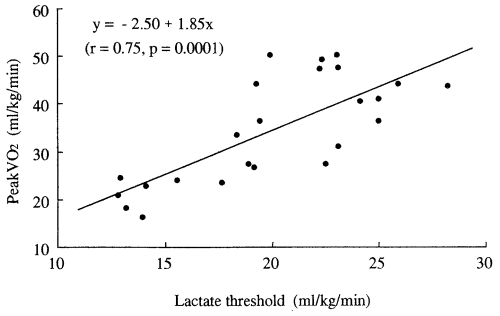

Fig. 3. Correlation between peak $\dot{V}O_2$ and lactate threshold.

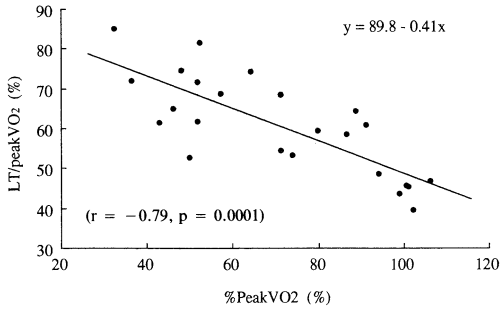

Fig. 4. Correlation between LT/peak $\dot{V}O_2$ ratio and %peak$\dot{V}O_2$.

stronger ($r = 0.91$, $p = 0.0001$) when the value was expressed as milliliters per minute. A significant negative correlation between the LT/peak$\dot{V}O_2$ ratio and %peak$\dot{V}O_2$ was also observed, as illustrated in Figure 4; and the difference in the ratio between controls and patients with CHD was significant ($p < 0.0005$). This result means that exercise tolerance above LT (anaerobic exercise tolerance) was lower in patients with CHD, and its increase was more significant in the increase in peak$\dot{V}O_2$ in controls.

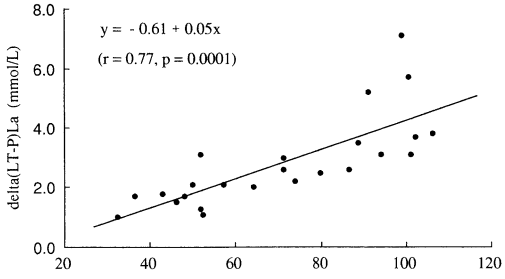

Fig. 5. Correlation between the increase in lactate from LT to peak exercise [Δ(LT − P)La] and %peak$\dot{V}O_2$.

Relation Among the Increase in Lactate Concentration, Decrease in BE from LT to Peak Exercise, and Exercise Tolerance

Both the increase in lactate concentration and the decrease in BE from LT to peak exercise were correlated with the %peak$\dot{V}O_2$ ($r = 0.77$, $p = 0.0001$ and $r = -0.62$, $p = 0.001$, respectively) (Figs. 5, 6). The change in acid–base balance was defined by the exercise capacity over the LT.

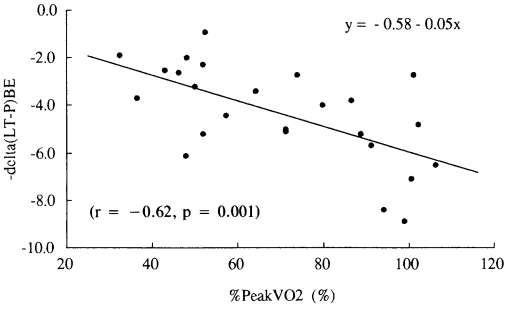

Fig. 6. Correlation between the decrease in base excess from LT to peak exercise [Δ(LT −P)BE] and %peak$\dot{V}O_2$.

Discussion

Controversy continues regarding the definition of ''anaerobic threshold'' [9, 19, 25]. Many investigators, however, have recognized a phenomenon of abrupt increase in lactate concentration as exercise intensity increases and metabolic (lactic) acidosis develops. To detect the threshold precisely and objectively, several methods have been developed, including the V-slope method, the log-log transformation of lactate concentration and $\dot{V}O_2$, and the ramp exercise protocol [24]. the validity of these methods and their reproducibility have been studied in adults [4, 6–8, 13, 18, 20], but there have been few such studies in pediatric patients, including those with CHD.

The LT and VT, as indices of cardiorespiratory function during exercise in patients with CHD and in healthy children, have been studied by Reybrouck et al. [14, 15], Cooper et al. [5], and other investigators; and variations with age, gender, and physical activity have been evaluated as well. Previous studies, however, were performed in children who had relatively good physical function; they included healthy children, patients with a left-to-right intracardiac shunt, or those who had undergone an operation for an atrial septal defect [16]. We selected 25 patients whose exercise tolerance ranged widely from cyanotic CHD to those with a history of Kawasaki disease who had normal exercise tolerance, and investigated the relation between LT and VT and between these parameters and %peak$\dot{V}O_2$. Furthermore, we attempted to confirm the clinical validity and feasibility of our original protocol for measuring such thresholds.

In a conventional incremental protocol, such as the Bruce protocol (familiar to pediatricians), there is a rate of increase in work rate that is inappropriate for patients with low exercise tolerance. Therefore we developed a ramp-like progressive exercise protocol so the patients could perform exercise testing safely and we could determine the LT and VT without difficulty.

With 1 minute of incremental exercise on a treadmill as a ramp protocol on a cycle ergometer, as proposed by Whipp et al. [24], the validity and feasibility of the detecting the AT and the maximum $\dot{V}O_2$ were demonstrated by Davis et al. [7]. In children, however, especially those with CHD who have a low exercise tolerance, few studies have been reported.

In 1 of our 25 subjects (4%) the LT was difficult to analyze by two-segment linear regression because of a steady increase in lactate concentration. VT(VE) was determined in each case (100%). VT(V-sl) was not determined in 3 of 25 subjects (12%) because a steady increase in R made it difficult to find the intersection by two-segment linear regression lines in the $\dot{V}CO_2$ versus $\dot{V}O_2$ plots. In previous studies by Caiozzo et al. [4], Davis et al. [6], and Wasserman et al. [22], the probability of determining the VT(VE) by one parameter of R was relatively low compared with that for the other ventilatory and gas exchange parameters. It is our impression that VT(VE) can be determined without difficulty [4, 6]. For the detection of LT, VT(V-sl), and VT(VE), there was no significant difference in the proportion of the determinable ratio ($df = 2$, total $\chi^2 = 0.102$, NS). In previous pediatric studies there has been no discussion about cases in which thresholds could not be determined. In 257 healthy children aged 5–18 years, VT(VE) was determined for all subjects by Reybrouck et al. [14]. On the other hand, in a study by Cooper et al. [5] VT(VE) was not determined in 5 of 114 children (4%) aged 6–17 years. In our previous study of 73 healthy subjects 5–24 years, VT(VE) was not determined in 5 (7%) [11]. In our experience with young children who are not accustomed to exercise testing, measurements of gas exchange variables tended to fluctuate, and it was therefore difficult to detect the thresholds. To avoid these obstacles, we made the following modifications: First, we considered a ramp-like protocol on a treadmill to be as suitable as that on a bicycle [24]; second, each patient was allowed to become accustomed to the protocol; and third, the values measured breath-by-breath were transformed by interpolation into plots constructed using a 30-second moving average. After these procedures, the VT was determined in most subjects in this study.

Both VT(VE) and VT(V-sl) correlated well with LT. Correlation coefficient values of the three thresholds expressed as milliliters per minute were higher than those expressed as milliliters per kilogram per minute, as previously noted [4]. The differences in $\dot{V}O_2$ that resulted from changes in the method were not significant on average. However, a difference in $\dot{V}O_2$ of >4.0 ml/kg per minute at threshold according to the three methods was observed in 3 of 24 subjects (12.5%) when LT and VT(V-sl) were compared, and in 1 each (4%) when LT and VT(VE) or VT(VE) and VT(V-sl) were compared (Table 5). Theoretically, the values of both VT(VE) and VT(V-sl) might be expected to be slightly higher than that of LT [3]. Probably because the 1-minute sampling interval of lactate concentration was adequate to cause this error, no difference was observed in this study among the three thresholds, as reported by Beaver et al. [3], Dickstein et al. [8], and Shimizu et al. [18]. Interobserver error, on average, was also not significant among the experienced evaluators, but the difference among the values according to A, B, and C (Table 6) was > 4.0 ml/kg per minute in 2 of 13 cases (15%), similar to the difference observed as a result of the three methods (Table 6). It may cause a problem in clinical applications for accurate evaluation of exercise tolerance in patients with CHD.

Table 5. Differences in VO_2 at threshold according to method

Difference (ml/kg/min)	LT − VT(VE)	LT − VT(V-sl)	VT(VE) − VE(V-sl)
0–2.0	18 (75%)	16 (67%)	16 (73%)
2.0–4.0	5 (21%)	5 (21%)	5 (23%)
4.0–	1 (4%)	3 (12%)	1 (4%)

VO_2, oxygen uptake; LT, lactate threshold; VT(VE), ventilatory threshold determined by ventilatory equivalents for O_2 uptake and CO_2 output; VT(V-sl), VT determinede by the V-slope method.

The difference in the threshold/peak$\dot{V}O_2$ ratio between controls and patients with CHD was greater than the difference in $\dot{V}O_2$ at threshold (Table 3). An increase in anaerobic exercise tolerance influenced individual exercise tolerance, especially in patients with relatively high exercise tolerance. The correlation must thus have been stronger between VT or LT and peak$\dot{V}O_2$ in patients with low exercise tolerance compared with that in patients with relatively high exercise tolerance, and it was suggested that VT was more useful for predicting peak$\dot{V}O_2$, especially in patients with CHD with low exercise tolerance.

Judging from changes in lactate concentration and BE during progressive exercise, the magnitude of the change in the acid–base balance was apparently influenced by the exercise capacity above threshold in the pediatric patients, as it is in adults.

These data demonstrate that even in pediatric patients with poor exercise tolerance metabolic acidosis does occur during progressive exercise, and VT(VE) and VT(V-sl) can be determined in most patients by continuous ventilatory and gas exchange measurements using our original exercise protocol on a treadmill. These VTs

Table 6. Differences in VO_2 at threshold according to evaluator

Difference (ml/kg/min)	A − B	A − C	B − C
0–2.0	10 (77%)	11 (85%)	10 (77%)
2.0–4.0	1 (8%)	2 (15%)	1 (8%)
4.0–	2 (15%)	0 (0%)	2 (15%)

VO_2, oxygen uptake.
A, B, and C are experienced evaluators.

were useful for evaluating exercise tolerance in pediatric patients with CHD, although differences that should be considered when evaluating submaximal exercise tolerance, as noted in studies of adults [8, 18, 20], were observed in $\dot{V}O_2$ at VTs that resulted from using different methods and evaluators.

References

1. Beaver WL, Wasserman K, Whipp BJ (1985) Improved detection of lactate threshold during exercise using a log-log transformation. *J Appl Physiol 59*:1936–1940
2. Beaver WL, Wasserman K, Whipp BJ (1986) A new method for detecting anaerobic threshold by gas exchange. *J Appl Physiol 60*:2020–2027
3. Beaver WL, Wasserman K, Whipp BJ (1986) Bicarbonate buffering of lactic acid generated during exercise. *J Appl Physiol 60*: 472–478
4. Caiozzo VJ, Davis JA, Ellis JF, Azus JL, Vandagriff R, Prietto CA, McMaster WC (1982) A comparison of gas exchange indices used to detect the anaerobic threshold. *J Appl Physiol 53*:1184–1189
5. Cooper DM, Weeiler-Ravell D, Whipp BJ, Wasserman K (1984) Aerobic parameters of exercise as a function of body size during growth in children. *J Appl Physiol 56*:628–634
6. Davis JA, Frank MH, Whipp BJ, Wasserman K (1979) Anaerobic threshold alterations caused by endurance training in middle-aged men. *J Appl Physiol 46*:1039–1046
7. Davis JA, Vodak P, Wilmore JH, Vodak J, Kurts P (1976) Anaerobic threshold and maximal aerobic power for three modes of exercise. *J Appl Physiol 41*:544–550
8. Dickstein K, Barvik S, Aarsland T, Snapinn S, Karlsson J (1990) A comparison of methodologies in detection of the anaerobic threshold. *Circulation 81* [Suppl II]:38–46
9. Green HJ, Hughson RL, Orr GW, Ranney DA (1983) Anaerobic threshold, blood lactate, and muscle metabolites in progressive exercise. *J Appl Physiol 54*:1032–1038
10. Itoh H, Taniguchi K (1989) Ramp exercise testing for patients with heart failure (in Japanese). *Coronary 6*:41–49
11. Ohuchi H (1993) Anaerobic threshold in children: evaluation of anaerobic threshold with ramp treadmill exercise testing (abstract). *Acta Cardiol Paediatr Jpn 8*:493
12. Palgi Y, Gutin B, Young J, Alejandro D (1984) Physiologic and anthropometric factors underlying endurance performance in children. *Int J Sports Med 5*:67–73
13. Poster JD, Gorman KM, Klein HS, Cline CJ (1987) Ventilatory threshold: measurement and variation with age. *J Appl Physiol 63*:1519–1525
14. Reybrouck T, Weymans M, Stijns H, Knops J, van der Hauwaert L (1985) Ventilatory anaerobic threshold in healthy children. *Eur J Appl Physiol 54*:278–284
15. Reybrouck T, Weymans M, Stijns H, von der Hauwaert LG (1986) Ventilatory threshold for evaluating exercise performance in children with congenital left-to-right intracardiac shunt. *Pediatr Cardiol 7*:19–24
16. Reybrouck T, Bisschop T, Dumoulin M, von der Hauwaert LG (1991) Cardiorespiratory exercise capacity after surgical closure of atrial septal defect is influenced by the age at surgery. *Am Heart J 122*:1073–1078
17. Rowland TW, Green GM (1989) Anaerobic threshold and the determination of training target heart rates in premenarchal girls. *Pediatr Cardiol 10*:75–79
18. Shimizu M, Myer J, Buchanan N, Walsh D, Kraemer M, McAuley P, Froelicher VF (1991) The ventilatory threshold: method, protocol, and evaluator agreement. *Am Heart J 122*:509–516
19. Stanley WC, Gertz EW, Wisneski JA (1985) Systemic lactate kinetics during graded exercise in man. *Am J Physiol 249*:595–602
20. Surtin MJ, Cobb FR (1990) The anaerobic threshold in chronic heart failure. *Circulation 81* [Suppl II]:47–58
21. Wasserman K (1984) The anaerobic threshold measurement in exercise testing. *Clin Chest Med 5*:77–88
22. Wasserman K, Whipp BJ, Koyal SN, Beaver WL (1973) Anaerobic threshold and respiratory gas exchange during exercise. *J Appl Physiol 35*:236–243
23. Wasserman K, Hansen JE, Sue DY, Whipp BJ (1987) *Protocol for exercise testing: principles of exercise testing and interpretation.* Lea & Febiger, Philadelphia, pp 58–71
24. Whipp BJ, Davis JA, Torres F, Wasserman K (1981) A test to determine parameters of aerobic function during exercise. *J Appl Physiol 50*:217–221
25. Yeh MP, Gardner RM, Adams TD, Yanowitz FG, Crapo RO (1983) ''Anaerobic threshold'': problems of determination and validation. *J Appl Physiol 55*:1178–1186