Very Early Lactate Threshold in Healthy Young Men as Related to Oxygen Uptake Kinetics

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Abstract: We assessed the correspondence between the V-slope ventilatory threshold (VT) and the lactate threshold (LT) by using a distinctive slow submaximal ramp protocol to ensure that sufficient data points exist around the threshold. Twenty healthy young men participated. A submaximal test based on a prior maximal test (25 watt/min, medium ramp) was performed with an individual slow-ramp protocol (6–17 watt/min, slow ramp), in which the time to reach the VT workload was estimated to be 10 minutes. The LT was determined visually by detecting a rise above the resting value, without or with log–log transformation (LT1, LT2). The point at which the blood lactate exceeded the minimal difference (LMD) of 2 resting values was also calculated.

The VT appeared significantly earlier under the slow-ramp protocol compared to the medium-ramp protocol (from 19.3 ± 3.9 to 15.0 ± 4.0 mL/kg/min VO2, P < 0.001). The mean LT1 and LT2 values appeared even earlier than the VT (LT1, P = 0.004; LT2, P = 0.002) (LT1, 11.9; LT2, 13.4; LMD, 17.0; VT, 15.0 mL/kg/min VO2). As the percent of peak VO2 each occurred at 29.9%, 33.7%, 42.5%, and 37.8%. The VT correlated significantly with LT1, and LMD (r = 0.61, 0.64, 0.80; P = 0.004, 0.002, <0.001). Mean blood lactate showed a similar trend (1.30, 1.43, 1.81, 1.68 mmol/L, respectively).

Furthermore, the ΔVO2/Δ work rate slope increased (from 10.8 ± 0.9 to 11.5 ± 0.9; P = 0.01) with the slow ramp, and the lower LT was associated with the greater increase in slope (LT1, r = −0.47, P = 0.03; LT2, r = −0.59, P = 0.005), that is, the lower LT was an indication that on the faster medium ramp the slope would decrease. The LMD and VT did not show this relation.

Under slow-ramp exercise testing in healthy young men, the VT appeared earlier than under medium-ramp exercise testing. In addition, the LT appeared even earlier (at approximately 30% of peak VO2) than the VT, although they correlated. This very early onset of LT was, however, associated with evidence of reduced oxygen uptake kinetics.

INTRODUCTION

The lactate threshold (LT) and the ventilatory threshold (VT)—determined by using respiratory measures—are the 2 most common submaximal measures of exercise tolerance.1,2 LT and VT are generally considered to agree with each other,3 but this remains controversial.5

The purpose of the present study was to assess how closely VT and LT correspond to each other, by using a special exercise protocol devised for this purpose. Most of the previous studies with lactate sampling during incremental exercise used a maximal exercise protocol.1,4–6 Blood was sampled throughout the exercise period, resulting in fewer sampling points at the most critical period near the threshold. We devised a submaximal slow-ramp protocol that lasted for 12 minutes, during which the subjects would exercise only to a point just beyond VT. With this exercise protocol we expected to obtain a longer and stable pre-LT baseline.

In addition, after closely examining previous studies which included individual lactate curves,4–6 we were impressed that some young normal subjects (10%–30%) exhibited arise in the lactate level very early or almost immediately after the start of incremental exercise, although it is generally agreed that LT occurs at approximately 50% of the oxygen uptake (VO2)max in normal subjects.1,7 These features were mentioned by some of the authors themselves.4,5 We wondered whether the variability of LT as the percentage of VO2max in normal subjects might be much larger, particularly toward the lower end, and if this is true, is there a physiological significance to the very low LT in normal subjects in terms of oxygen uptake kinetics? The rise of lactate is generally considered to represent a limitation in oxygen availability in the working muscle, and it is associated with a less-fit condition for aerobic exercise.1

We chose to primarily use the V-slope method (VO2 vs carbon dioxide output [VCO2] plot) to determine the VT. Relative to 2 other conventional methods using ventilatory equivalents and end-tidal gas concentrations,1 it is assumed that the V-slope method more directly corresponds to changes in lactate levels because the acid component (H+) of lactic acid is buffered by HCO3–, producing excess CO2 which is not derived from oxidative phosphorylation1 (the term “nonmetabolic excess CO2” is used here in accord with the literature).9

Abbreviations: BP = break point, LMD = lactate above minimal difference, LOA = level of agreement, LT = lactate threshold, LT1 = lactate threshold determined from raw data, LT2 = lactate threshold determined after log–log transformation of data, VA = alveolar ventilation, VCO2 = carbon dioxide output, VE = minute ventilation, VO2 = oxygen uptake, VT = ventilatory threshold.
METHODS

Participants
The study participants were 20 healthy male college students: 10 were members of various college sports clubs (although not at an intercollegiate level), and the remaining 10 were less physically active. Their mean age was 21.0 ± 2.4 years, the mean height was 175.0 ± 6.3 cm, and the mean weight was 66.6 ± 10.2 kg. Written informed consent was obtained from all participants before the study.

Exercise Testing
Cardiopulmonary exercise testing was performed by using a stationary bicycle (StrengthErgo 8; Mitsubishi Electric Engineering, Tokyo) and a breath-by-breath gas analyzer (AE-300S; Minato Ikagaku, Tokyo). Exercise tests were carried out on 2 separate days. Maximal exercise was performed by using a ramp protocol of 25 watt/min on day 1 (medium ramp), and submaximal exercise of 6 to 17 watt/min (slow ramp) was performed on day 2. The submaximal test was based on the day 1 test results and was designed to allow the individual participants to reach VT in approximately 10 minutes.

Each participant performed the tests in the afternoon at approximately the same time 1 week apart. The submaximal exercise duration was set to a total of 12 minutes. Ramp exercise was always preceded by a 2-minutes warm-up period at 20 watts during the maximal and 10 watts during the submaximal exercise protocol. The gas analyzer was calibrated for volume and O2 and CO2 concentrations before each test. For the gas data analysis, 10-second means from the gas analyzer system were used.

Blood Lactate Sampling
Blood was sampled by using a finger-stick device. Three fingers (the left 3rd, 4th, and 5th) were prepared by the application of a topical vasodilator (Finalgon cream, nonivafarming, Tokyo) and a breath-by-breath gas analyzer (AE-300S; Minato Ikagaku, Tokyo). Exercise tests were carried out on 2 separate days. Maximal exercise was performed by using a ramp protocol of 25 watt/min on day 1 (medium ramp), and submaximal exercise of 6 to 17 watt/min (slow ramp) was performed on day 2. The submaximal test was based on the day 1 test results and was designed to allow the individual participants to reach VT in approximately 10 minutes.

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entire V-slope and the lactate curve of the same participant (Figure 1A,B).

The point where the V-slope crossed the diagonal line of \( R = 1 \) during the submaximal testing (R1P) was determined. In 8 participants, the submaximal exercise test ended before the lines crossed each other. All 20 cases of co-plots are included in Supplementary File S1, http://links.lww.com/MD/A416.

Oxygen Uptake Kinetics (\( \Delta VO_2/\Delta \text{Work Rate} \))

The VO2–work rate relation\(^1,16\) during ramp exercise testing was evaluated by plotting the work rate on the x-axis and VO2 on the y-axis. Both maximal and submaximal exercise data were plotted on the same graph. The initial time delay was removed from the analysis.\(^16\) Each slope was calculated by using linear regression for the max and submax tests, respectively. All 20 plots showing this relation are included in Supplementary File S2, http://links.lww.com/MD/A416.

Statistical Analysis

Results are given as mean ± SD. Paired data were compared by means of a repeated measures analysis of variance (ANOVA) followed by the Holms test for pairwise comparison. Correlations between variables were assessed by using Pearson correlation coefficients (r). Statistical analyses were performed with Statistics for Excel 2012 (Social Survey Research Information Co., Tokyo).

When assessing the agreement of VT and LT qualitatively, we used a reported level of agreement of VT (200 ML/kg/min \( VO_2 \)) as an index of agreement between the 2.\(^{17}\) Our experience (170 ML/kg/min \( VO_2 \)) also generally agrees with the above reported level of agreement.

This research protocol was approved by the institutional review board of Sapporo Ryokuai Hospital.

RESULTS

The basic exercise data are summarized in Table 1. Except for the VT (max) and peak (max) values, the values were those obtained during submaximal exercise. As shown in Table 2, during submaximal testing using the slow ramp, VT appeared unexpectedly much earlier than it did under maximal testing using the 25-watt/min ramp (VT, from 19.3 ± 3.9 to 15.0 ± 4.0 mL/kg/min \( VO_2 \), \( P < 0.001 \)). Therefore, VT as the percentage of the peak fell from 48.6 ± 7.4% to 37.8 ± 8.2%.

All 20 cases showing the changes in the V-slope VT induced by the ramp shift from the medium to slow ramp are included in Supplementary File S3, http://links.lww.com/MD/A416. In line with this, the lactate thresholds also appeared very early, only at 29.9% ± 9.1% (LT1) and 33.7% ± 7.3% (LT2), respectively, of the peak VO2, whereas LMD appeared at 39% of the peak VO2.

### TABLE 1. Basic Exercise Data Summary

|                         | Medium Ramp (Day 1) | Slow Ramp (Day 2) |
|-------------------------|---------------------|-------------------|
| Peak heart rate, bpm    | 183.0 ± 12.9        | 144.0 ± 19.6*     |
| Peak work rate, watt    | 231.9 ± 39.1        | 134.8 ± 35.4*     |
| Ramp protocol, watt/min | 25                  | 10.5 ± 2.9*       |
| Exercise time, second   | 514.2 ± 92.1        | 720*              |
| Peak VO2 weight*, mL/kg/min | 39.7 ± 5.0       | 27.0 ± 6.3*       |
| Peak R                  | 1.19 ± 0.07         | 1.01 ± 0.05*      |
| Peak lactate, mmol/L    | 7.18 ± 1.81         | 4.05 ± 1.15*      |

Values are mean ± SD of 20 participants. \( R = \) respiratory exchange ratio, \( VO_2 = \) oxygen uptake.

\(^* P < 0.001\) compared to medium ramp (day 1).
were significantly correlated with VT (VT vs LT1, ¼ 0.79; VT vs LT2, ¼ 0.64, P < 0.001). Additionally, the mean lactate level at VT during maximal exercise tended to be less than that at the corresponding VO2 during submaximal exercise (2.6 vs 3.3 mmol/L, P < 0.05 versus LT2).

As shown in Figure 2, the LTs and LMD (mL/kg/min VO2) were significantly correlated with VT (VT vs LT1, r = 0.61, P = 0.004; VT vs LT2, r = 0.64, P = 0.002; VT vs LMD, r = 0.80, P < 0.001), and they were also significantly correlated with each other (LT1 vs LT2, r = 0.81; LT1 vs LMD, r = 0.84; LT2 vs LMD, r = 0.79; P < 0.001). Additionally, the mean lactate level at VT during maximal exercise tended to be less than that at the corresponding VO2 during submaximal exercise (2.6 vs 3.3 mmol/L, P = 0.08).

When examined individually in 10 cases, LT1 agreed with VT within 200 mL of VO2. In the other 10 cases, however, LT1 appeared much earlier. In these latter 10 cases, the first lactate BP (LT1) was not detected at all by the V-slope. A typical example of this is shown in Figure 1A. Such cases are marked accordingly in Supplementary File S1, http://links.lww.com/MD/A416. We reasoned that in these cases the initial CO2 storage (rightward shift of the V-slope) obscured the increasing lactate level (leftward shift). The mean LT2 (log–log transformation) was somewhat higher. LT2, because of log transformation, probably tended to capture a change in slope as it did not assume the initial flat or level line before the threshold. The mean LMD (minimal difference method), although very close to VT, did not fall on any particular BP.

The mean blood lactate level at LT1 was not different from that at rest because it assumed a flat segment without any lactate increase before the threshold (see the LT determinations in the Methods section). The mean LT2 lactate level was significantly greater than the resting lactate level but slightly lower than the mean lactate level at VT (P < 0.001). The mean LMD was significantly greater than the mean VT lactate level (P = 0.03). The mean lactate at VT was 1.68 mmol/L, only slightly lower than the onset of the blood lactate accumulation of 2 mmol/L10 and, on the average, approximately 0.4 mmol/L above the resting lactate value.

In order to assess whether these low thresholds (LT, VT) brought about by a slow ramp were physiologically meaningful, we sought to determine the relation with oxygen uptake kinetics (ΔVO2/Δ work rate). As a group the mean ΔVO2/Δ work rate

| TABLE 2. VO2 weight−1, HR, and Lactate at Each Stage |
|--------------------------------|------------------|------------------|
| VO2 weight−1, mL/kg/min | HR, bpm | Lactate, mmol/L |
|------------------------|---------|----------------|
| Rest | 4.4 ± 0.6 | 77.9 ± 5.7 | 1.29 ± 0.25 |
| LT1 | 11.9 ± 4.2** | 95.9 ± 14.6** | 1.30 ± 0.25 |
| LT2 | 13.4 ± 3.4** | 100.1 ± 13.6** | 1.43 ± 0.30** |
| LMD | 17.0 ± 5.0** | 110.6 ± 14.1** | 1.81 ± 0.25** |
| VT (slow ramp) | 15.0 ± 4.0** | 104.5 ± 12.3** | 1.68 ± 0.33** |
| VT (medium ramp) | 19.3 ± 3.9 | 124.8 ± 18.3 | |
| R1P (slow ramp) | 23.5 ± 6.3 | 131.4 ± 14.8 | 2.97 ± 0.64 |
| Peak (medium ramp) | 39.7 ± 5.0 | 183.0 ± 12.9 | 7.18 ± 1.81 |

Values are mean ± SD of 20 participants. LMD = lactate above minimal difference, HR = heart rate; LT = lactate threshold; VT = ventilatory threshold; R1P = the point where the V-slope crosses the diagonal line of R = 1.0. In 8 cases, R1P was not observed.

* P < 0.05 versus rest (repeat ANOVA followed by Holm adjusted for 5 comparisons).
** P < 0.001 versus LT2.
§ P < 0.001 versus LT1.
‖ P < 0.001 versus LT2.
‖‖ P < 0.001 versus R1P.
\$ P < 0.05 versus LMD. Statistical tests were performed only for rest, LT1, LT2, LMD, and VT (slow ramp).

FIGURE 2. Relationship between the lactate threshold (LT1, LT2, LMD) and VT with the submaximal protocol. The tendency for LT1 and LT2 points to appear earlier than VT is readily seen. LMD = lactate above minimal difference, LT1 = lactate threshold determined from raw data, LT2 = lactate threshold determined after log–log transformation of data, VT = ventilatory threshold.
increased significantly from 10.8 ± 0.9 (max) to 11.5 ± 0.9 (submax) (P = 0.03). The co-plotting of the VO2–work rate relation during the maximal and submaximal protocols in each case showed that in 7 of the 20 cases (#7, #9, #11, #14, #15, #18, and #20), there was visually a very early clear departure of 2 plots or slopes soon after the start of the ramp protocol, instead of midway through the exercise (at VT) as reported in normal individuals.1,18

As shown in Figure 3, the degree of improvement or increase in the ΔVO2/Δ work rate slope from the medium ramp to the slow ramp was significantly correlated with LT1 and LT2 (r = −0.47, P = 0.03; r = −0.59, P = 0.005), that is, the lower LT was an indication that on the faster medium ramp the slope would decrease, indicating reduced oxygen uptake kinetics. The increase in the ΔVO2/Δ work rate slope did not correlate with LMD or VT, but it significantly correlated with the peak VO2 (r = −0.49, P = 0.02).

Interestingly, although the blood lactate level had generally exhibited an exponential or curvilinear increase, as reported in previous incremental exercise studies,1,3,10,19 in the present study, 11 cases (#4, #5, #7, #10, #14, #15, #16, #17, #18, #19, and #20) visually exhibited a step-like pattern with multiple BPs, particularly during the lighter work rate. Likewise some V-slopes exhibited a similar pattern, an example is shown in Figure 1B. All 20 individual graphs of the V-slope and lactate curve are provided in Supplementary File S1, http://links.lww.com/MD/A416.

The ventilatory equivalent and end-tidal methods detected VT in only 10 participants under the submaximal protocol, although it was detected for all participants under the maximal protocol.

The results of the VT and LT validation analyses were as follows. The mean S1 (slope) was not significantly different from 1 (mean slope ± SD, 0.993 ± 0.081; P = 0.687). When the next data point was added in the analysis, the average S1 was already significantly different from 1 (mean slope ± SD, 1.051 ± 0.101; P = 0.035). Subsequent analyses yielded the same results (significantly different from 1). The mean pre-LT slope was not significantly different from 0 (mean slope ± SD, 0.00003 ± 0.0002; P = 0.948). When the next data point was added, the average slope was significantly different from 0 (mean slope ± SD, 0.00019 ± 0.0002; P = 0.002). Subsequent analyses yielded the same results with the slope significantly different from 0.

DISCUSSION

This study aimed to reveal in detail the relation or correspondence between LT and VT by using a distinct submaximal exercise protocol with frequent lactate sampling. After we conducted a critical examination of the published reports with individual lactate curves, we felt that there was often an inadequate number of data points leading to a threshold,4–6 particularly because in these studies involving normal subjects, the blood lactate level at times seemed to increase almost immediately after the start of exercise (at a very light work rate), conflicting with the accepted notion of LT appearing at approximately 50% of VO2max. We felt that a slower incremental protocol might reveal more information about the initial process of lactate increase (LT).

The first major finding of our study was a decrease in VT when the exercise protocol was shifted from the medium ramp to the slow ramp. We did not quite expect this because we had believed that varying the incremental or ramp work rate would not alter the VT as reported by some researchers.20,21 However, in a further search of the literature, we found that the VT or LT has been reported in some papers to be protocol-dependent.22–24 However, in a further search of the literature, we found that the VT or LT has been reported in some papers to be protocol-dependent.22–24 The slower ramp yielded lower thresholds. Based on the VT results, it is also very likely that the LT also appeared earlier in the blood under the slow-ramp condition, although we did not obtain every-minute sampling of lactate during maximal exercise. As it is physiologically unlikely that slow-ramp exercise produces more lactate than medium-ramp exercise does in the muscle at the same work rate or VO2, we suspect that this finding resulted from longer diffusion times of lactate under slow-ramp exercise.10 We therefore concur that when the VT or LT is used as a standard measure of exercise tolerance, the test duration (or work rate) should be within a certain range based on the individual’s VO2max; currently 8 to 12 minutes of maximal exercise testing is recommended.7
Our mean VT as a percentage of the peak VO$_2$ was very low (30%–34%) compared to the reference values reported elsewhere. According to a summary statement $^7$, VT usually occurs at approximately 50% to 60% of the %VO$_2$max (ranging from 35% to 80%). Our low value was most likely due to the slow-ramp protocol we used.

The V-slope may miss a lactate BP early in the exercise when the blood lactate levels begin to increase before S1 is established (transition phase of the V-slope). We propose the following mechanism for this discrepancy: an increase in the tissue CO$_2$ storage $^{13}$ would shift the V-slope rightward, whereas increasing lactate levels with an increase in excess CO$_2$ would shift the V-slope leftward, thus interfering with each other (see Figure 2A). Instances in which this problem appears to occur are marked in Supplementary File S1, http://links.lww.com/MD/A416.

An early first lactate BP is most likely a transient light work-rate phenomenon. We know that during light steady-state exercise the lactate level rises above resting values, but it is not sustained and in time decreases to baseline. However, the results of the present study suggest that this small rise in lactate (LT1 and LT2) is physiologically meaningful because it was associated with the ramp-dependent changes in oxygen uptake kinetics (ie, the ΔVO$_2$/Δ work rate slope). Exercise training studies using incremental protocols seem to show a shift of the whole lactate curve to the right, including the first portion of the curve that shows only a small rise in lactate. $^{25,26}$

In the present study, the changes in oxygen uptake kinetics did not correlate with the VT, probably because the VT missed the LT when the latter appeared very early, as we pointed out above. Neither did it correlate with the LMD. It was interesting to note that only the earliest-appearing thresholds (LT1 and LT2) were sensitive markers of reduced oxygen uptake kinetics. On the other hand, oxygen uptake kinetics significantly correlated with peak VO$_2$, probably because oxygen uptake kinetics in principle cumulatively affect the transitional O$_2$ uptake process up to the peak during incremental exercise testing.

We were somewhat surprised to find an early departure of two VO$_2$–work rate slopes with the 25 watt/min medium- and slow-ramp protocols. We had expected to see a departure at around the VT, as reported previously. $^{18}$ The departure at the VT or LT is physiologically logical. We thus speculate that this early departure of the 2 slopes signifies that a mismatch between oxygen uptake kinetics and increasing work rate (ramp) has occurred at this early stage of incremental exercise, resulting in an equally early rise of lactate. Our results are similar to those a study of patients with heart failure showing a reduction in the greater improvement in oxygen uptake kinetics. It remains to be elucidated how this seemingly physiological limitation of the very early lactate threshold associated with depressed

With regard to the difference in exercise parameters between the physically active and inactive subjects, the active subjects tended to have better indices of exercise tolerance, but they were not significant. The number of subjects we had was probably not enough to discern the possible differences, and the absolute differences in exercise tolerance between the active and inactive subjects were not large enough. The mean peak VO$_2$ for the active subjects was only 42 mL/kg/min. When we recruited volunteers for the study, we wanted to have a good mix of active and inactive students.

The submaximal slow-ramp exercise protocol we used in this study was designed solely to examine the relation between the LT and VT in detail and is therefore not indicated for routine exercise testing. However, it may be an interesting experimental exercise protocol to use because it seems to reflect the lactate changes occurring in the muscle much better than the standard exercise protocols. A stable baseline before LT is obtained with exercise training. However, it may be an interesting experimental exercise protocol to use because it seems to reflect the lactate changes occurring in the muscle much better than the standard exercise protocols. A stable baseline before LT is obtained with exercise training. Therefore, it is possible to determine LT in those with a low LT with more confidence.

With the exercise intensity well below VO$_2$max, it has the potential to measure an index of exercise tolerance in the range of ordinary everyday activities with applications for all subjects ranging from cardiac patients and normal subjects to athletes.

**CONCLUSIONS**

In this study, a slow-ramp submaximal protocol was used to ensure enough relevant data points around thresholds. Compared with the standard medium-ramp maximal exercise the mean VT as a percentage of the peak VO$_2$ fell from 49% to 38%, and the LT appeared even earlier (30%–34% of VO$_2$max).

We assessed the physiological significance of the very early appearance of the VT or LT in these healthy young subjects using changes in oxygen uptake kinetics (ΔVO$_2$/Δ work rate slope) that ensued from a shift of the exercise protocol from the medium- to slow-ramp. The lower LT correlated with the greater improvement in oxygen uptake kinetics. It remains to be elucidated how this seemingly physiological limitation of the very early lactate threshold associated with depressed
uptake kinetics in healthy young males impacts their daily activities.

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