Constant Load Exercise at Gas Exchange Threshold is Accompanied by a Distinct Elevation in Blood Lactate Level

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Abstract

Background: The gas exchange threshold (GET) is determined during incremental exercise (Inc-Ex) testing. It is generally considered to be a safe training intensity, with little or no elevation in blood lactate (BLa). However, actual exercise training at GET is carried out primarily as a constant load exercise (CL-Ex). The dynamics of BLa during CL-Ex at GET have not been studied. This study was conducted particularly among the elderly population.

Methods: We recruited 20 healthy elderly individuals (H: age 69.4±6.8 years) and 10 patients with cardiovascular diseases or under medication for cardiovascular risk factors (P: age 73.0±8.8 years). On day 1, we determined GET during symptomatic maximal Inc-Ex. On day 2, CL-Ex at GET intensity was performed for 20 min. Arterialized blood lactate levels were determined.

Results: The mean BLa at GET during Inc-Ex was 1.51±0.29 mmol/L in H and 1.78±0.42 mmol/L in P ($p < 0.05$). During CL-Ex, BLa increased significantly more than that at GET, reaching a steady state level of 2.65±1.56 (H) and 2.53±0.95 (P) mmol/L (ns), with a mean respiratory exchange ratio (RER) of 0.94±0.05 (H) and 0.93±0.05 (P) (ns). Oxygen uptake (VO_2) also reached a steady state in all participants. All participants were able to complete CL-Ex with mean perceived exertion ratings (Borg/20) of 11.8±1.3 (H) and 12.2±1.3 (P) (ns).

Conclusions: CL-Ex at GET occurred at distinctly increased BLa levels; however, BLa reached a steady state, together with VO_2 and RER, indicating that exercise intensity was metabolically moderate.

Introduction

The gas exchange threshold (GET) or ventilatory anaerobic threshold (VAT) is a useful measure of exercise tolerance. Unlike peak or maximal oxygen uptake, it does not require maximal effort. It is considered by some to be a safe optimal initial training intensity for cardiac patients in cardiac rehabilitation [1, 2]. At the GET, blood lactate (BLa), a traditional primary indicator of metabolic exercise intensity, shows only a minimal increase (0.5 mmol/L above the baseline) [3, 4, 5]. However, exercise training itself is primarily performed using a constant load protocol. Quantitative data regarding lactate levels when GET-level exercise is maintained over a 20- to 30-min period (constant load exercise: CL-Ex) have not been reported, including data on VO_2 kinetics, individual's perceived rate of exertion, and tolerability of exercise. Although data above and below the GET and at various percentages of VO_2max [6] have been reported [7, 8], no study to date has assessed CL-Ex specifically at the GET.

As we generally deal with the elderly population in cardiac rehabilitation, we focused on this population as the principal participants of this investigation.

Methods

Subjects

The study required that all participants were between the ages of 60 and 80 years. We recruited 10 patients who were under medication for cardiovascular diseases (n = 5) or cardiovascular risk factors (n = 5) (group P, age: 73.0 ± 8.8 years; male: 8). Cardiovascular disease etiologies included post-coronary artery bypass graft surgery for coronary artery disease (n = 2), myocardial infarction (n = 1), and valvular heart disease (n = 2). Cardiovascular risk factors included hypertension (n = 10), impaired glucose tolerance or diabetes mellitus (n = 1), and hyperlipidemia (n = 6). Twenty healthy participants matched for age (group H, age: 69.4 ± 6.8 years; male: 9) were recruited for comparison (Table 1). To estimate the daily activity levels of the participants, the International Physical Activity Questionnaire (IPAQ) short form was administered [9].

Table 1
Clinical characteristics of study participants

Characteristics		**Healthy group [H: n = 20]**	**Patient group [P: n = 10]**
Age	[years]	69.4 ± 6.8	73.0 ± 8.8
Sex		M:9, F:11	M:8, F:2
Height	[cm]	159.4 ± 5.9	164.7 ± 3.8
Body weight	[kg]	56.9 ± 8.3	67.1 ± 10.5
BMI		22.3 ± 2.2	24.8 ± 4.1
CTR	[%]		47.9 ± 4.7
BNP	[pg/dL]		73.9 ± 126.4
LVEF	[%]		68.1 ± 13.4
IPAQ-SF	[MET-min/week]	2082 ± 1857	3895 ± 4371
Comorbidity			
Hypertension	[n (%)]	0 (0)	10 (100)
Dyslipidemia	[n (%)]	0 (0)	6 (60)
Impaired glucose tolerance	[n (%)]	0 (0)	1 (10)
Obesity	[n (%)]	2 (10)	4 (40)

Data are presented as mean ± S.D. Obesity is defined as BMI > 25 kg/m^2. Significant differences in clinical characteristics such as age, BMI, and physical activity (IPAQ-SF) were not observed between group H and group P.

CTR, cardio-thoracic ratio; BMI, body mass index; BNP, brain natriuretic peptide; LVEF, left ventricular ejection fraction; IPAQ-SF, international physical activity questionnaire–short form.

Exclusion criteria included change in medication within 6 months, infection within 2 weeks, body temperature greater than 37.5 °C, chronic atrial fibrillation or flutter, permanent pacemaker, and presence of

orthopedic conditions rendering the individual unfit for exercise testing. In addition, we excluded participants taking warfarin or other anticoagulants or metformin for diabetes.

Exercise Testing

Cardiopulmonary exercise testing (CPET) was performed using a stationary bicycle (StrengthErgo 8; Mitsubishi Electric Engineering, Tokyo) and a breath-by-breath gas analyzer (AE-300S; Minato Ikagaku Co., Tokyo). Exercise tests were carried out on 2 separate days (mean interval between the 1st - and 2nd -day tests: 4.1 ± 2.3 days). On day 1, symptomatic maximal exercise was performed using a ramp protocol of 10 W/min (Inc-Ex: incremental exercise), with GET determination. On day 2, Inc-Ex with the 10 W/min ramp protocol was performed up to the GET point, after which a constant load at the GET level work rate was initiated and maintained for a total exercise duration of approximately 25 min (Fig. 1). Before the experiment, it was planned that the total duration of the exercise (Inc-Ex + CL-Ex) on day 2 be 25 min for each participant. The duration of Inc-Ex varied among participants because of the different GET levels. Consequently, mean Inc-Ex duration was 3.2 ± 1.1 min, and the mean CL-Ex duration was 21.8 ± 1.1 min. Thus, all graphs, tables, and texts denoting 25 min of CL-Ex represent approximately 22 min of CL-Ex. Warm-up exercises were performed for 2 min at 10 W.

We used 10-s average data for all analyses. The output was obtained from a gas analyzer system.

Gas Exchange threshold

We determined the GET during Inc-Ex testing on day 1 to determine the CL-Ex testing work rate for day 2. The GET was visually determined using the modified V-slope method, as described by Sue et al. [10], which is a modification of the method described by Beaver et al. [11]. The details of this method as practiced by us have been published previously [12, 13]. In summary, this V-slope method (Fig. 2) draws a line parallel to the respiratory exchange ratio (RER) = 1 diagonal line through the data points, referred to as the pre-GET baseline. The point where the data points begin to deflect toward the left (forming an angle < 180°) is selected as the GET. Data points preceding the parallel line (with angle < 180°) are disregarded. This method fixes the pre-GET slope as the baseline, making it easy to see a deflection. At the inception of Inc-Ex, the carbon dioxide production (VCO_2) increase in the blood and at the mouth is delayed against the VO_2 increase because of a larger CO_2 tissue storage capacity [12]. Therefore, the V-slope itself is shifted to the right [12]. A line drawn parallel to the RER = 1 diagonal signifies a change in the rate of (delta VCO_2/delta VO_2) of 1.0, in contrast to the conventionally calculated RER (simple division of moment-to-moment VCO_2 by VO_2) (Fig. 2). The point at which this index begins to increase above 1.0 is the GET deflection point. A baseline representing a constant rate of change of 1.0 is often readily visible during the early stage of ramp exercise [12, 13]. References 12 and 13 include as supplemental material readings of the GET for each case analyzed in each study. This is the basis of our method for identifying the GET.

Blood Lactate

Blood was sampled using a fingerprick. A topical vasodilator (Finalgon cream, nonivamide butoxyethyl; Boehringer Ingelheim, Gaithersburg, MD) was applied to three fingers of the left hand (2nd, 3rd, and 4th).

After 10 min, the cream was removed and the entire left hand, including the distal part of the forearm, was placed in a water bath at 43–45 °C for 10 min [3, 14]. BLa levels were determined using Lactate Pro LT-1730 (Arkray, Kyoto, Japan). The instrument was calibrated using a calibration strip before each exercise.

On day 1, blood samples were collected at rest (× 2), during the warm-up exercise (× 2), and at each minute during the ramp exercise. On day 2, blood samples were collected every minute up to the GET point, and every 5 min during the entire 25-min Ex period (IncEx + CL-Ex).

Rate of Perceived Exertion and Miscellaneous Measures

The rate of perceived exertion was obtained using the Borg scale. Left ventricular ejection fraction (LVEF) was obtained using the Teichholz method. Brain natriuretic peptide (BNP) was determined by chemiluminescent enzyme immunoassay.

Statistical Analysis

Data are presented as the mean ± SD. Unpaired data were analyzed using Student's t-test. Paired data were analyzed using a paired t-test. Testing for VO_2 steady state in each case during CL-Ex involved comparing the last exercise dataset (25-min data) to the preceding 4 datasets (data at every 5 min). A 1-min dataset consisted of 6 data points of 10 s each. A repeated one-way analysis of variance (ANOVA) was performed, followed by a post-hoc Bonferroni correction. The p value was expressed as p × the number of comparisons, 4, and $p < 0.05$ was considered to indicate statistical significance, while $p > 0.05$ indicated that the exercise was at a steady state level. Comparison between groups H and P was performed using a repeated two-way ANOVA. The percent maximal heart rate (% MHR) at the GET was calculated as (HR at GET/peak HR) × 100. The percent heart rate reserve (% HRR) was calculated as ((peak HR – HR at GET)/(peak HR – resting HR)) × 100. In addition to the pre-planned 5-min analysis (lactate sampling point) over the entire 25-min Ex period (Inc-Ex + CL-Ex), data analysis based on the start of FL-Ex as time point zero (0) was also performed.

Statistical analyses were performed with Statistics for Excel 2012 (Social Survey Research Information Co., Tokyo).

Ethical Considerations

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and was approved by the Ethical Committee (Institutional Review Board: IRB) of Sapporo Ryokuai Hospital (approval number: 19 − 1). Informed consent was obtained from all participants for their participation in the study and for the publication of this report. The authors confirm that there is no identifying information concerning the participants in the manuscript and that the information has been fully anonymized. Furthermore, the authors affirm that all mandatory health and safety procedures were followed in the course of conducting any experimental work reported in this paper.

Results

The clinical characteristics of the participants are summarized in Table 1. Group P had a higher proportion of males, with significantly higher mean height and weight compared with group H. The total MET minutes per week according to the IPAQ-SF was not significantly different between groups H and P, respectively (p = 0.119). This result is similar to the average of a broader healthy Japanese population of the same age range [15]. One group H participant and 3 group P participants reported vigorous intensity, as defined in the questionnaire.

Change in variables during CL-Ex

BLa level, oxygen uptake, RER, and heart rate (HR) of both groups during CL-Ex are shown in Figs. 3–6 and Tables 2–4.

Table 2
Primary cardiopulmonary data at rest and at peak exercise

			Healthy group [H: n = 20]		Patient group [P: n = 10]	
			Inc-Ex (Day 1)	CL-Ex (Day 2)	Inc-Ex (Day 1)	CL-Ex (Day 2)
Rest	VO_2	[ml/min]	239 ± 41	225 ± 35	253 ± 50	265 ± 52 *
	VO_2/wgt	[ml/kg/min]	4.3 ± 0.8	4.0 ± 0.5	3.8 ± 0.6	3.9 ± 0.4
	HR	[bpm]	68.9 ± 10.7	67.3 ± 9.8	65.1 ± 5.8	64.9 ± 7.1
	Lactate	[mmol/L]	1.17 ± 0.32	1.16 ± 0.26	1.34 ± 0.30	1.24 ± 0.25
Peak [Day 1]	Work rate	[watt]	105.5 ± 21.8	-	103.2 ± 23.4	-
	VO_2	[ml/min]	1400 ± 316	-	1318 ± 335	-
	VO_2/wgt	[ml/kg/min]	24.7 ± 4.4	-	19.5 ± 3.7 *	-
	RER		1.15 ± 0.09	-	1.16 ± 0.13	-
	HR	[bpm]	143.6 ± 19.8	-	128.4 ± 15.3 *	-
	Lactate	[mmol/L]	5.55 ± 1.55	-	5.80 ± 2.58	-
	RPE		16.2 ± 2	-	17.1 ± 1.4	-

VO_2, oxygen uptake; VO_2/wgt, oxygen uptake per weight; HR, heart Rate; CL-Ex, constant load exercise; Inc-Ex, incremental exercise; RPE, rate of perceived exertion; RER, respiratory exchange ratio.

* Significant (p < 0.05) for Healthy group vs. Patient group

Table 3
Cardiopulmonary data during exercise at GET

		Healthy group [H: n = 20]		Patient group [P: n = 10]	
		Inc-Ex (Day 1)	CL-Ex (Day 2)	Inc-Ex (Day 1)	CL-Ex (Day 2)
Work rate	[watt]	41.8 ± 10.2		41.1 ± 12.2	
VO_2	[ml/min]	678 ± 136	760 ± 144 *	700 ± 170	840 ± 193 *
VO_2/wgt	[ml/kg/min]	12.1 ± 2.6	13.5 ± 2.5 *	10.3 ± 1.5	12.4 ± 1.6 *
%Peak	[%]	49.4 ± 8.4	55.7 ± 10.7 *	54.4 ± 9.9	65.2 ± 10.5 †
RER		0.85 ± 0.05	0.94 ± 0.05 *	0.87 ± 0.07	0.93 ± 0.05 *
HR	[bpm]	91.1 ± 12.6	99.7 ± 14.2 *	84.0 ± 6.2	95.0 ± 11.9 *
Lactate	[mmol/L]	1.51 ± 0.29	2.65 ± 1.56 *	1.78 ± 0.42 ‡	2.53 ± 0.95 *
RPE		-	11.8 ± 1.3	-	12.2 ± 1.3
On day 1, GET was determined during Inc-Ex. On day 2, GET level denotes the 25-min value during CL-Ex at					
the work rate corresponding to GET VO_2 on day 1.					
VO_2, oxygen uptake; VO_2/wgt, oxygen uptake per weight; GET, gas exchange threshold; HR, heart Rate; CL-Ex, constant load exercise; Inc-Ex, incremental exercise; RPE, rate of perceived exertion; RER, respiratory exchange ratio.					
* Significant ($p < 0.01$) for Inc-Ex vs. CL-Ex					
† Significant ($p < 0.05$) for Inc-Ex vs. CL-Ex					

Table 4
Variables as a function of time elapsed from the start of CL-Ex

CL-Ex n = 30		start of CL				
	[min]	0	6.8 ± 1.1	11.8 ± 1.1	16.8 ± 1.1	21.8 ± 1.1
Lactate	[mmol/L]	1.56 ± 0.44	2.29 ± 0.75 *†	2.46 ± 0.94 *†	2.55 ± 1.15 *†	2.61 ± 1.27 †
VO_2	[ml/min]	681 ± 142	770 ± 157 *†	783 ± 159 *†	780 ± 153 *†	786 ± 163 †
VO_2/wgt	[ml/kg/min]	11.4 ± 2	12.9 ± 2.3 *†	13.1 ± 2.4 *†	13.1 ± 2.5 *†	13.1 ± 2.3 †
R		0.86 ± 0.07	0.95 ± 0.06 *†	0.93 ± 0.05 *†	0.94 ± 0.05 *†	0.94 ± 0.05 †
HR	[bpm]	85.7 ± 10.3	92.2 ± 12.3 †	94.5 ± 13.1 *†	95.1 ± 13.3 *†	98.4 ± 14.0 †
VO_2, oxygen uptake; VO_2/wgt, oxygen uptake per weight; HR, heart Rate; CL-Ex, constant load exercise; CL-Ex, constant load exercise; RPE, rate of perceived exertion; RER, respiratory exchange ratio.						
* Not significantly different (p > 0.05) vs. 25-min value						
† Significant (p < 0.05) vs. start of CL value						

Blood Lactate

The mean BLa levels were 1.50 ± 0.37 (H) and 1.69 ± 0.55 (P) mmol/L at the start of CL-Ex (the end of ramp Inc-Ex) and increased further during CL-Ex (Fig. 3). These values reached a steady state during the last 10 min in Group H and in the last 5 min in Group P. The steady-state lactate level was 1.42 ± 1.16 mmol/L above the value recorded at the GET point during Inc-Ex. We also visually checked for the trend in each case (supplemental file). Three cases in Group H appeared to show an increasing pattern (cases 6, 12, and 16). However, random noise often makes concrete characterization difficult.

Oxygen uptake, RER, and HR

Mean oxygen uptake followed the same pattern as that of BLa, reaching a steady state during the last 10 min of CL-Ex (Fig. 4). No individual case showed an increasing pattern (Supplemental File). RER also followed the same pattern as that of VO_2 (Fig. 5), with mean RER remaining below 1.0. In contrast, HR did not reach the steady state, increasing progressively during CL-Ex instead (Fig. 6). The mean %MHR and %HRR at GET of all participants (n = 30) were 64.7 ± 7.8 and 30.8 ± 9.0, respectively, with no significant difference between the two groups (Supplemental File 5). On average, the increase in BLa after time zero (start of CL-Ex) was much greater than that of VO_2 (compare Fig. 3 and Fig. 4).

Rate of Perceived Exertion

The rate of perceived exertion (Borg scale: 6–20) during CL-Ex was not significantly different between the two groups (group H: 11.8 ± 1.3 vs. group P: 12.2 ± 1.3; p = 0.431) (Table 3). The Borg scale range was 9–14 in group H and 9–13 in group P. All participants completed the total exercise protocol of 25 min.

There were no significant differences between the two groups with respect to BLa and CPET parameters (no interaction by two-way ANOVA). There were no significant differences in BLa and CPET parameters between the GET during Inc-Ex (day 1) and the work load of the Inc-Ex/CL-Ex transition (day 2) (Table 3).

Adverse effects of exercise testing

Minor adverse effects were observed during the experiment. Sporadic PVCs were observed in 4 cases during Inc-Ex and in 5 cases during CL-Ex. PACs were observed in 1 case during Inc-Ex and in 4 cases during CL-Ex. One of these participants developed transient intermittent supraventricular tachycardia (100–110 bpm) during the last 5 min of CL-Ex. A significant ST segment change without angina was observed in one case; this case was excluded from the study.

There were no adverse effects concerning fingertip blood sampling, which was conducted frequently over a short time period.

Discussion

This study aimed to examine lactate dynamics during a fixed-load exercise at the work rate of the GET, as determined during Inc-Ex. This was done because the GET level of exercise is often suggested as a convenient initial work rate for cardiac rehabilitation [1, 2], and it is known that with the often-employed percentage of maximal VO_2 approach, the same percentage prescription results in a very inhomogeneous metabolic profile, including blood lactate, in different individuals [16]. The GET level exercise is expected to produce a more homogenous response. One study [17], the primary purpose of which was to assess the arterialized and venous lactate concentration difference during constant-load exercise, investigated lactate levels at the lactate threshold in young male participants. Although LT was determined by lactate measurement (not by GET) and respiratory variables were not reported, the lactate time trend was similar to our results.

The mean BLa increase at the GET was approximately 0.5 mmol/L above the resting level, which is consistent with the results of our and others' previous reports [3, 4, 5]. Therefore, we can say that this GET level of exercise induces only minimal lactate elevation during Inc-Ex. However, as the continuation of this GET level exercise as a CL-Ex produced a clear increase in the lactate level (1.38 ± 1.21 mmol/L above the resting level), the GET level exercise at this stage cannot be called an exercise that produces only the minimal level of lactate. Further increases in the GET level during CL-Ex may be the result of 2 factors: 1) lactate is formed in the exercising muscle and takes time to reach the bloodstream to be detected [18, 19]; 2) the preferential energy source varies with exercise duration [20]. During Inc-Ex, the workload is continually increased, which may favor glycogen breakdown and induce lactate formation in the working muscle; this is then released with a time delay.

In spite of GET-level exercise being accompanied by distinct elevations in lactate, overall mean changes in lactate, VO_2, and RER revealed the attainment of a steady state, although each parameter reached a steady state with different delays during CL-Ex. Previous studies have mostly analyzed changes in blood lactate during steady state exercise using arterialized blood collected from healthy young people [17, 21]. In addition, some previous studies used mixed-venous blood, one of which reported no increase in blood lactate at 60 ± 3% VO_2 max [22]. The problems with venous sampling are well known [23, 24].

In our study, CL-Ex at the GET level was individually tolerable for all elderly individuals included in this study. All participants showed significant elevation in BLa during the GET level constant load exercise. The concept of increased lactate levels during exercise has evolved in recent years [25]. Evidence suggests that the increase in BLa is not due to hypoxia, particularly when exercise is not severe, but is instead likely due to increased glycolysis under aerobic conditions [26]. Muscle biopsy studies show decreased muscle glycogen levels, even if the exercise intensity is not severe [26, 27, 28]. The steady state reached by mean VO_2, RER, and BLa strongly suggests that our GET level exercise was essentially aerobic in nature. Furthermore, elevated BLa itself may serve as a metabolic signal to stimulate more efficient aerobic energy production [29]. Therefore, an increase in BLa may be a necessary component of optimal exercise training. In this sense, GET-level exercise training can be a good starting point for cardiac rehabilitation.

An explanation is required for the CL-Ex protocol we employed in this study: approximately 3 min of Inc-Ex followed by CL-Ex, instead of step-wise introduction of CL-Ex, as is generally performed [30, 31]. We conducted the study in this manner for the following reason: if we introduce a GET-level work load as a step function, during the first short period, the subject may incur a sudden, undue energy demand. This could generate lactate in the muscle, which may appear in the blood with a delay and interfere with the interpretation of the subsequent BLa during CL-Ex. However, by employing an Inc-Ex protocol, as we routinely do, halting Inc-Ex as soon as we detect the GET (with minimal lactate increase), and transitioning into CL-Ex, we can observe how the naturally occurring GET behaves in CL-Ex.

The first limitation of the study concerns our FL exercise protocol. In this study, we defined a GET-level exercise as an exercise intensity (W) at which the GET in mL of VO_2 appeared. It is known that for a step-wise initiation of CL-exercise, there is a delay in the increase of VO_2, which is known as the mean response time. This delay in the response to VO_2 increases with exercise intensity [32, 33]. Therefore, when the work rate at the GET VO_2 is taken as the GET work rate, it may result in overestimation of the GET work rate because the work rate is, in a sense, ahead of VO_2. However, there is no currently widely used or standard way to correct for this, although a quantitative way to correct for this has been reported and seems promising [32]. Therefore, our GET-level FL-exercise protocol, which is not corrected for this, may well be overestimating the individual “true” GET level CL-Ex. Despite this, the average respiratory and metabolic responses reached a steady state.

Other limitations of this study include the fact that the size of the sample comprising participants with cardiovascular diseases was not sufficient. Particularly, no difference was observed between the healthy

controls and the patient population. Further studies are required to investigate GET-level CL-exercise in cardiac patients with reduced exercise capacity.

Second, only the elderly population was studied. Although lactate dynamics in a younger population are unlikely to be very different at the GET, they may also need to be studied.

Third, the GET is visually determined, and individual GET values determined by different investigators can vary significantly, although the mean values may not show a significant difference [34]. Therefore, there is a possibility that a similar investigation, if conducted by other investigators, may not produce similar results. It would be very interesting to see other studies of a similar nature performed.

In summary, the BLa level during constant-load exercise at GET intensity showed a greater increase (by approximately 1 mmol/L) than it did at the GET during incremental exercise. Nevertheless, BLa reached a steady state, together with VO_2 and RER (below 1.0), suggesting that the exercise was primarily aerobic. This GET-level constant-load exercise protocol allowed all elderly participants to complete the 25-min exercise with fairly light to somewhat hard mean perceived exertion. Furthermore, the results suggest that increased blood lactate might serve as a stimulus for furthering aerobic energy metabolism.

Abbreviations

GET
gas exchange threshold; VAT:ventilatory anaerobic threshold; Inc-Ex:incremental exercise; CL-Ex:constant load exercise; CPET:Cardiopulmonary exercise testing; VO_2:Oxygen uptake; VCO_2:carbon dioxide production; BLa:blood lactate; RER:respiratory exchange ratio; IPAQ:International Physical Activity Questionnaire; LVEF:Left ventricular ejection fraction; BNP:Brain natriuretic peptide; ANOVA:A repeated one-way analysis of variance

Declarations

Acknowledgments

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The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation, and the results of the present study do not constitute endorsement by BMC Sports Science, Medicine, and Rehabilitation.

Authors' contributions

KK, HN and MA developed the study concept and were involved in the design and implementation of the study. KK, TK and MM delivered the program content to participants. KK, KI, TK, HN and HN acquired the data. KK, TK and AH analyzed the data. KK and HN prepared the manuscript. MA contributed to drafts of the manuscript and approved the final draft. All authors read and approved the final manuscript.

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This study did not receive any funding support. This work was performed at the Cardiac Rehabilitation Center, Sapporo Ryokuai Hospital, Sapporo, Japan.

Availability of data and materials

The dataset used in the current study is available from the corresponding author on request.

Ethics approval and consent to participate

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and was approved by the Ethical Committee (Institutional Review Board: IRB) of Sapporo Ryokuai Hospital (approval number: 19-1). Informed consent was obtained from all participants for their participation in the study and for the publication of this report. The authors confirm that there is no identifying information concerning the participants in the manuscript and that the information has been fully anonymized. Furthermore, the authors affirm that all mandatory health and safety procedures were followed in the course of conducting any experimental work reported in this paper.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Conflicts of Interest and Source of Funding

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Figures

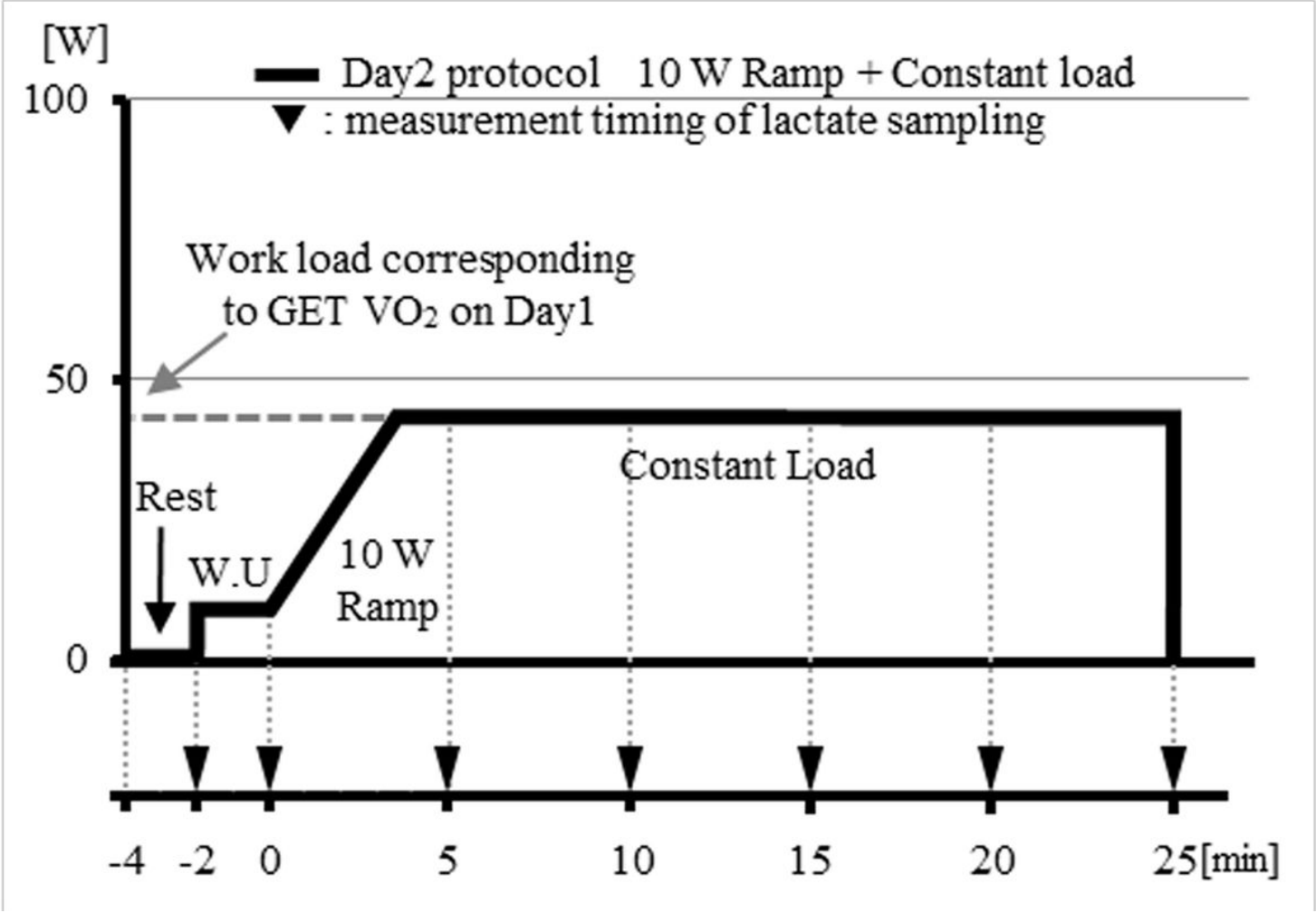

Figure 1

Day 2 exercise protocol The start of ramp exercise is set to zero (0). The total exercise duration of the ramp and CL-Ex was set at 25 min. The time to GET varied depending on the individual participant; the mean was 3.2 ± 1.1 min. Blood lactate was sampled twice at rest, twice during warm-up, and every minute during ramp exercise. It was also sampled every 5 min during the total exercise duration of 25 min.

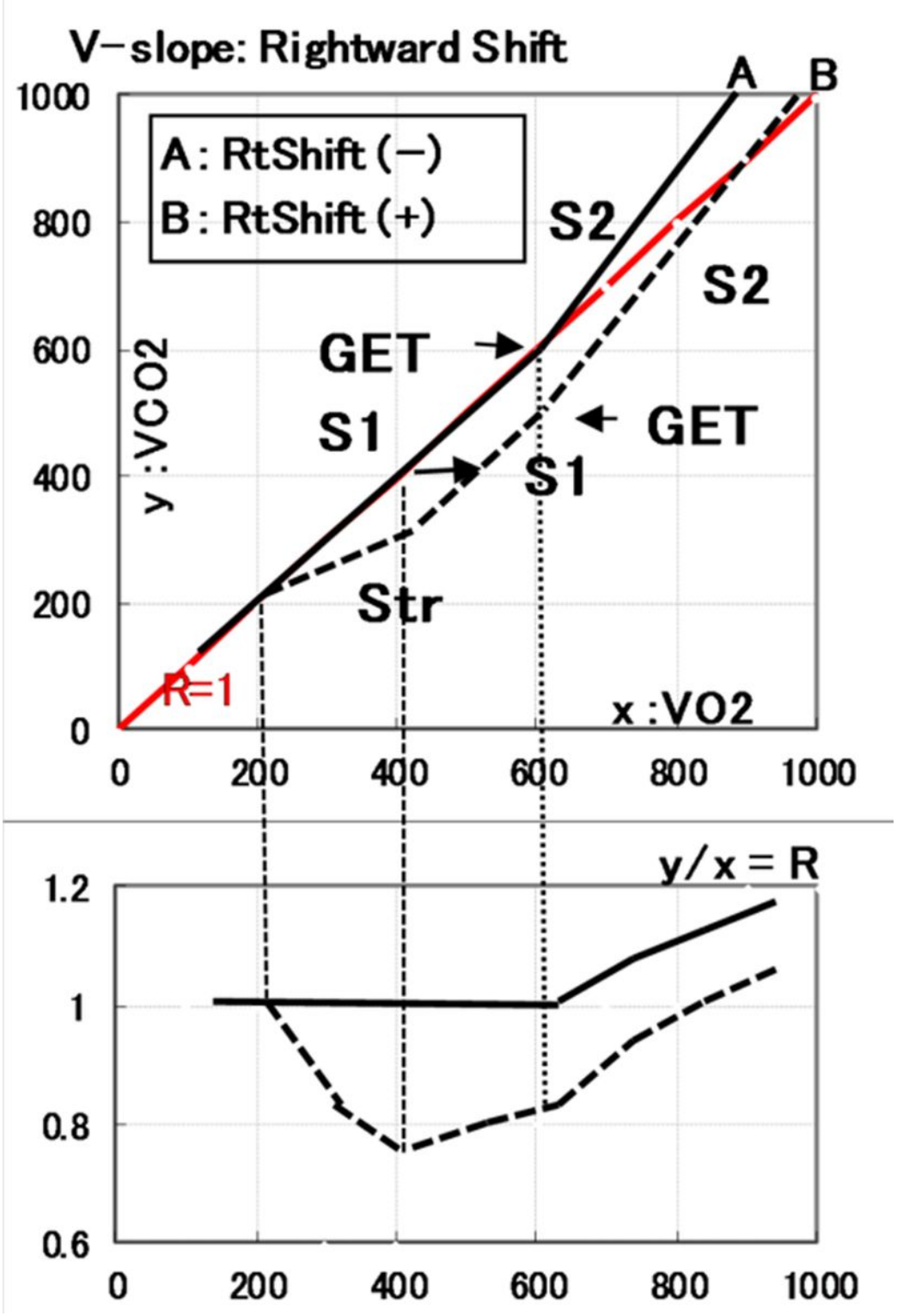

Figure 2

Determination of GET: diagram The x-and y-axes are set at simple arbitrary values (0 to 1000) to explain the principle of the rightward shift of the V-slope (upper panel) and its consequences on the RER calculation (lower panel). V-slope “A” shows no rightward shift. “B” shows a RtShift of 100 mL (horizontal arrow to right). For “A”, during S1, the RER (VCO2/VO2) equals the change in the rate of (delta VCO2/delta VO2). Both variables were constant at 1.0. For “B”, the rate of change is not equal to RER. The rate of

change was constant at 1.0, whereas RER was not constant. Str, S transient is the segment in transition prior to the establishment of S1; S1, pre-GET baseline; GET, gas exchange threshold; S2, post-GET segment; RtShift; rightward shift of V-slope

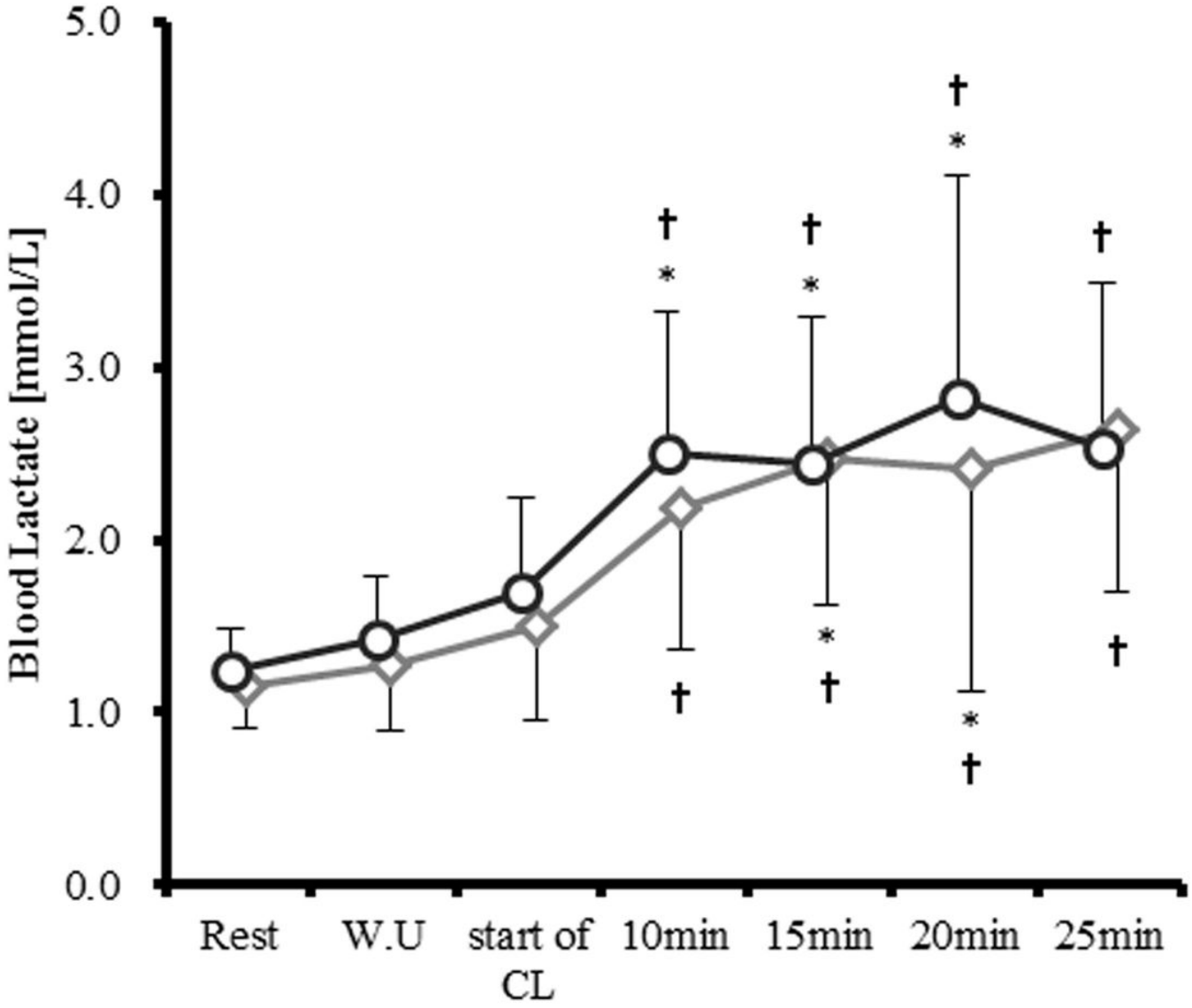

Figure 3

Blood lactate (BLa) response during constant load exercise (CL-Ex) Healthy group (□) and patient group (□) BLa response during CL-Ex. Data are presented as mean ± S.D. CL-Ex (day 2) consisting of ramp exercise for an average of 3 min and constant load exercise for 22 min, for a total exercise duration of 25 min (see Methods for details). * Not significantly different ($p > 0.05$) vs. 25-min value. □$p < 0.05$ vs. start of CL [Healthy: 1.50±0.37, Patient: 1.69±0.55 mmol/L]

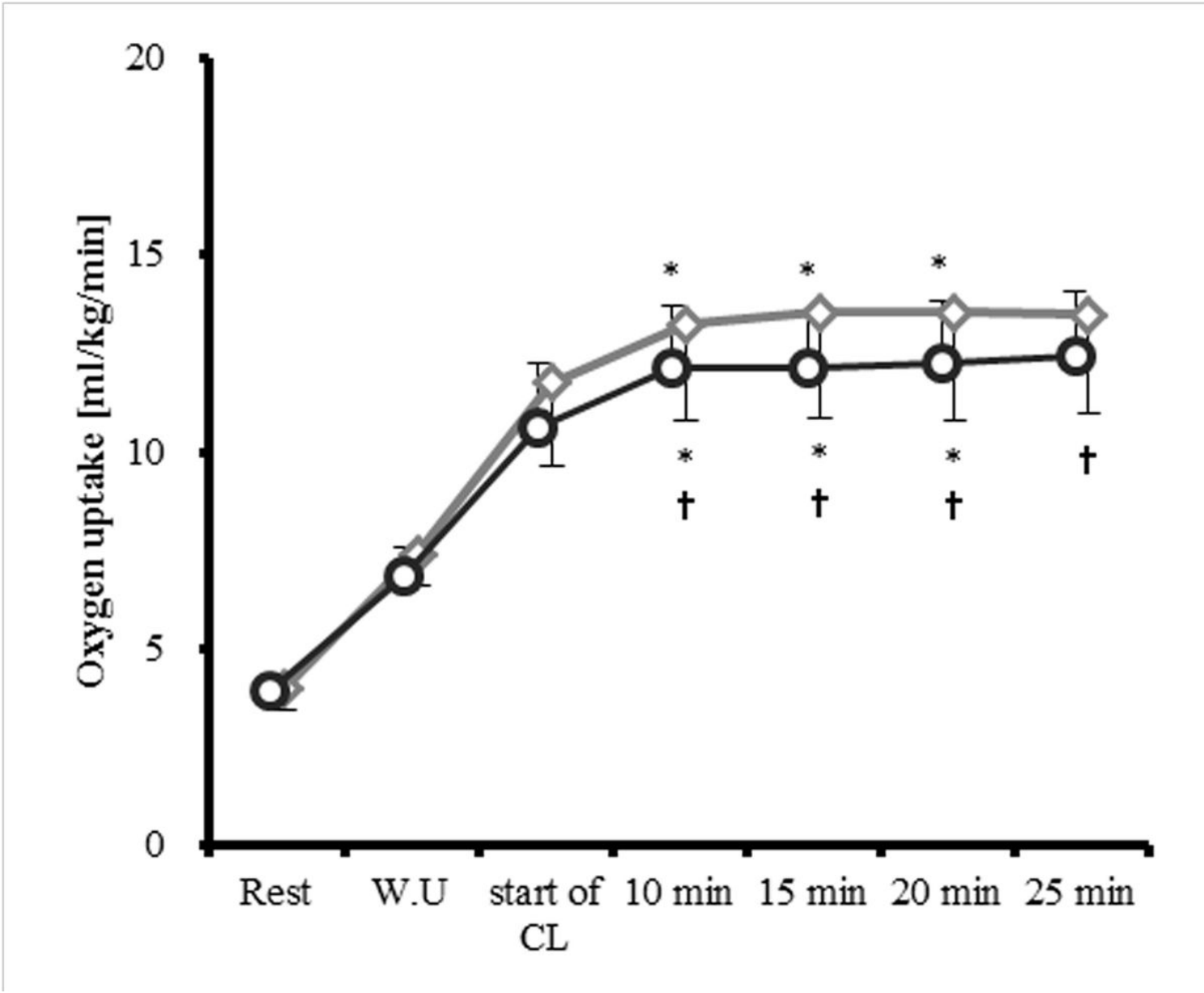

Figure 4

Oxygen uptake during constant load exercise (CL-Ex) Healthy group (□) and patient group (■) oxygen uptake (VO2/wgt) response during CL-Ex. Data representations are the same as those shown in Figure 2. * Not significantly different ($p > 0.05$) vs. 25-min value. †$p < 0.05$ vs. start of CL [Healthy: 11.7±2.1, Patient: 10.6±1.6 ml/kg/min]

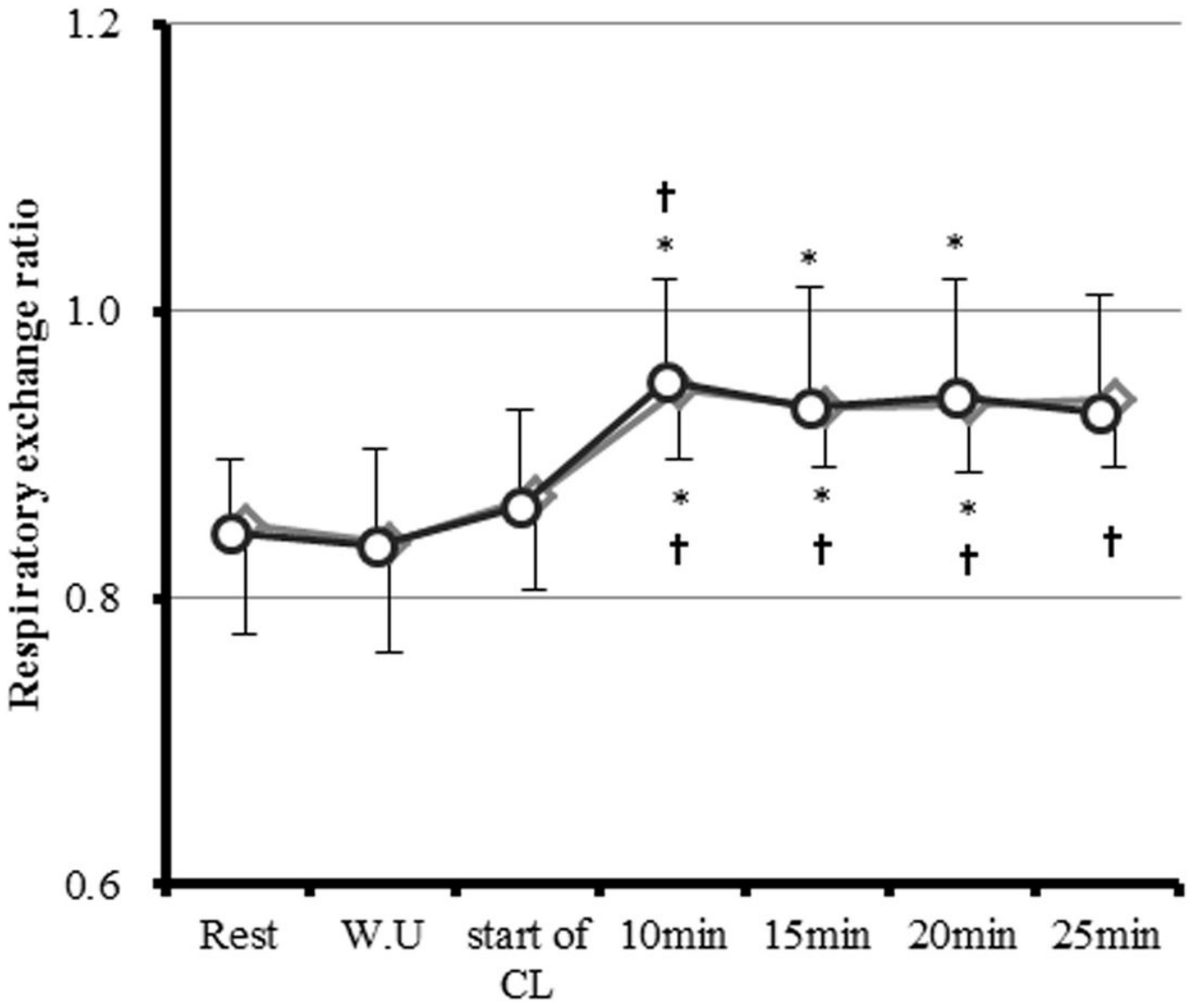

Figure 5

Respiratory exchange ratio (RER) during constant load exercise (CL-Ex) Healthy group (□) and patient group (■) RER response during CL-Ex. Data representations are the same as those shown in Figure 2. * Not significantly different ($p > 0.05$) vs. 25-min value. †$p < 0.05$ vs. start of CL [Healthy; 0.87±0.09, Patient; 0.86±0.07]

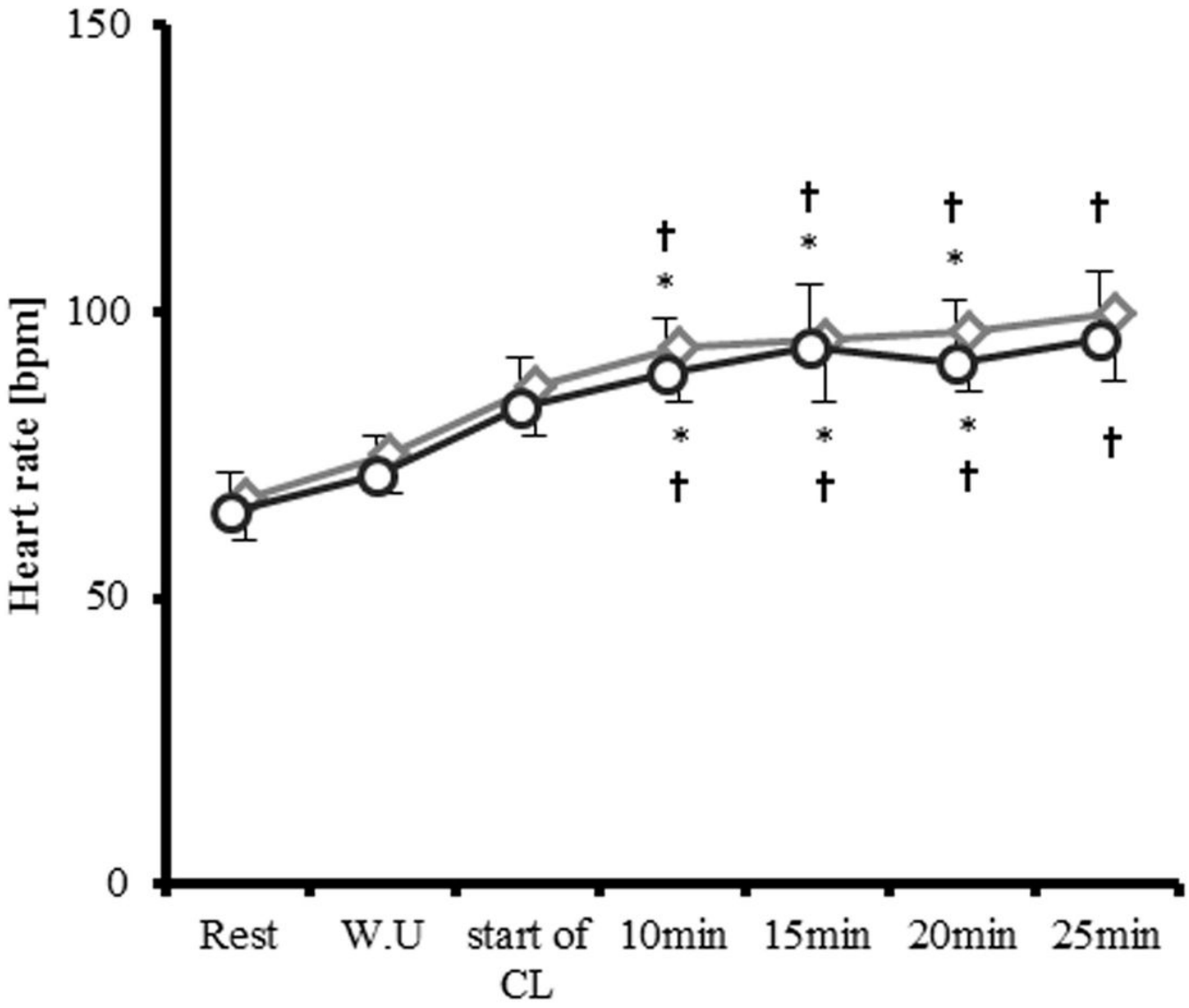

Figure 6

Heart rate (HR) during constant load exercise (CL-Ex) Healthy group (□) and patient group (■) HR response during CL-Ex. Data representations are the same as those shown in Figure 2. * Not significantly different ($p > 0.05$) vs. 25-min value. †$p < 0.05$ vs. start of CL [Healthy; 87.0±11.0, Patient; 83.3±8.7 bpm]

Supplementary Files

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