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Gas exchange threshold to guide exercise training intensity of older individuals during cardiac rehabilitation

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Abstract

The gas exchange threshold (GET), which is determined during incremental exercise (Inc-Ex) testing, is often considered a safe training intensity for cardiac rehabilitation. However, there are only a limited number of reports on the actual implementation of this method. We assessed the applicability of GET-guided exercise using a constant load exercise (CL-Ex) protocol.

We recruited 20 healthy older individuals (healthy, age: 69.4 ± 6.8 years) and 10 patients with cardiovascular diseases or risk factors (patient, age: 73.0 ± 8.8 years). On day 1, we determined the GET during symptomatic maximal Inc-Ex. On day 2, CL-Ex at work rate (watt: W) where the GET manifested during Inc-Ex (therefore, not corrected for the known oxygen response delay) was maintained for 20 minute. Arterialized blood lactate (BLa) levels were also determined.

Oxygen uptake reached a steady state in all participants, with a mean respiratory exchange ratio of <1.0. The mean BLa at the GET during Inc-Ex was $1.51 \pm .29$ $\text{mmol}\cdot\text{l}^{-1}$ in the healthy group and $1.78 \pm .42$ $\text{mmol}\cdot\text{L}^{-1}$ in the patient group, which was about .5 $\text{mmol}\cdot\text{L}^{-1}$ above the resting level. During CL-Ex, BLa increased significantly over the value at the GET (Inc-Ex). However, it reached a steady-state level of 2.65 ± 1.56 (healthy) and 2.53 ± 0.95 (patient) $\text{mmol}\cdot\text{L}^{-1}$. The %peak oxygen uptake, %peak heart rate, and % heart rate reserve during CL-Ex were 58.8 ± 11.5, 71.8 ± 10.3, and 44.9 ± 17.4, respectively. All participants could complete CL-Ex with mean perceived exertion ratings (Borg/20) of 11.8 ± 1.3 (healthy) and 12.2 ± 1.3 (patient). These heart rate-related indices and exertion ratings were all within the recommended international guidelines for cardiac rehabilitation.

CL-Ex at the GET appears to be the optimal exercise intensity for cardiac rehabilitation.

Abbreviations: %HRR = %heart rate reserve, ANOVA = analysis of variance, BLa = blood lactate, CL-Ex = constant load exercise, CPET = cardiopulmonary exercise testing, GET = gas exchange threshold, HR = heart rate, Inc-Ex = incremental exercise, RER = respiratory exchange ratio, VCO_2 = carbon dioxide, VO_2 = oxygen uptake.

Keywords: cardiac rehabilitation, cardiopulmonary exercise testing, gas exchange threshold, older population, ventilatory anaerobic threshold

1. Introduction

The gas exchange threshold (GET), also known as the “ventilatory anaerobic threshold”, is a useful measure of exercise tolerance. GET is defined as the value of oxygen uptake (VO_2), where carbon dioxide (VCO_2) starts to increase disproportionately against VO_2 (a deflection point in the VO_2 vs VCO_2 relation using the V-slope method). This usually coincides with the elevation of blood lactate (BLa) levels.[1–4] Unlike peak or maximal oxygen uptake, GET is observed at 50% to 60% of VO_2max.[5,6] Therefore, GET is considered as the optimal initial training intensity for cardiac rehabilitation.[7–9]

Recently, GET-based personalized training programs, conducted in efforts to increase the efficacy of rehabilitation programs, are gaining popularity.[10–13] Traditional programs based on a certain percentage of maximal heart rate (HR) have resulted in widely differing lactate values; however, exercising at the same percentage of maximal HR or VO_2 did not result in a similar lactate response.[14] Therefore, one may argue that this traditional exercise protocol does not address the individual’s metabolic profile. In contrast, exercise based on GET is tailored to the individual’s metabolic profile,[6,15] and therefore should be a good index to guide exercise intensity in cardiac rehabilitation.

In Japan, cardiac rehabilitation is covered by the National Health Insurance. Cardiopulmonary exercise testing (CPET) using a respiratory gas analyzer system was also reimbursed. These circumstances have made the use of CPET very popular

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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before the start of cardiac rehabilitation. The Japan Circulation Society,[7] Japanese Association of Cardiac Rehabilitation,[16] as well as American and European Heart Associations[1] have recommended the use of ventilatory anaerobic threshold as a physiological means of tailoring of exercise intensity to individuals' metabolic profiles. However, while implementing GET-guided exercise (conventionally, with an average 20 minute-constant work rate protocol), some experts in Japan have identified the actual work rate is lower than the work rate when GET manifests during incremental testing (such as using the HR recorded 1 minute prior to GET). We believe that this was based on the concern of going beyond a threshold for gas exchange by using the actual GET work rate itself. Additionally, there is a margin of error in determining the inter-individual and intra-individual variations in the GET.[17,18] Furthermore, there is no widely accepted means of correcting for VO_2 in translating incremental exercise (Inc-Ex) GET to constant load exercise (CL-Ex) work rate, which can be easily applied in everyday settings. It is known that the lag in VO_2 response during Inc-Ex results in CL-Ex VO_2 exceeding that of a GET work rate obtained during incremental tests.[19,20] The definition of "GET-level" training remains ambiguous. Most of the GET-based training studies[10,11,13] used a work rate or heart rate slightly below the GET level determined during Inc-Ex. A physiological way to correct for the lag in VO_2 response has been recently reported.[19–21] However, it requires an extra exercise step of 6 minute of CL-Ex before the Inc-Ex to determine GET.[22] The implementation of this method in clinical settings has not yet been reported.

We hypothesized that based on our prior experience in cardiac rehabilitation, in which we also adopted the method of going back 1 minute for correcting work rate, we deemed that applying an "uncorrected'" work rate (work rate where GET appeared during Inc-Ex) for a constant-load 20-minute would be tolerated by most older subjects without undue physiological stress and within the accepted perceived sense of exertion for cardiac rehabilitation. The goal of the study was to collect data on VO_2, lactate dynamics, scores of perceived exertion, and the rate of completion of this CL-Ex during this protocol. It was expected to generate valuable baseline data on which we could build a more specific approach to GET-level exercise in a clinical setting.

As our participants of cardiac rehabilitation programs usually come from the older population, older individuals were chosen for this investigation.

2. Methods

2.1. Subjects

The study required all participants to be 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) (Patient, age: 73.0 ± 8.8 years). Cardiovascular disease etiologies included post-coronary artery bypass graft surgery (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 individuals matched for age (Healthy, age: 69.4 ± 6.8 years) 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.[23]

Table 1

Clinical characteristics of study participants.

Characteristics		Healthy group [n = 20]	Patient group [n = 10]
Age	[yrs]	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	[$\mathrm{pg\cdot dl^{-1}}$]		73.9 ± 126.4
LVEF	[%]		68.1 ± 13.4
IPAQ-SF	[$\mathrm{MET\text{-}min\cdot wk^{-1}}$]	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 $>25\ \mathrm{kg\cdot m^{2\cdot-1\cdot}}$ Significant differences in clinical characteristics such as age, BMI, and physical activity (IPAQ-SF) were not observed between healthy and patient groups.

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

Exclusion criteria included changes in medication within 6 months, infection within 2 weeks, chronic atrial fibrillation or flutter, permanent pacemaker, and presence of orthopedic conditions that rendered the individual unfit for exercise testing. In addition, we excluded participants who took warfarin, other anticoagulants, or metformin for diabetes.

2.2. 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 conducted 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 $10\ \mathrm{W\cdot min^{-1}}$ (Inc-Ex) with GET determination. On day 2, Inc-Ex was performed using a ramp protocol of $10\ \mathrm{W\cdot min^{-1}}$ 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 minute (Fig. 1). Before the experiment, the total duration of the exercise (Inc-Ex + CL-Ex) on day 2 was planned to be 25 minute for each participant. The duration of Inc-Ex varied among participants because of the different GET levels. Consequently, the mean Inc-Ex duration was 3.2 ± 1.1 minute and the mean CL-Ex duration was 21.8 ± 1.1 minute. Thus, all graphs, tables, and texts denoting 25 minute of CL-Ex represent approximately 22 minute of CL-Ex. Warm-up exercises were performed for 2 minute at 10 W. We used 10-s average data for all analyses.

2.3. Gas exchange threshold

We determined the GET during Inc-Ex testing on day 1 to determine the CL-Ex work rate on day 2. The GET was visually determined using the modified V-slope method as described by Sue et al,[24] which is a modification of the method described by Beaver et al.[25] The details of this method have been published

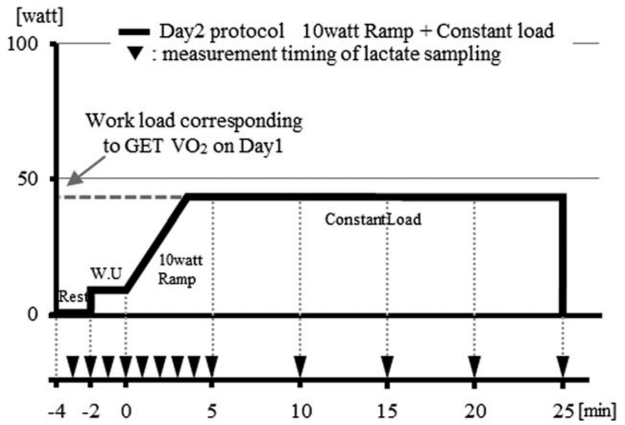

Figure 1. Day 2 exercise protocol. The time at the start of the ramp exercise was set to zero (0). The total exercise duration of the ramp and CL-Ex was set to 25 min. The time to GET varied depending on the participants. The mean was 3.2 ± 1.1 min. BLa was sampled twice at rest, twice during warm-up, and then every minute during the ramp exercise. It was also sampled every 5 min for a total exercise duration of 25 min. BLa = blood lactate, CL-Ex = constant load exercise, GET = gas exchange threshold, VO_2 = oxygen uptake, W.U. = warming up.

previously.[18,26] In summary, this V-slope method (Fig. 2) involves drawing a line parallel to the respiratory exchange ratio (RER) = 1 diagonal line through the data points, which is referred to as the pre-GET baseline (S1). The point at which the data begin to deflect toward the left is selected as the GET. The data points preceding the parallel line were disregarded. A line drawn parallel to the RER = 1 diagonal signifies a change of 1.0 in the rate of (Δ VCO_2/Δ VO_2) (Fig. 2). Therefore, the point at which this index begins to increase above 1.0 is the GET deflection point.[18,26] Previous studies included actual readings of the GET for each analyzed case. We used this approach in our study to identify the GET.

2.4. Blood lactate

Blood was sampled using a finger prick. A topical vasodilator was applied to the 2nd, 3rd, and 4th fingers of the left hand. The vasodilator was removed after 10 minute, and the entire left hand, including the distal part of the forearm, was placed in a water bath at 43 to 45°C for 10 min.[2,27] BLa levels were determined using Lactate Pro LT-1730 (Arkray, Kyoto, Japan). The instrument was calibrated using a calibration strip prior to each exercise session.

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 minute during the entire 25-minute exercise period (Inc-Ex + CL-Ex, Fig. 1).

2.5. Rate of perceived exertion and miscellaneous measures

The rate of perceived exertion was measured using the Borg scale. Left ventricular ejection fraction was determined using the Teichholz method. Brain natriuretic peptide levels were determined using a chemiluminescent enzyme immunoassay.

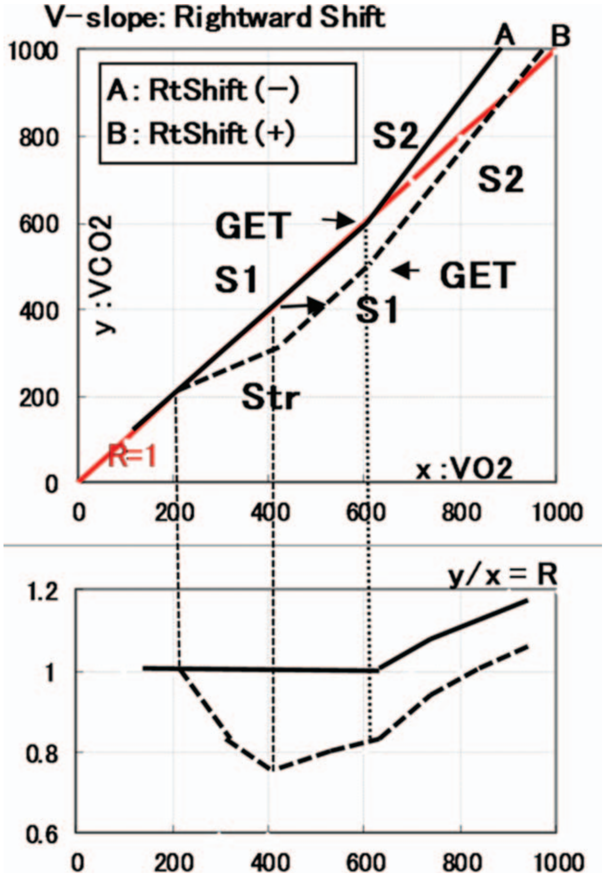

Figure 2. Determination of GET: diagram. The x-and y-axes are set at simple arbitrary values (0-1000) to explain the rightward shift of the V-slope line (upper panel) and its consequences on the RER calculation (lower panel). The V-slope line “A” shows no rightward shift. “B” shows a rightward shift of 100 mL (horizontal arrow to right). For “A”,’ during S1, the RER (VCO_2/VO_2) equals the change in the rate of (Δ VCO_2/Δ VO_2). Both variables were kept constant at 1.0. For “B”, the rate of change is not equal to the RER. The rate of change was constant at 1.0, whereas the RER was not constant. Str (S transient) is the segment in transition prior to the establishment of S1. GET = gas exchange c threshold, RtShift = rightward shift of V-slope line, S1 = pre-GET baseline, S2 = post-GET segment, VO_2 = oxygen uptake, VCO_2 = carbon dioxide.

2.6. Statistical analysis

Data are presented as the mean ± SD. Unpaired data were analyzed using Student *t* test. Paired data were analyzed using paired *t* tests. Testing for VO_2 steady state in each case during CL-Ex involved comparing the last exercise dataset (25-minute data) to the preceding 4 datasets (data at every 5 minute). The 1-minute dataset consisted of 6 data points of 10 second each. A repeated 1-way analysis of variance (ANOVA) was performed, followed by post hoc Bonferroni correction. The P value was expressed as $P \times$ the number of comparisons (4, $P < .05$), with a value $< .05$ considered to be significant. On the other hand, $P > .05$ indicates that the exercise was at a steady-state level. Comparisons between the healthy and patient groups were performed using a repeated 2-way ANOVA. In addition to the pre-planned 5-minute analysis (lactate sampling point) over the entire 25-minute exercise period (Inc-Ex + CL-Ex), data analysis based on the start of CL-Ex as time point zero (0) was also performed.

The %peak VO_2 at GET was calculated as (VO_2 at CL-Ex 25 min/peak VO_2) × 100. The %peak HR at GET was calculated as (HR at CL-Ex 25 min/peak HR) × 100. The %heart rate reserve (%HRR) at GET was calculated as (GET at CL-Ex 25 min HR - resting HR)/(Peak HR - resting HR). Peak values denote those recorded during the Inc-Ex.

2.7. Ethical considerations

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of Sapporo Ryokuai Hospital (approval number: 19–1). Informed consent was obtained from all study participants. There is no identifying information concerning the participants in the manuscript, and the information has been fully anonymized.

3. Results

The clinical characteristics of the participants are summarized in Table 1. The total metabolic equivalent minutes per week according to the international physical activity questionnaire–short form was not significantly different between the healthy and patient groups ($P = .119$). This result is similar to the average of a broader healthy Japanese population in the same age range.[28]

3.1. Change in variables during CL-Ex (Figs. 3–6, Tables 2–4)

3.1.1. Oxygen uptake, respiratory exchange ratio, and heart rate. The mean oxygen uptake reached a steady state during the final 10 minute of the CL-Ex (Fig. 4). RER also followed the same pattern as that of VO_2 (Fig. 5), remaining below 1.0. In contrast, HR did not reach a steady state, increasing progressively during CL-Ex (Fig. 6). At GET, the ratios of CL-Ex/Inc-EX values of VO_2 and HR were 115% and 111%, respectively (n = 30). There were no significant differences between the 2 groups with respect to CPET parameters (no interaction found by 2-way ANOVA). There were no significant differences in CPET parameters between the GET during Inc-Ex (day 1) and the workload of the Inc-Ex/CL-Ex transition (day 2) (Table 3). The %peak VO_2, %peak HR, 0%HRR values are shown in Table 3. All values were within the recommended range for exercise intensity according to various international and national cardiac rehabilitation guidelines,.[1,7,8]

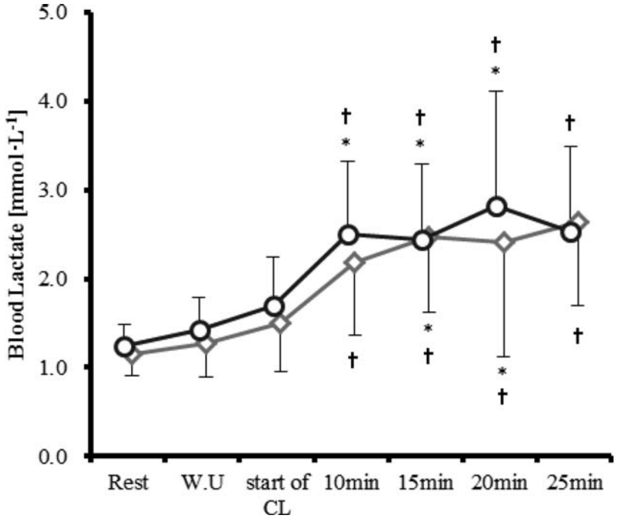

Figure 3. Blood lactate (BLa) response during constant load exercise (CL-Ex). BLa response of the healthy group (◇) and patient group (○) during CL-Ex. Data are presented as mean ± S.D. CL-Ex (day 2) consisting of ramp exercise for an average of 3 min and CL-Ex for 22 min, for a total exercise duration of 25 min (see Methods for details). * Not significantly different ($P > .05$) vs 25-min value. †$P < .05$ vs start of CL [Healthy: 1.50 ± 0.37, Patient: 1.69 ± 0.55 mmol□L^{-1}].

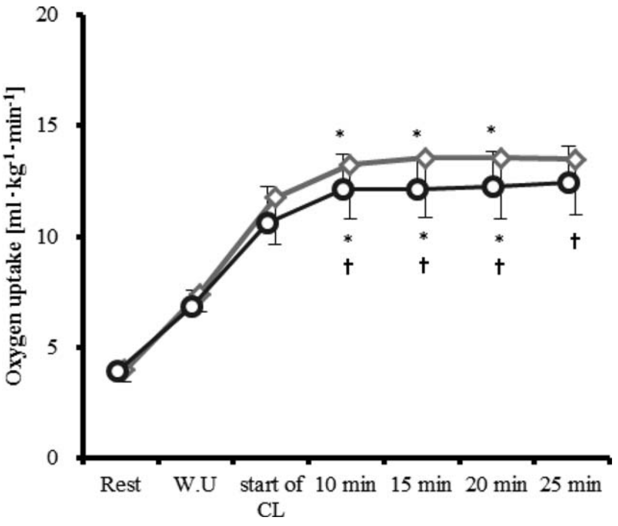

Figure 4. Oxygen uptake during constant load exercise (CL-Ex). Oxygen uptake (VO_2/weight) response of the healthy group (◇) and patient group (○) during CL-Ex. The data representations are the same as those shown in Figure 2. *Not significantly different ($P > .05$) vs 25-min value. †$P < .05$ vs start of CL [healthy: 11.7 ± 2.1, patient: 10.6 ± 1.6 ml·kg^{-1}·min^{-1}].

3.1.2. Blood lactate. The BLa levels at the start of CL-Ex (the end of ramp Inc-Ex) increased further during CL-Ex (Fig. 3). However, these values reached a steady state during the final

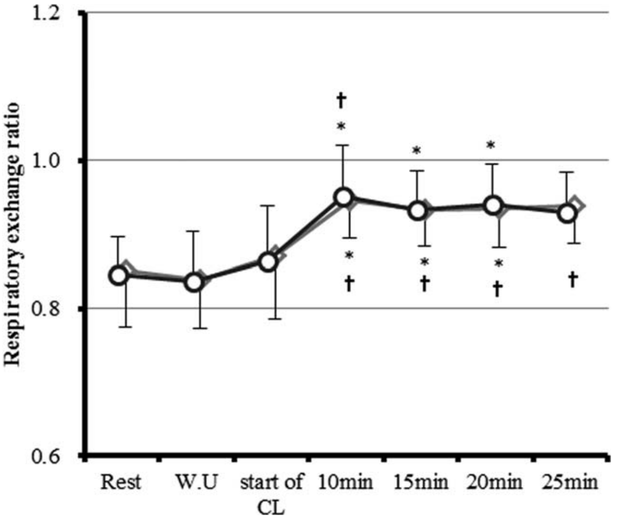

Figure 5. Respiratory exchange ratio (RER) during constant load exercise (CL-Ex). RER response of the healthy group (◇) and patient group (○) during CL-Ex. The data representations are the same as those shown in Figure 2. *Not significantly different ($P > .05$) vs 25-min value. †$P < .05$ vs start of CL [healthy; 0.87 ± 0.09, patient; 0.86 ± 0.07].

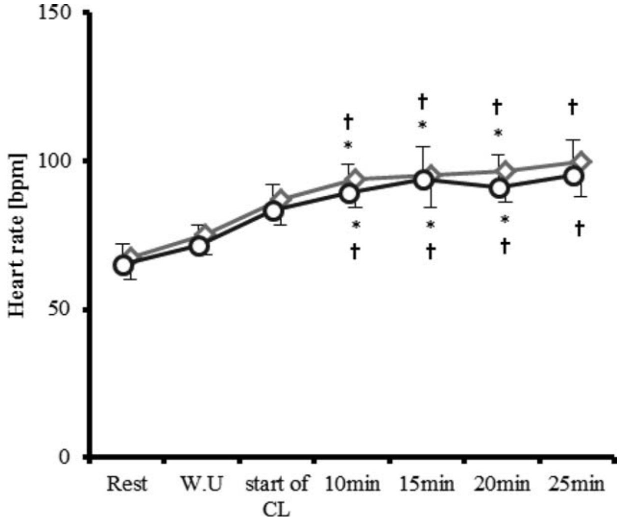

Figure 6. Heart rate (HR) during constant load exercise (CL-Ex). HR response of the healthy group (◇) and patient group (○) during CL-Ex. The data representations are the same as those shown in Figure 2. *Not significantly different ($P > .05$) vs 25-min value. $^{\dagger}P < .05$ vs start of CL [healthy; 87.0 ± 11.0, patient; 83.3 ± 8.7 bpm].

10 minute in the healthy group and final 5 minute in the patient group. The steady-state lactate level was 1.42 ± 1.16 $\text{mmol}\cdot\text{L}^{-1}$ above the value recorded at the GET point during Inc-Ex. The increase in BLa after the start of CL-Ex was much greater than that of VO_2 or HR. At GET, the ratio of the CL-Ex/Inc-Ex values of BLa was 158%. There were no significant differences between the 2 groups with respect to BLa. There were no significant differences in BLa between the GET during Inc-Ex (day 1) and the workload of the Inc-Ex/CL-Ex transition (day 2) (Table 3).

3.1.3. Rate of perceived exertion. The rate of perceived exertion (Borg scale: 6-20) during the CL-Ex was not significantly different between the 2 groups (Table 3). The Borg scale range was 9 to 14 and 9 to 13 in the healthy and patient groups, respectively. All participants completed the exercise protocol for 25 minutes.

3.1.4. Adverse effects of exercise testing. One participant developed transient intermittent supraventricular tachycardia (100-110 bpm) during the final 5 minute of the CL-Ex. A significant ST-segment change without angina was observed in 1 case; this case was excluded from the study.

4. Discussion

This study aimed to assess the VO_2, BLa dynamics, and perceived rates of exertion during GET-level CL-Ex (“uncorrected”) based on the results of GET during Inc-Ex. The rationale behind our methodology was that the GET level of exercise is often recommended as an initial work rate for cardiac rehabilitation.[7–9] While the often-employed percentage of maximal VO_2 approach results in a very heterogeneous metabolic profile (including BLa) in different individuals,[14] GET-level exercise is expected to produce a more homogenous and consistent response targeted at an individually appropriate exercise intensity. Although GET-guided exercise training has been recommended,[1,7,16] the exact implementation of this protocol remains unclear. In Japan, exercise therapists in a clinical setting routinely use HR that has been recorded 1 minute prior to the appearance of GET (during Inc-Ex) as an initial target HR during CL-Ex. One guideline suggests a 10 W reduction in work rate when a 10 $\text{W}\cdot\text{min}^{-1}$ incremental test is used.[1] Most GET-guided training programs use the same type of simple practical adjustment for the overestimation described as follows: initially 10 bpm below GET-HR[12] or 80% of the work intensity of GET.[10] The need for correction arises from the fact that if 1 uses the HR or VO_2 as recorded during Inc-Ex tests, the measurements may be underestimated; however, the HR or VO_2 level will increase to a higher level during CL-Ex. Because of the delay in VO_2 and HR changes during CL-Ex,[19,20] a decrease or correction of the target work rate is required. Currently, correction is performed arbitrarily in the clinical setting. A newer, more physiological, and quantitative method for correcting VO_2 delay has been proposed.[19,20] However, the method requires 1 or more intersessions of an extra 6 minute of CL-Ex before the routine Inc-Ex test. Therefore, this strategy has not yet been routinely applied to cardiac rehabilitation.

We chose to use the GET work rate exactly as it manifested during Inc-Ex, which was “uncorrected”.’ The consequence of not correcting of exercise intensity was revealed by the increase in HR and VO_2 during the implementation of CL-Ex (greater exercise intensity during CL-Ex than anticipated from “uncor-

Table 2

Primary cardiopulmonary data at rest and peak exercise.

			Healthy group [n = 20]		Patient group [n = 10]	
			Inc-Ex (Day 1)	CL-Ex (Day 2)	Inc-Ex (Day 1)	CL-Ex (Day 2)
Rest	VO_2	[$\text{ml}\cdot\text{min}^{-1}$]	239 ± 41	225 ± 35	253 ± 50	265 ± 52*
	VO_2/weight	[$\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$]	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	[$\text{mmol}\cdot\text{l}^{-1}$]	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	[$\text{ml}\cdot\text{min}^{-1}$]	1400 ± 316	–	1318 ± 335	–
	VO_2/weight	[$\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$]	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	[$\text{mmol}\cdot\text{l}^{-1}$]	5.55 ± 1.55	–	5.80 ± 2.58	–
	RPE		16.2 ± 2	–	17.1 ± 1.4	–

CL-Ex = constant load exercise, HR = heart rate, Inc-Ex = incremental exercise, RER = respiratory exchange ratio, RPE = rate of perceived exertion, VO_2/wgt = oxygen uptake per weight, VO_2 = oxygen uptake.
*Significant ($P < .05$) for healthy group vs patient group.

Table 3

Cardiopulmonary data during exercise at gas exchange threshold.

		Healthy group [n=20]			Patient group [n=10]		
		Inc-Ex (day 1)	CL-Ex (day 2)		Inc-Ex (day 1)	CL-Ex (day 2)	
		GET	Start of CL-Ex (GET)	End of CL-Ex	GET	Start of CL-Ex (GET)	End of CL-Ex
Work rate	[watt]		41.8 ± 10.2			41.1 ± 12.2	
VO_2 (%increase)	[$ml \cdot min^{-1}$]	678 ± 136	661 ± 117	$760 \pm 144^{*,\dagger}$ (1.13 ± 0.11)	700 ± 170	721 ± 183	$840 \pm 193^{*,\dagger}$ (1.21 ± 0.14)
VO_2/weight (%increase)	[$ml \cdot kg^{-1} \cdot min^{-1}$]	12.1 ± 2.6	11.7 ± 2.1	$13.5 \pm 2.5^{*,\dagger}$ (1.12 ± 0.11)	10.3 ± 1.5	10.6 ± 1.6	$12.4 \pm 1.6^{*,\dagger,\ddagger}$ (1.21 ± 0.12)
%Peak	[%]	49.4 ± 8.4	48.3 ± 9.1	$55.7 \pm 10.7^{*,\dagger}$	54.4 ± 9.9	55.6 ± 9.4	$65.2 \pm 10.5^{*,\dagger}$
RER		0.85 ± 0.05	0.85 ± 0.06	$0.94 \pm 0.05^{*,\dagger}$	0.87 ± 0.07	0.86 ± 0.07	$0.93 \pm 0.05^{*}$
HR (%increase)	[bpm]	91.1 ± 12.6	87.0 ± 11.0	$99.7 \pm 14.2^{*,\dagger}$ (1.10 ± 0.10)	84.0 ± 6.2	83.3 ± 8.7	$95.0 \pm 11.9^{*,\dagger}$ (1.14 ± 0.10)
%MHR	[%]	64.0 ± 8.5	61.3 ± 8.8	$70.6 \pm 11.3^{\dagger}$	66.0 ± 6.2	65.2 ± 6.0	$74.3 \pm 7.7^{*,\dagger}$
%HRR	[%]	30.9 ± 9.9	25.4 ± 11.5	$43.6 \pm 19.4^{*,\dagger}$	30.5 ± 7.4	28.6 ± 9.5	$47.6 \pm 13.1^{*,\dagger}$
Lactate (%increase)	[$mmol \cdot L^{-1}$]	1.51 ± 0.29	1.50 ± 0.37	$2.65 \pm 1.56^{*,\dagger}$ (1.75 ± 0.87)	$1.78 \pm 0.42^{\ddagger}$	1.69 ± 0.55	$2.53 \pm 0.95^{*,\dagger}$ (1.40 ± 0.37)
RPE		–		11.8 ± 1.3	–		12.2 ± 1.3

On day 1, GET was determined during Inc-Ex. Data for day 2 shows the start of CL-Ex (reached at GET work rate) and the 25-min value during CL-Ex at the work rate corresponding to GET VO2 on day 1.

-Exercise intensity (%MHR) = HR/MHR.

-Target heart rate = exercise intensity (%MHR) × MHR.

-Exercise intensity (%HRR) = (GET or CL-Ex 25 min HR − rest HR)/(Peak HR − rest HR).

-Target heart rate = exercise intensity × (MHR − rest HR) + rest HR.

VO2 = oxygen uptake, VO2/weight = oxygen uptake per weight, GET = gas exchange threshold, HR = heart rate, MHR = maximum heart rate, CL-Ex = constant load exercise, Inc-Ex = incremental exercise, RPE = rate of perceived exertion, RER = respiratory exchange ratio, %MHR = %heart rate maximum, %HRmax = %maximum heart rate, %HRR = %heart rate reserve.

[*] Significant ($P < .05$) for GET in Inc-Ex vs the end of CL-Ex.

[†] Significant ($P < .05$) for the start vs the end of CL-Ex.

[‡] Significant ($P < .05$) for healthy vs patient.

rected” GET level). However, we found that the exercise intensity expressed during CL-Ex was within the recommended range of % peak VO_2, %peak HR, %HRR, and perceived rate of exertion.[1,7,8] This was achieved with a 100% completion rate of the protocol exercise. Therefore, we believe that this method of administering GET-guided exercise training with a slow ramp protocol such as $10\,W \cdot min^{-1}$ is quite feasible as a simple and practical method when used in older populations. Additionally, the fact that BLa levels were elevated during CL-Ex may have implications for the training effect. It has been suggested that elevated BLa levels may serve as a metabolic signal to stimulate more efficient aerobic energy production.[29–32] This phenomenon is sometimes referred to as “lactormone”.[30] Therefore, an increase in BLa level 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. If GET-level CL-Ex (provided it can be exactly implemented) produces only minimal or no blood lactate elevation (above resting level), the exercise intensity may not be sufficient for effective training. Moreover, the elevated value can be used to evaluate the effect of training by monitoring its decrease.

Further explanation is required for the use of the CL-Ex protocol employed in this study; that is, the use of approximately 3 minute of Inc-Ex prior to CL-Ex, instead of the usual stepwise introduction of CL-Ex.[33,34] We theorized that using a stepwise introduction of the GET-level workload may cause an individual to experience a sudden and 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 routinely performed), we halted Inc-Ex as soon as we detected the GET (with minimal lactate increase) and transitioned into CL-Ex.

This study has some limitations. First, the “uncorrected” GET-guided method is only applicable to slow ramp protocols. A more physiologically sound GET-guided exercise training method[19,20] should be instituted for more rapid ramp protocols, such as for younger populations. The price of not “correcting” is

Table 4

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

CL-Ex n=30	[min]	Start of CL 0	6.8 ± 1.1	11.8 ± 1.1	16.8 ± 1.1	21.8 ± 1.1
Lactate	[$mmol \cdot l^{-1}$]	1.56 ± 0.44	$2.29 \pm 0.75^{*,\dagger}$	$2.46 \pm 0.94^{*,\dagger}$	$2.55 \pm 1.15^{*,\dagger}$	$2.61 \pm 1.27^{\dagger}$
VO_2	[$ml \cdot min^{-1}$]	681 ± 142	$770 \pm 157^{*,\dagger}$	$783 \pm 159^{*,\dagger}$	$780 \pm 153^{*,\dagger}$	$786 \pm 163^{\dagger}$
VO_2/weight	[$ml \cdot kg^{-1} \cdot min^{-1}$]	11.4 ± 2	$12.9 \pm 2.3^{*,\dagger}$	$13.1 \pm 2.4^{*,\dagger}$	$13.1 \pm 2.5^{*,\dagger}$	$13.1 \pm 2.3^{\dagger}$
R		0.86 ± 0.07	$0.95 \pm 0.06^{*,\dagger}$	$0.93 \pm 0.05^{*,\dagger}$	$0.94 \pm 0.05^{*,\dagger}$	$0.94 \pm 0.05^{\dagger}$
HR	[bpm]	85.7 ± 10.3	$92.2 \pm 12.3^{\dagger}$	$94.5 \pm 13.1^{*,\dagger}$	$95.1 \pm 13.3^{*,\dagger}$	$98.4 \pm 14.0^{\dagger}$

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

[*] Not significantly different ($P > .05$) vs 25-min value.

[†] Significant ($P < .05$) vs start of CL value.

known to be smaller for lower work rate tests.[19,20] Second, the sample size of participants with cardiovascular diseases was insufficient. In particular, no differences were observed between the healthy and patient groups. This may be because the study did not include cardiac patients with greater severity. Third, the GET is visually determined, and individual GET values determined by different investigators can vary significantly.[17] Therefore, there is a possibility that a similar investigation may not produce similar results. Further studies with a similar nature that address these limitations are recommended.

Although to our knowledge, our study is the only study using CL-Ex at GET, 1 study[35] investigated lactate levels at the lactate threshold in young men. Although GET was not used and respiratory variables were not reported, the lactate patterns in the aforementioned study were similar to our results.

If this uncorrected GET protocol proves to be excessive in routine clinical application, then a simple practical correction factor may be applied, such as a 5 to 10 reduction in work rate. Follow-up studies are needed to further address this point. Furthermore, the range of ramp exercise protocol (Inc-Ex) for older people is only approximately between 5 and 20 W·min^{-1}. We have planned to conduct similar studies to the current one at 5, 15, and 20 W/min and explore an approximate correction for each Inc-Ex-based program.

In conclusion, the proposed protocol physiologically elicited "supra-GET" levels of exercise intensity. However, the average perceived rate of exertion and the 100% protocol completion rate of participants imply that using a CL-Ex protocol based on the "uncorrected" GET work rate as determined during Inc-Ex is a feasible and safe strategy to employ in the older population. The resulting elevated lactate levels may elicit sufficient oxidative stress, which is critical for the training effect. In addition, lactate may act as a metabolic signal to stimulate more efficient aerobic energy production during exercise (termed the "lactormone" effect) (Supplemental digital content File. 1 - BLa, http://links.lww.com/MD2/A568, Supplemental digital content File. 2 - VO2, http://links.lww.com/MD2/A569, Supplemental digital content File. 3 - HR, http://links.lww.com/MD2/A570, Supplemental digital content File. 4 - RER, http://links.lww.com/MD2/A571).

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The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. They do not constitute an endorsement by medicine.

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