The temporal relationship of thresholds between muscle activity and ventilation during bicycle ramp exercise in community dwelling elderly males

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Abstract. [Purpose] To compare the appearance time of the ventilatory threshold point and the electromyographic threshold in the activity of the vastus lateralis, rectus femoris, biceps femoris long head and gastrocnemius lateral head muscles during ramp cycling exercise in elderly males. [Subjects and Methods] Eleven community dwelling elderly males participated in this study. Subjects performed exercise testing with an expiratory gas analyzer and surface electromyography to evaluate the tested muscle activities during ramp exercise. [Results] The electromyographic threshold for rectus femoris was not valid because the slope after electromyographic threshold was not significant as compared to that before electromyographic threshold. The slope of the regression line for vastus lateralis was significantly decreased after electromyographic threshold while biceps femoris and gastrocnemius were increased. The electromyographic threshold appearance times for vastus lateralis and gastrocnemius were significantly earlier than ventilatory threshold point. There were no difference in electromyographic threshold appearance times among three muscles. [Conclusion] These results suggest that the increase in the slope of the regression line after electromyographic threshold for vastus lateralis was decreased, possibly indicating to postpone muscular fatigue resulting from the activation of biceps femoris and gastrocnemius as biarticular antagonists. This recruitment pattern might be an elderly-specific strategy.

Key words: Electromyographic threshold, Ventilatory threshold, Community dwelling elderly males

INTRODUCTION

Decreased aerobic capacity is a risk factor for all-cause mortality in Japanese men1). In addition, cardiorespiratory fitness is a strong predictive factor of death in elderly individuals2). Therefore, improving aerobic capacity in elderly individuals is thought to prolong not only the average life expectancy, but also the healthy life expectancy, which may have significant medical, social, and medico-economic influences.

In the setting of rehabilitation training, prescribed exercise programs often include aerobic exercise with constant work load using a bicycle ergometry aimed at maintaining and improving the aerobic capacity of the patient. The most important consideration when prescribing aerobic exercise is determining the exercise intensity. If the exercise intensity is too high, it...
may result in injuries to the musculoskeletal system or an increased load on the heart, leading to accidents during exercise. However, if the exercise intensity is too low, the prescribed exercise provides only a weak effect, requires more time until the manifestation of the effect, and results in a poor rate of exercise adherence. Therefore, it is necessary to determine the appropriate intensity for aerobic exercise. The gold standard exercise intensity keeps the patient near their anaerobic threshold (AT point), which is the point at which the dominant mechanism in adenosine triphosphate (ATP) production switches from aerobic to anaerobic metabolism. When considering the risk-benefit profile of therapeutic exercise, using the AT point is recommended as an index to determine the optimal exercise intensity. When determining the AT point in the clinical setting, the ventilatory threshold (VT) point is determined by implementing a cardiopulmonary exercise test (CPX) using an expired gas analyzer. However, while aerobic exercise is prescribed for many patients requiring rehabilitation training, the number of patients with heart disease in whom cardiac rehabilitation is begun without implementing an exercise test is increasing in Europe and the United States. One reason for this is that CPX imposes a heavy burden on the patient’s body, possibly aggravating symptoms in patients who have a vulnerable physical condition or motor organ disease, particularly in the legs. Therefore, strict evaluation of the VT point using CPX is often avoided in these cases. Because this trend likely also exists in Japan, the exercise intensity should be adjusted using not only subjective symptoms but also an objective surrogate index that allows the prediction of the VT point in patients in whom the VT point has not been evaluated. One of the objective indices is the target heart rate calculated by the Karvonen method, in which the target heart rate is obtained as the product of the coefficient and the predicted maximum heart rate (220 − age). Because the heart rate responds most sensitively to exercise intensity, it is considered reasonable to determine the optimal exercise intensity based on the heart rate. However, β-blockers and other drugs that influence the circulatory system also affect the heart rate variability. Therefore, in patients on these types of drugs, the predicted maximum heart rate may deviate from the actual maximum heart rate. In addition, blunting of the rate response during exercise causes difficulty in determining the coefficient and thus the target heart rate. Patients with hypertension, a representative cardiovascular disease, total approximately 43 million in Japan, and patients being treated for hypertension account for more than 50% of individuals in their 60s and more than 60% of those in their 70s. This means that heart rate can be used as the index for determining the exercise intensity in less than 50% of the elderly population when recommending aerobic exercise for this subgroup of patients. Thus, an index other than the heart rate is necessary for determining the optimal exercise intensity for elderly individuals.

There are effector systems for both the respiratory and circulatory systems as determinants of aerobic capacity. The oxygen consumption of skeletal muscles during exercise determines the workload of the respiratory and the circulatory system via the chemoreceptor reflex. Therefore, it is speculated that the VT point can be predicted from the intensity of and variations in the activity of working muscles during exercise. In addition, such an index is advantageous because it is minimally influenced by medications, in contrast to the heart rate. In a bicycle ergometry study in healthy young subjects, Nagata et al. obtained the inflection point at which the integrated myoelectric potential of the vastus lateralis (VL), measured by surface electromyography, began to increase non-linearly and demonstrated that the oxygen uptake (VO₂) at the inflection point was closely correlated with the VO₂ at the AT point. This suggests that the inflection point for the VL can be an index for the aerobic capacity. According to Moritani et al., the inflection point, as manifested by a non-linear increase in the muscle activity, may be attributable to an increase in the recruitment of fast twitch motor units and motor unit rate coding needed to maintain the required energy supply for contraction. There have been many studies that examined the inflection point obtained due to changes in the activity of the skeletal muscles of the lower limbs during ergometry exercise. The examined muscles are usually quadriceps femoris muscles such as the VL or the rectus femoris (RF) which agonist muscle during pedaling, and their antagonist muscles, such as the biceps femoris long head (BF). In a study that evaluated the inflection points of these three muscles, the inflection points at which these muscles began to increase non-linearly manifested near the respiratory compensation point (RC point), i.e., the delayed ventilatory threshold (VT₂), and the inflection point occurred later than the VT point. However, all of these studies targeted only young participants with a high exercise tolerance, such as professional cyclists or other athletes, and did not include elderly subjects. The properties of skeletal muscle differ greatly between elderly and young individuals. The number of motor units decreases with aging, and the relative excess of decreased motor neurons over the decrease in the number of muscle fibers causes an increase in the mean innervation ratio of motor units in elderly individuals. Decreases in the number of motor units and muscle fibers along with atrophy lead to muscle weakness. In addition, the composition of muscle fibers changes with age, such that there is a relative decrease in type II fibers and an increase in type I fibers. There have been no reports documenting whether an appropriate inflection point can be obtained from changes in muscle activity in elderly individuals or whether there is any difference between this inflection point in elderly versus young people. The present study aimed to examine the temporal relationship between the inflection point of muscle activity and the VT point in community dwelling elderly males, and thereby determine which muscle can provide an index of exercise intensity in the elderly.

SUBJECTS AND METHODS

Eleven community dwelling elderly males participated in this study (67.7 ± 3.2 years, BMI 22.4 ± 1.7 kg/m²). The subject selection criteria were: having a fitness habit (physical activity at least 30 min a day two times a week for one year), not having been instructed by a physician to refrain from physical exercise, having no current or past history of respiratory,
circulatory, or metabolic diseases possibly limiting physical activity, not taking medication, and no low back pain or leg pain during cycling exercise. Written informed consent was obtained from the subjects after the study procedure had been fully explained. This study was approved by the ethics committee for research of the Kinjo University (approval number: 26-07, 27-29).

Muscle activity during the exercise session was measured by surface electromyography (TeleMyo2400 EM-401, Noraxon, Inc., USA). The following muscles were VL, RF, BF and gastrocnemius lateral head (GL) (on the right side). After appropriate skin preparation, disposable electrodes (Bluesensor P-00-S, METS, Japan) were placed parallel to the muscle fibers. Skin impedance was measured with an impedance checker (EM-570, Noraxon, Inc., USA), ensuring that the skin-electrode impedance was kept below 5 kΩ. The sampling frequency was 3,000 Hz.

CPX was conducted using an expired gas analyzer (AT-1100A, ANIMA Corp.) and a bicycle ergometry (EC-MD100, Cateye). Blood pressure, heart rate, and oxygen saturation were monitored in subjects wearing an electrocardiogram (ECG) recorder (ECG-1550, Nihon Cohden Corp.), a stress blood pressure monitor (Tango, SunTech Medical, Inc.), and a pulse oximeter (Oximate S-101, Shimei Medical). The blood pressure monitor was attached to the participant’s right upper arm and the pulse oximeter to the left index finger. The saddle was set at a level that allowed the subject’s right knee to achieve approximately 20° of flexion when the right pedal was at the lowest point. The foot was placed on the pedal with the toes protruding from the front part of the pedal and fixed with a pedal strap fastened over the instep to an appropriate tightness.

The ramp protocol was used with incremental loading of 10 W per minute. Incremental loading was begun after 4 min of sitting at rest on the saddle and 4 min of warm-up pedaling. The cadence was 50–60 rotations per minute. The subject was instructed as appropriate to stare ahead and not tilt forward excessively during pedaling. Beginning with the start of exercise loading, blood pressure was measured every 1 min and the subjective intensity of exercise was evaluated by the Borg scale separately for chest symptoms and lower limb symptoms.

Because this study enrolled elderly subjects, the CPX discontinuation criteria included objective findings (ECG abnormalities, blood pressure, heart rate, and pedaling status) as well as subjective symptoms (19 [very hard] or higher score on the Borg scale for the chest or lower limbs). The blood pressure discontinuation criteria were a systolic blood pressure>200 mmHg or a decrease of 10 mmHg or more from the level at the beginning of exercise. The heart rate exceeded 90% of the subject’s predicted maximum heart rate (220 – age). The pedaling status was failure to maintain pedaling at 50 rotations/min for approximately 10 s or more. Exercise loading was discontinued immediately when it met the CPX discontinuation criteria, and a 4 min cooldown at 20 W was provided. Subsequently, the subject received hydration and was allowed to leave the room after their blood pressure and heart rate were restored to pre-exercise levels. No subjects had physical abnormalities after exercise testing.

Analog signals of recorded myogenic potentials were subjected to analog-to-digital (AD) conversion and entered into a personal computer. The electromyographic waveforms obtained were processed with a 30–500 Hz band-pass filter and then subjected to full-wave rectification, normalization at the rectified peak level for the maximum voluntary contraction, and root mean square (RMS) processing at 50 ms intervals. In this study, the mean level of muscle activity was obtained for each incremental 1 W, and the mean level of muscle activity for a 6 s interval was calculated. When the data obtained immediately before the end of exercise loading did not span the designated 6 s interval, the data were excluded from data processing. To minimize individual differences in electrical charge, the mean level of muscle activity for each 6 s interval during the exercise period was normalized by the mean level of muscle activity for 30 s (from the 211st to 240th second) during the warm-up. Time-series data obtained and processed using these procedures were used for piecewise regression analysis, and the point that gave the maximum inflection in the muscle activity (electromyographic threshold: EMGT) was obtained. Calculation of the EMGT using linear regression has been performed by other researchers who conducted similar studies. Two regression lines crossing at an arbitrary point were applied, and the point that gave the maximum summation of the residual sums of squares of the two regression lines was considered the EMGT. The slopes of the two regression lines around the EMGT were determined as the pre-slope (regression line before the EMGT: pre-slope; regression line after the EMGT: post-slope) and the coefficient of determination (R²) for evaluating the accuracy of the derived EMGT were obtained.

The VO₂, CO₂ elimination (VCO₂), minute expiratory ventilation (VE), fraction end-tidal oxygen (FETO₂), and fraction end-tidal CO₂ (FETCO₂) were obtained from the expired gas data during CPX, and the VT point was determined by two raters. Using the V-slope method, the VT point was determined as the point at which VE/VCO₂ was unchanged or decreased but VE/VO₂ was increased, or FETCO₂ was unchanged or decreased but FETO₂ was increased. The pre- and post-slope values were compared to verify the validity of the calculated EMGT for the 4 tested muscles. If both slopes were not parametric according to the Shapiro-Wilk test, the pre- and post-slopes were compared using the Wilcoxon signed rank test. Next, the EMGT appearance time which verified their validity and the VT point time were compared. Each EMGT time was expressed relative to the VT point time (with the VT point considered 100%). If the EMGT times were parametric according to the Shapiro-Wilk test, the EMGT time and VT point time were compared using Tukey’s honestly significant difference test. We utilized PASW statistics 18.0 (IBM SPSS) statistical software for all analyses. For all tests, a p value<0.05 was considered statistically significant.
RESULTS

The averaged total time of CPX was 406.4 ± 94.4s, and end point was that eight was the elevation of blood pressure and three was elevation of heart rate. The VT point time was 84.9 ± 9.9% relative to total exercise time.

Comparing the slopes before and after EMGT, the post-slope in the VL decreased significantly (p<0.01), whereas the post-slope in the BF (p<0.01) and GL (p<0.01) increased more than pre-slope. There was no difference between the pre- and post-slopes in the RF.

Comparing the EMGT appearance times for the VL, BF, and GL with the VT point, the EMGT appearance times for VL (p<0.0001) and GL (p<0.05) were significantly earlier than the VT point, and the EMGT for BF tended to proceed at the VT point (p=0.08). The EMGT appearance times did not differ across the 3 muscles (Table 1).

DISCUSSION

The non-linear increase in EMG activity may reflect the additional recruitment of fast twitch motor units to compensate for the deficit in contractility resulting from the impairment of fatigued motor units10, 15). In previous studies in which the non-linear increase point of muscle activity was obtained by RMS processing, the EMGT was confirmed in the various muscles examined15–21). Thus, previous studies have shown that the EMGT is closely associated with ventilation kinetics15, 18, 21).

However, most of the previous studies that determined the EMGT enrolled athletes who had a very high exercise tolerance, such as professional cyclists and triathletes, because of the characteristic features of CPX. No studies have examined the EMGT in elderly participants, even though elderly patients represent a core target population for rehabilitation. In this study examining elderly persons, the EMGT values for four muscles associated with pedaling actions, i.e., the VL, RF, BF, and GL, were determined and compared with the time to reach the VT point. A valid EMGT was found for three muscles, the VL, BF, and GL, excluding the RF. Interestingly, the post-slope increased compared with the pre-slope in the BF and GL, whereas there was a decrease in the post-slope in the VL. In addition, the EMGT occurred earlier than the VT point in the VM and GL.

When the angle was regarded as 0° for the pedal at the highest point, 180° at the lowest point, and 90° at the midpoint between the highest and lowest points during forward rotation, the monoarticular VL and vastus medialis muscles began to be activated just before the highest point and remained active until just past 90°. In particular, there was a peak at approximately 30°, indicating that these muscles were in charge of downward pedaling (down-stroke) via extension of the knee25). On the other hand, the biarticular RF muscle began to be active earlier than the vastus muscles, showing muscle activity that began at approximately 270° and was maintained past the highest pedal point until approximately the same point as the vastus muscles, with its peak obtained near the highest point25). Compared with the vastus muscles, the RF had a longer time phase for one pedal rotation and reached its peak activity earlier. This is because, like the vastus muscles, the RF is responsible for both down-stroke pedaling via knee extension after reaching the highest point and pulling up the pedal (up-stroke) via hip flexion. Because the quadriceps oxidative capacity, which is the product of the volume of the quadriceps femoris muscle and VO2, during bicycle ergometry is correlated with the change in the whole body VO226), it is apparent that the VL and RF play major roles in pedaling a bicycle ergometry in both kinematic and metabolic aspects.

Studies of the EMGTs of the VL and RF have occasionally been reported in the literature. Lucia et al.15) conducted a study of elite cyclists to obtain the EMGT at two points for the VL and RF under incremental exercise loading, based on changes in the muscle activity, and reported that delayed manifestation of the EMGT (EMGT\textsubscript{Th2}) was found after the RC point (VT\textsubscript{2}). In a study by Thomas and Stephane18), who examined cyclists and triathletes, the EMGT was obtained just before the RC point in these two muscles. Racinais et al.21) conducted a similar study in cyclists, and demonstrated that the EMGT of the VL occurred after the RC point, whereas that of the RF occurred near the RC point, similar to the findings of Lucia et al.15) and Lucia et al.21).
In their study, the appearance time of the EMGT in the BF also occurred after the RC point, similar to the VL. The results of these studies conducted in athletes are consistent in that the EMGT occurred at approximately the RC point in the VL, RF, and BF; thus, the EMGT appeared after the VT point. In a study of professional road cyclists conducted by Hug et al., there was no difference between the workload at the EMGT (EMGt1/2) and that at the RC point (VT1). On the other hand, in this study of elderly participants, the EMGT was not obtained for the RF, but it was observed before the VT point in both the VL and GL, and it non-significantly tended to precede the VT point in the BF. The coefficients of determination in these cases were high. It is noteworthy that the activity of the VL showed a decrease in its slope after the EMGT. None of the previous studies of the EMGT in young athlete found a decrease in the slope of increasing muscle activity after the EMGT. A decrease in the post-slope of the VL represents a decrease in the slope of increasing muscle activity, and indicates that the additionally recruited motor units for incremental loading is decreasing. The EMGT appearance time in the VL was approximately 54.2% of the time to reach the VT point. Thus, it is speculated that the energy supply in the VL is sufficiently provided by aerobic metabolism at the EMGT, presumably precluding the possibility that this muscle was in a state of fatigue. This finding indicates that the EMGT appearance point in the VL of elderly individuals should be considered from other viewpoints, rather than simply considering the neurophysiological or metabolic aspects. The level of activity of the monoarticular VL muscle was greater than that of the biarticular RF and BF muscles when pedaling a bicycle ergometry. According to the Ericson’s study, that examined the muscle activity patterns when pedaling a bicycle ergometry at 54% of the maximum exercise intensity, the knee extensors produced 39% of the total positive mechanical work compared with the hip extensors 27%, ankle planter flexors 20%, knee flexors 10%, hip flexors 4%. The activity of biarticular muscles such as the RF is small, whereas the activity of monoarticular muscles such as the VL, vastus medialis muscle, and soleus muscle is relatively high at 54% of the maximum exercise intensity. Namely, the monoarticular VL is the agonist muscle when pedaling an ergometry at an exercise intensity near the VT point level. Studies that measured the muscle fiber conduction velocity (MFCV) of the VL during ergometry found that the MFCV increased with increasing exercise intensity in young participants. On the other hand, the MFCV in elderly did not increase with a gradual increase in exercise intensity, regardless of the participant’s level of training. This finding and the results of our present study suggest that the absence of a linear increase in the muscle activity of the VL in response to incremental exercise loading is a characteristic feature of VL activity in the elderly. With increasing age, there are decreases in skeletal muscle strength, capillary density in muscle, and ATP production efficiency, leading to decreased muscle endurance. It is presumed that the agonist muscle, the VL, is not increased continuously in elderly persons, as it is in young persons, to postpone fatigue reducing the workload of this muscle. The findings of the present study suggest that the decrease in the slope of the increasing VL activity is supported by antagonistic biarticular muscles such as the BF and GL. During pedaling, the BF begins to become active just before 0°, and it shows moderate activity from just after 90° to near 180°. The activity of the GL was observed from approximately 30° to just before 180° and from approximately 180° to near 270°, showing a bimodal pattern. The peaks of its activity were found just over 90° and near 270°, with the former peak practically synchronized with that of the BF. The BF and GL are similar to the VL in that they act during the down-stroke. However, when the muscle activity peaks of these muscles were compared, a peak was found near 30° in the VL, whereas it occurred just past 90° in the BF and GL, showing a slight divergence in the time phase of the activity peaks. More specifically, even in the same down-stroke, the peak is found in the former half of the down-stroke in the VL and the latter half of the down-stroke in the BF and GL. We speculate that in elderly persons the time phase of dominant muscle strength is changed slightly during the down-stroke of pedaling in response to incremental exercise loading, to provide fine adjustment and prevent the VL from becoming fatigued. The hip extensors and ankle planter flexors contribute greatly to produce the total mechanical work during bicycle next to knee extensors. BF as hip extensor and GL as ankle planter flexor would support the work load for prime mover VL as knee extensor. Furthermore, the monoarticular agonist and its biarticular antagonist muscles activate together as a pair during the propulsive phase. This paired action occurs between the joint torque necessary to contribute to joint power and the torque necessary to establish the direction of the force on the pedal. These findings suggest that the decrease in the slope of the increasing activity of the agonist muscle, VL, in pedaling is supported by the antagonist muscle, BF and GL, and thereby the muscle endurance of the VL is preserved.

On the other hand, the femur biarticular muscle RF, like the BF, did not show any response to a decrease in the post-slope after the EMGT of the VL. Because the RF is involved in pulling the pedal up as well as the down-stroke, and strapped pedaling were used in this study, this study provided a motion environment suitable for an increase in the action of the RF. However, there were no significant changes between the pre- and post-slope of the RF, yielding no valid EMGT for the RF. In a study of professional road cyclists, Racinais et al. examined young cyclists, found that the RMS activity of the RF was significantly lower than for both VL and BF from 14–15 to 95–96% of the maximum oxygen uptake (VO2max), and the muscle activity of the RF increased steeply at an intensity approximately near the VO2max. Chin et al. also showed that the activation of the RF is lower than that of the VL or vastus medialis muscle throughout the majority of the ramp exercise. In a study using near-infrared spectroscopy (NIRS), Hikichi et al. found that the deoxygenation threshold in the VL was observed in many subjects, whereas no subjects showed such a threshold in the RF. Considering these findings and the results of our study, it is presumed that the RF characteristically increases its muscle activity rapidly near the RC point, where other agonist muscles are fatigued and struggle to provide sufficient contractile force against the exercise load. We speculate that the EMGT of the RF might appearance to activate during not only down-stroke but also up-stroke to pull the pedal under high intensity. Because elderly participants were examined in this study, the discontinuation criteria for CPX included the upper limits of blood pressure and
heart rate to proper risk management. Therefore, the VT point could be confirmed in all subjects, while the RC point was not. If the upper limits of blood pressure and heart rate had not been utilized as discontinuation criteria, and exercise had continued until the RC point, valid EMGTs might have been extracted from the observed changes in the activity of the RF.

This study has some limitations. The incremental intensity of the ramp load and cadence were set at low levels to ensure proper risk management in elderly subjects, compared with previous studies that targeted young athletes. In addition, because there were also upper limits for blood pressure and heart rate that constituted the discontinuation criteria for CPX, no subjects discontinued CPX because their subjective symptoms reached the established upper limits. The appearance time of the VT point occurred at approximately 85% of the total exercise time, indicating that exercise did not continue long after the VT point. Therefore, not all subjects continued to exercise until the RC point, resulting in the failure to extract the EMGT of the RF. Another limitation is the small number of subjects. It is necessary to further study this issue in a larger number of subjects.

The purpose of this study was to determine an index of the VT point, using skeletal muscle activity to determine a safe and effective exercise intensity, to facilitate aerobic exercise in elderly persons. Because ramp load to evaluate the VT point is a method of loading devoid of a steady state, the increase in VO₂ follows the increase in exercise intensity, with a time lag. Thus, there is a risk of overloading if constant work load is conducted at the time of the VT point obtained by ramp load. Therefore, when prescribing the exercise intensity for constant work load, it is necessary to prescribe a lower intensity than that at the VT point. The EMGT of the BF obtained in this study occurred at approximately 75% of the VT point, and therefore the exercise intensity near at the point of the appearance of the EMGT of the BF may be useful as an indication of the optimal intensity of exercise for bicycle ergometry. We intend to further study whether exercise tolerance can be increased by exercise utilizing constant work load at the exercise intensity that allows the appearance of the EMGT of the BF.

The results of this study showed that, in community dwelling elderly male subjects undergoing bicycle ergometry exercise with incremental loading, the EMGTs of the VL and GL occurred before the VT point, whereas the EMGT of the BF tended to occur just prior to the VT point. Our results suggest that the slope of the increasing activity of the VL was decreased in order to postpone VL fatigue, the agonist muscle for pedaling motion, and this was supported by the antagonist biarticular BF and GL muscles. On the other hand, the EMGT of the RF may appear at a high intensity, when other muscles are fatigued. The appearance of the EMGT of the BF as observed in male subjects of advanced age may be useful as an index of the optimal intensity of aerobic exercise for bicycle ergometry.

REFERENCES

3) Wasserman K, McIlroy MB: Detecting the threshold of anaerobic metabolism in cardiac patients during exercise. Am J Cardiol, 1964, 14: 844–852. [Medline] [CrossRef]


33) Layeg G, Haseler Lj, Richardson RS: Reduced muscle oxidative capacity is independent of O2 availability in elderly people. Age (Dordr), 2013, 35: 1183–1192. [Medline] [CrossRef]

