Regional differences in blood flow and oxygen consumption in resting muscle and their relationship during recovery from exhaustive exercise

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Mizuno, Masaki, Yuichi Kimura, Takashi Iwakawa, Keiichi Oda, Kenji Ishii, Kiichi Ishiwata, Yoshio Nakamura, and Isao Muraoka. Regional differences in blood flow and oxygen consumption in resting muscle and their relationship during recovery from exhaustive exercise. J Appl Physiol 95: 2204–2210, 2003. First published July 25, 2003; 10.1152/japplphysiol.00197.2003.—This investigation evaluated regional differences in blood flow and oxygen consumption and their relationship in exercised muscle during recovery from exhaustive exercise. Five healthy men performed exhaustive one-legged cycling exercise. Positron emission tomography was used to measure blood flow, oxygen uptake, and oxygen extraction in the quadriceps femoris muscle before and after exercise. Regions of interest included five areas of the muscle (two proximal, one central, and two distal), which were evenly spaced across the muscle. Before exercise, blood flow and oxygen consumption decreased significantly (P < 0.05) in the direction from the proximal to the distal portions; blood flow declined from 2.0 ± 0.5 to 1.4 ± 0.3 ml·100 g−1·min−1, and oxygen consumption decreased from 0.21 ± 0.04 to 0.17 ± 0.02 ml·100 g−1·min−1. In contrast, these gradients in blood flow and oxygen consumption diminished during recovery after exercise. Consequently, there was a positive relationship between changes in blood flow and oxygen consumption in an exercised muscle during recovery after exercise (r = 0.963, P < 0.01). These changes became larger in the direction from proximal to distal portions: blood flow increased from 2.9 ± 0.7 to 3.9 ± 0.8 and oxygen consumption from 1.4 ± 0.1 to 1.8 ± 0.4 times resting values. These results suggest that hemodynamic variables are heterogeneous within a muscle both at rest and during recovery from exercise and that there is a systematic difference in these variables in the direction from proximal to distal regions within the quadriceps femoris muscle.

BLOOD FLOW AND OXYGEN SUPPLY to skeletal muscle increase in parallel with oxygen demand and exercise intensity when measured in the whole body (24) and in an individual limb (2, 21). Moreover, at the microvascular level, there is a direct coupling between blood flow in the capillaries and energy metabolism induced by electrical stimulation of a skeletal muscle (5). In contrast to the relationship between blood flow and oxygen consumption during exercise, previous studies (3, 4, 16) have suggested that oxygen supply is not directly regulated by oxygen demand in the skeletal muscle during recovery from exercise, based on a difference in the time course of both variables after exercise.

Concerns about hemodynamic measures and possible problems involved in measuring arteriovenous difference in oxygen levels have been reviewed (28). In addition, a recent study reported that the technique based on Fick’s principle could not detect regional changes in the forearm muscles during a handgrip exercise (6, 27). Because absolute changes in blood flow and oxygen consumption are smaller during recovery after exercise than during exercise, it is possible that conventional techniques cannot detect small changes during recovery. Moreover, blood flow is heterogeneous in the skeletal muscle of animals (13, 18) and humans (11, 12).

To more clearly understand the relationship between blood flow and oxygen demand in skeletal muscle during and after exercise, it is necessary to first identify factors such as differences in regional distribution of blood flow during and after exercise, technical problems in measuring hemodynamics, and heterogeneous recovery in a uniform muscle. To date, the regional distribution of oxygen supply and demand within a limb and/or muscles has not been measured during recovery from exercise.

Recently developed advanced methodologies, especially imaging modalities such as magnetic resonance imaging and positron emission tomography (PET), provide more information than conventional methodologies to measure local and regional functions in the human body. PET provides a noninvasive imaging technique to assess various biochemical and physiological functions in living tissues and can quantify hemodynamic variables in the skeletal muscle with a higher spatial resolution than conventional techniques. The purpose of this study was to evaluate regional differ-

Address for reprint requests and other correspondence: Y. Kimura, Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, 1-1, Naka, Itabashi, Tokyo 173-0022, Japan (E-mail: ukimura@ieee.org).
ences in hemodynamic parameters within an exercised muscle and to examine their relationship during recovery from exercise. Muscle blood flow, oxygen consumption, oxygen extraction fraction, and blood volume were measured in skeletal muscle by PET before and after one-legged exhaustive cycling exercise.

**METHODS**

**Subjects**

Five healthy men participated in this study (age 20—24 yr, height 168–178 cm, weight 62—79 kg). The subjects were fully informed of the purpose, nature, and potential risks of the experiments and gave their written, informed consent to participate in this study. The Ethics Committee of the Tokyo Metropolitan Institute of Gerontology approved the study protocol.

**Experimental Procedures**

The subjects were instructed to abstain from drinking alcohol and caffeine and to avoid heavy exercise for 24 h before the study. They were fasted overnight (>12 h) before the experiment. The experimental protocol is summarized in Fig. 1. After 30 min of supine rest, a catheter was inserted into a radial artery to withdraw blood for measuring plasma radioactivity, percentage of oxygen saturation, and hemoglobin content. The subjects were positioned supine to place the femoral regions of both legs in the PET scanner. Eight minutes of transmission scanning was first performed to correct photon attenuation, and then emission scans were performed to measure muscle blood flow, oxygen uptake (VO2), and blood volume using inhalation of [15O]CO2, [15O]O2, and [15O]CO, respectively. After the PET scans, subjects performed one-legged cycling exercise on a cycle ergometer (model 232C50, Combi, Tokyo, Japan) in a seated position. The right leg exercised while the left leg remained stationary on the ergometer frame. The pedaling rate was set at 80 revolutions per minute and was controlled by a metronome. Exercise intensity was set at 30 W for the first 3 min, followed by increments of 6 W every minute until exhaustion. Exhaustion was defined as the point at which subjects were unable to maintain the pedaling rate. The subjects were familiarized with this exercise protocol in advance. Ten minutes after the end of exercise, the second PET measurement was performed with the same procedure as that used before exercise.

To prevent misalignment between before- and after-exercise PET images, the PET camera was carefully positioned with the use of a laser marker equipped in the PET camera. The subject’s legs were immobilized with a plastic cover to prevent displacement of legs during the PET scan.

**Measurements of Physiological Functions**

**Systemic parameters.** Heart rate (HR) and blood pressure (BP) were measured simultaneously with an automatic BP analyzer (EBP300, Minato Medical Science, Tokyo, Japan) applied to the upper part of the left arm. Pulmonary VO2 was measured with an automatic gas analyzer (MG360, Minato Medical Science) and an automatic respiration monitor (RM300, Minato Medical Science). HR and pulmonary VO2 were monitored every 30 s at rest and during exercise. During recovery from exercise, HR and BP were recorded every 10 min, and pulmonary VO2 was recorded 10, 20, 40, 60, and 80 min after exercise. Time constants of the recovery rate (τ, min) of HR and pulmonary VO2 were calculated by fitting a single-exponential curve extending from peak values to pre-exercise values in Eq. 1, which represents a modified model for the off transient (22)

\[
Y(t) = P - X \cdot (1 - \exp^{-\frac{t}{\tau}})
\]

where \(Y\) is each parameter after exercise, \(P\) is the peak value obtained during exercise (i.e., exhaustion), \(X\) is the difference between peak and preexercise values, and \(\tau\) is time.

**PET parameters.** All radioactive gases were synthesized with a small cyclotron (CYPRIS-370, Sumitomo Heavy Industries, Tokyo, Japan). The PET camera (HEADTOMEX, Shimadzu, Kyoto, Japan) had an axial field of view of 200 mm, consisting of four ring detectors, providing a set of 32 slice images at center-to-center intervals of 6.25 mm with an image spatial resolution of 4.2-mm full width at half maximum and an axial resolution of 4.5-mm full width at half maximum. The subjects received radioactive gases that were diluted with room air ([15O]CO2: 0.75/100; [15O]O2 and [15O]CO: 0.15/100, vol/vol). Arterial blood was continuously withdrawn at a flow rate of 3 ml/min, and the radioactivity was measured with the use of an online radioactivity detector system (beta counter, Shimadzu). Arterial blood was sampled 0, 1, 3, 5, 7, and 8.5 min after gas inhalation, and radioactivity was measured with a well-type gamma counter (BSS, Shimadzu) to calibrate the count from the beta counter. All data were corrected for dead time, decay, dispersion, and photon attenuation before data analysis.

**Calculation of blood flow.** The subjects simultaneously underwent a 4-min continuous inhalation of [15O]CO2 (1,500 MBq/ml) and an 8-min static PET scan. The blood flow...
(ml·100 g⁻¹·min⁻¹) value was calculated by using an autoroadiographic method (23)
\[ C(t) = f \cdot \int_0^\infty C_a(t)dt - \frac{f}{p} \cdot \int_0^\infty C(t)dt \]  
(2)
where C and Ca indicate the radioactivity content in tissue and arterial plasma, respectively; f denotes blood flow; and p is the partition coefficient of water in the skeletal muscle, a constant with a fixed value of 0.95 (23).

Calculation of oxygen extraction fraction and VO₂. The subjects simultaneously underwent an 8.5-min continuous inhalation of [¹⁵O]CO (2,000 MBq/ml) and an 8.5-min static emission scan. The oxygen extraction fraction (OEF) was calculated with the use of Eq. 3 (8, 10)
\[ C = \frac{\text{OEF} \cdot \text{A}_o + f \cdot \text{A}_w}{\text{V}} \]  
(3)
where A₀ represents radioactivity of [¹⁵O]O₂ in arterial blood and A_w represents radioactivity of the metabolite of [¹⁵O]O₂ ([¹⁵O]H₂O) in arterial blood. Cₐ₀₂ (the oxygen content in the arterial blood) was calculated with Eq. 4
\[ C_{02} = 1.39 \cdot \% \text{Sat} \cdot \text{Hb} \]  
(4)
\[ \text{VO}_2 (\text{ml}·100 \text{g}^{-1}·\text{min}^{-1}) \] was calculated with Eq. 5
\[ \text{VO}_2 = \text{OEF} \cdot f \cdot C_{02} \]  
(5)
Calculation of blood volume. The subjects received a 4-min continuous inhalation of [¹⁵O]CO mixed room air (2,000 MBq/ml); a 6-min static PET scan was then performed after a 2-min room air inhalation. The blood volume (ml/100 g) value was calculated from Eq. 6 (19)
\[ \text{Blood volume} = \frac{\text{A}_o}{\text{Tco}} \cdot \frac{1}{\text{R}} \]  
(6)
where A₀ and Tco represent the radioactivity of [¹⁵O]CO in arterial blood and tissue, respectively, and R represents the tissue-to-large vessel hematocrit ratio. The value of R applied was 0.91 (19).

Regions of interest. The center of the 200-mm axial view of the PET camera was positioned at a point equivalent to 50% of the length between the greater trochanter and the knee joint. Five slices were selected for further investigation: 1) the center of the axial field of view (middle), 2) 31 mm (proximal-31 mm) and 3) 62 mm (proximal-62 mm) from the center in the proximal direction, and 4) 31 mm (distal-31 mm) and 5) 62 mm (distal-62 mm) from the center in the distal direction. Regions of interest (ROIs) were placed over the quadriceps femoris muscles in both thighs on the PET images with a reference to the images of the transmission scan. In the selection of the ROIs, large vessels appearing as hot spots were carefully avoided and sufficient distance was maintained between the body surface and bone. Consequently, the total volumes of ROIs were as follows (mean ± SD): for proximal-62 mm, 40.8 ± 4.5 cm³; for proximal-31 mm, 40.5 ± 6.1 cm³; for middle, 34.9 ± 5.3 cm³; for distal-31 mm, 30.3 ± 4.5 cm³; and for distal-62 mm, 27.9 ± 4.8 cm³. Identical ROIs were applied for data both before and after exercise.

Statistical Analysis
All data are presented as means ± SE. For systemic parameters, one-way ANOVA for repeated measurements followed by Scheffé’s post hoc test was performed to test differences between pre- and postexercise values. Student’s unpaired t-test was performed to test differences between time constants for HR and pulmonary VO₂. To test portion dependency for PET parameters, the Kendall’s rank correlation coefficient was applied. For PET parameters in pre- and postexercise, two-way ANOVA (time and leg) for repeated measurements was performed to test the effect of exercise in each portion. The factor “time and leg” indicates comparisons between pre- and postexercise and between nonexercised and exercised leg, respectively. When an F test was significant, pairwise comparisons were performed with Scheffé’s post hoc test. Linear relationships between parameters were tested with Pearson’s correlation coefficients. Values of P < 0.05 were considered statistically significant.

RESULTS
Systemic Parameters
The parameters measured at exhaustion are shown in Table 1, and the time courses of systemic parameters after exercise are shown in Fig. 2. HR was significantly elevated for 20 min after exercise, but there were no significant changes in BP. Pulmonary VO₂ was elevated for 10 min after exercise. The T of HR was significantly slower than that of pulmonary VO₂ (Fig. 2, A and C): 11.1 ± 1.0 vs. 3.4 ± 0.2 min (P < 0.01). There were no significant differences in all systemic parameters between 30 and 80 min after exhaustive exercise when the PET scans were performed. These results indicate that steady state was achieved during the PET scan, which requires constant physiological function in the target organs.

PET Parameters
Examples of parametric images (subject 2) of hemodynamic parameters are shown in Fig. 3. Although systemic parameters reached to steady state, remarkable differences can be found between exercised and nonexercised legs in the PET images. Some anatomic structures are apparent in the PET images. Before exercise, muscle blood flow and VO₂ decreased significantly in the direction from the proximal to the distal portions (Fig. 4A). There were no significant differences in oxygen extraction fraction or in muscle blood volume among the portions measured. In contrast, during recovery from exercise, the gradient in muscle blood flow and VO₂ diminished (Fig. 4B). The changes in PET parameters before and after exercise are sum-

<table>
<thead>
<tr>
<th>Subject 1</th>
<th>Subject 2</th>
<th>Subject 3</th>
<th>Subject 4</th>
<th>Subject 5</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak HR, beats/min</td>
<td>153</td>
<td>178</td>
<td>189</td>
<td>194</td>
<td>181</td>
<td>17</td>
</tr>
<tr>
<td>Peak Pulmonary VO₂, ml/min</td>
<td>2,230</td>
<td>2,636</td>
<td>2,405</td>
<td>2,682</td>
<td>2,601</td>
<td>398</td>
</tr>
<tr>
<td>Peak Work Rate, W</td>
<td>96</td>
<td>126</td>
<td>138</td>
<td>162</td>
<td>130</td>
<td>24</td>
</tr>
<tr>
<td>Time to Exhaustion, min</td>
<td>14.1</td>
<td>18.6</td>
<td>20.1</td>
<td>24.1</td>
<td>19.0</td>
<td>3.6</td>
</tr>
</tbody>
</table>

HR, heart rate; VO₂, O₂ uptake.
Table 2. There were significant interactions, which indicated an effect of exercise on muscle blood flow in each portion, at distal-31 mm and distal-62 mm. Similarly, there were significant interactions in muscle \( \dot{V}O_2 \) in the middle and in both distal portions. In contrast, there was no significant interaction in oxygen extraction fraction in any portion. These results suggest a difference in recovery rates across the muscle.

The relationship between muscle blood flow and \( \dot{V}O_2 \) is shown in Fig. 5. Significant correlations emerged when intersubject averages of normalized muscle blood flow and \( \dot{V}O_2 \) by those preexercise values were plotted (\( r = 0.963, P < 0.01 \)).

**DISCUSSION**

The purpose of this study was to quantify, by PET, regional difference in blood flow and oxygen consumption in an exercised muscle and to clarify their relationship after exhaustive exercise.

**PET for Exercise Physiology**

PET is potentially an attractive technology for use in exercise physiology research because it enables quantitative visualization of regional hemodynamic parameters. Previous studies have shown high correlations between PET parameters and muscle blood flow as measured by venous occlusive plethysmography (20) and oxygen extraction fraction with the use of Fick’s principle (17). The hemodynamic data obtained in the present study are consistent with those reported in previous PET studies (17, 20). Resting muscle blood flow in the present study ranged from 0.8 to 4.4 ml·100 g\(^{-1}\)·min\(^{-1}\) (average: 1.8 ± 0.1 ml·100 g\(^{-1}\)·min\(^{-1}\)) and was comparable to values reported by Raitakari et al. (20) (range from 1.1 to 7.5 ml·100 g\(^{-1}\)·min\(^{-1}\); average 3.1 ± 1.7 ml·100 g\(^{-1}\)·min\(^{-1}\)). Likewise, resting muscle oxygen consumption in this study (0.19 ± 0.1 ml·100 g\(^{-1}\)·min\(^{-1}\)) was consistent with that measured by Nuutila et al. (17) (0.23 ± 0.1 ml·100 g\(^{-1}\)·min\(^{-1}\)).

PET has a low time resolution compared with conventional techniques to measure hemodynamic parameters; this point should be considered when studying events postexercise because these hemodynamic pa-

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**Fig. 2.** Changes in systemic parameters after exercise. A: heart rate, bpm, Beats, min. B: blood pressure. C: pulmonary \( \dot{V}O_2 \). *Significant difference from preexercise values, \( P < 0.05 \).

**Fig. 3.** Examples of positron emission tomography (PET) images of blood flow (top) and \( \dot{V}O_2 \) (bottom) in one subject (subject 2). Left: coronal images (immediately above the femur). Right: transaxial images at portions 62 mm from the center in the proximal direction (proximal-62), the center of the axial field (middle), and 62 mm from the center in the distal direction (distal-62). The right leg is the exercised leg, and the left leg is the nonexercised leg. Regions of interest are represented by red lines. White arrows indicate anatomic structures: A = femur; B = large vessel.
Regional Difference in Blood Flow and $\dot{V}O_2$ at Rest

Before exercise, the muscle blood flow and $\dot{V}O_2$ decreased significantly in the proximal to the distal direction (Fig. 4A). Use of an ultrasound-Doppler technique in humans has shown that resting blood flow and velocity are lower within the popliteal artery than within the superficial femoral artery (9). Decreases in blood flow in the present study, therefore, can be attributed to differences in the distance from the heart between the proximal and distal portions of the muscle. Another possible explanation may be related to the relationship between regional blood flow in a resting muscle and the percent content of slow oxidative fiber, as reported in studies on animals (13). Within a single muscle, there is a lower percentage of slow oxidative parameters change rapidly after exercise. In the present experimental protocol, PET measurements started 30 min after exhaustive exercise, when hemodynamics is expected to have reached a steady state following the dynamic changes immediately after exercise. No significant change in any systemic parameter was observed from 30 to 80 min after exercise (Fig. 2), suggesting that the hemodynamic variables achieved a steady state within 30 min after exercise.

During PET measurements, the subjects remained in a rested state to ensure consistency in the measurement duration of the hemodynamics. To minimize the effects of any preconditions and the duration of the PET measurements, which may have influenced the muscle contraction while subjects maintained posture, the subjects’ legs were fixed with a plastic cover. In addition, preexercise measurements of blood flow began after 30 min of rest in the spinal position.

Table 2. Changes of PET parameters before and after exhaustive exercise

<table>
<thead>
<tr>
<th>Portion</th>
<th>Nonexercised Leg</th>
<th>Exercised Leg</th>
<th>Comparison Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Time</td>
</tr>
<tr>
<td>Blood flow, $ml\cdot100\text{g}^{-1}\cdot\text{min}^{-1}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal-62</td>
<td>2.0 ± 0.5</td>
<td>2.2 ± 0.9</td>
<td>2.1 ± 0.6</td>
</tr>
<tr>
<td>Proximal-31</td>
<td>1.9 ± 0.5</td>
<td>2.3 ± 0.9</td>
<td>2.0 ± 0.6</td>
</tr>
<tr>
<td>Middle</td>
<td>1.9 ± 0.5</td>
<td>2.1 ± 0.7</td>
<td>1.9 ± 0.5</td>
</tr>
<tr>
<td>Distal-31</td>
<td>1.6 ± 0.4</td>
<td>1.8 ± 0.6</td>
<td>1.6 ± 0.4</td>
</tr>
<tr>
<td>Distal-62</td>
<td>1.4 ± 0.3</td>
<td>1.5 ± 0.5</td>
<td>1.4 ± 0.3</td>
</tr>
<tr>
<td>Oxygen extraction fraction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal-62</td>
<td>0.56 ± 0.03</td>
<td>0.47 ± 0.05</td>
<td>0.56 ± 0.05</td>
</tr>
<tr>
<td>Proximal-31</td>
<td>0.55 ± 0.03</td>
<td>0.51 ± 0.07</td>
<td>0.59 ± 0.04</td>
</tr>
<tr>
<td>Middle</td>
<td>0.59 ± 0.06</td>
<td>0.54 ± 0.06</td>
<td>0.57 ± 0.05</td>
</tr>
<tr>
<td>Distal-31</td>
<td>0.61 ± 0.05</td>
<td>0.59 ± 0.07</td>
<td>0.60 ± 0.05</td>
</tr>
<tr>
<td>Distal-62</td>
<td>0.64 ± 0.05</td>
<td>0.56 ± 0.08</td>
<td>0.60 ± 0.07</td>
</tr>
<tr>
<td>$\dot{V}O_2$, $ml\cdot100\text{g}^{-1}\cdot\text{min}^{-1}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal-62</td>
<td>0.21 ± 0.04</td>
<td>0.16 ± 0.03</td>
<td>0.21 ± 0.04</td>
</tr>
<tr>
<td>Proximal-31</td>
<td>0.20 ± 0.04</td>
<td>0.17 ± 0.02</td>
<td>0.21 ± 0.04</td>
</tr>
<tr>
<td>Middle</td>
<td>0.21 ± 0.03</td>
<td>0.18 ± 0.02</td>
<td>0.20 ± 0.03</td>
</tr>
<tr>
<td>Distal-31</td>
<td>0.15 ± 0.02</td>
<td>0.17 ± 0.02</td>
<td>0.18 ± 0.03</td>
</tr>
<tr>
<td>Distal-62</td>
<td>0.17 ± 0.02</td>
<td>0.13 ± 0.02</td>
<td>0.15 ± 0.02</td>
</tr>
</tbody>
</table>

Proximal-62 and proximal-31, 62 mm and 31 mm, respectively, from the center in the proximal direction; middle, center of the axial field; distal-62 and distal-31, 62 mm and 31 mm, respectively, from the center in the distal direction. Pre and Post, before and after exercise, respectively. The factors Time and Leg indicates multiple comparisons (Scheffe’s post hoc test) between pre- and postexercise and between nonexercised and exercised leg, respectively. Significance only as indicated; otherwise, no significance was found.
fibers in the distal than in the proximal portion (26, 29). In a study on human muscle, Lexell et al. (14) showed a lower percentage of slow oxidative fibers in the distal than in the proximal portion in vastus lateralis muscle. These previous reports have suggested the existence of a difference in muscle blood flow between the proximal and distal portions within a single muscle. In addition, in an in vitro study, Sullivan and Pittman (25) indicated that oxygen consumption in the skeletal muscle depended on the muscle fiber type and the capillary density.

**Regional Difference in the Extent of Recovery in Exercised Muscle**

Greig et al. (7) showed that nearly all muscle fibers are recruited at an exercise intensity eliciting 100% maximal VO2. In our protocol, all subjects exercised until exhaustion, which we assume would have recruited nearly all muscle fibers in quadriceps femoris muscle. There were no significant interactions of PET parameters in proximal portions of the muscle, although distal portions showed significant interactions of blood flow and VO2 (Table 2). Both blood flow and VO2 significantly increased in all portions investigated after exercise, and the increment became larger in the direction from the proximal to the distal portions (Fig. 5). These results suggest the presence of regional differences in the extent of recovery from exercise in an exercised muscle and are consistent with a previous study (15).

One possible interpretation of these regional differences relates to the effects of intramuscular pressure within single muscle. Ameredes and Provenzano (1) showed greater intramuscular pressure in the distal than in the proximal portion of a muscle. Higher intramuscular pressure would inhibit circulation during muscle contraction, which might be compensated during recovery after exercise. An alternative explanation is that regional differences may arise because of the presence of nonuniform muscle fiber type, as mentioned above. In the present study, there were differences in the regional parameters between different portions of the muscle preexercise (Fig. 4A), which might reflect lower oxidative capacity in the distal compared with the proximal portion, resulting in decreasing recovery rates in the distal portion. However, we did not measure muscle fiber type, and further investigation is required regarding any relationship to muscle fiber type in humans.

**Spatial Relationship Between VO2 and Blood Flow During Recovery From Exercise**

Previous studies reported a mismatch between blood flow and oxygen consumption during recovery after exercise (3, 4, 16). The time courses of HR and pulmonary VO2 observed in the present study are consistent with previous reports (see Fig. 2, A and B). BP remained unchanged, and the time constant of pulmonary VO2 was one-third that of HR. In addition, the PET data support measures of systemic parameters. Because there was a significant time effect of oxygen extraction fraction in the most proximal portions (P = 0.032, Table 2), oxygen extraction was lower after than before exercise. These results support previous reports (3, 4, 16) and demonstrate that excess perfusion may occur during recovery from exercise.

With regional blood flow distribution, however, PET showed a high correlation between muscle blood flow and VO2, demonstrating a tight coupling between oxygen supply and demand during recovery from exercise (Fig. 5). The inconsistency between systemic and regional PET parameters can be explained by differences in spatial resolution of hemodynamic measurements. PET was able to detect the coupling between hemodynamic variables, which might disappear with excess perfusion during recovery; this might be difficult to detect with measurement at the whole body and limb levels. Previous studies (3, 4, 16) that reported a “mismatch” between oxygen supply and oxygen demand used a technique based on Fick’s principle, which is regarded as the “gold standard” measure of hemodynamics in skeletal muscle. However, two recent studies (6, 28) demonstrated that this technique is not able to quantify local changes as well as near-infrared spectroscopy techniques. In addition, Berg et al. (5) showed a direct coupling between blood flow and energy metabolism induced by electrical stimulation in a microvascular system. Similarly, our data show a correlation between blood flow and oxygen consumption, indicating a consistent relationship between these hemodynamic variables during both exercise and postexercise recovery.

In conclusion, we found a significant gradient in blood flow and VO2 in resting muscle, decreasing in the direction from the proximal to distal portion; the magnitude of this gradient diminished after exhaustive exercise in recovering muscle. Consequently, during recovery from exercise, there was a significant positive relationship between changes in blood flow and oxygen consumption in the exercised muscle; this increment...
became larger in the direction from the proximal to distal portions. These results suggest that there is a systematic difference between proximal and distal regions in the quadriceps femoris muscle. The present study also demonstrates that, when evaluating cardiorespiratory parameters during and after exercise, it is important to measure both the time course and spatial changes in human skeletal muscle.

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