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COMPARISON OF TWO METHODS OF MEASURING FOREARM OXYGEN CONSUMPTION ($\dot{V}O_2$) BY NEAR INFRARED SPECTROSCOPY

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ABSTRACT

Near infrared spectroscopy (NIRS) was used to measure oxygen consumption ($\dot{V}O_2$) in the human forearm with two different methods. $\dot{V}O_2$ was measured in ten patients, first by inducing a forearm venous occlusion and then an ischemia. The mean value of $\dot{V}O_2$ was 3.3 ± 1.1 $\mu MO_2 \times 100\ g^{-1}\times min^{-1}$ during venous occlusion and 2.9±0.9 $\mu MO_2 \times 100\ g^{-1}\times min^{-1}$ during ischemia. The difference between the two means was 0.4 $\mu MO_2 \times 100\ g^{-1}\times min^{-1}$. A good agreement between the two methods was demonstrated. The results showed that NIRS is a useful tool for the measurement of $\dot{V}O_2$. The venous occlusion method was the method of choice because it could be easily repeated at the bedside without causing any discomfort to the patient. © *1997 Society of Photo-Optical Instrumentation Engineers.* [S1083-3668(97)01002-2]

1 INTRODUCTION

The study of the blood flow and $\dot{V}O_2$ of the limbs is of great relevance in exercise physiology and in patients with muscular and/or systematic diseases. Different invasive and noninvasive methods have been developed for assessing $\dot{V}O_2$.[1] Skeletal muscle $\dot{V}O_2$ is usually evaluated by separately measuring blood flow and the difference in arteriovenous O_2 content.[2,3] However, this invasive method is cumbersome and inconvenient to use in many physiological and clinical conditions. In recent years, research has been focused on the development of noninvasive optical techniques to monitor tissue functions.[4]

Near infrared spectroscopy (NIRS) has been used to measure oxygenation changes in skeletal muscle hemoglobin (Hb) under different conditions, such as ischemia and extreme exercise.[5–9]

Quantitative measures of [HbO_2] and [Hb] changes have been obtained by combining near-infrared absorption changes with optical path-length data. Skeletal muscle path lengths have been measured in volunteers under different conditions by time-resolved and phase-modulation spectroscopy.[10–12]

Measurements of skeletal muscle $\dot{V}O_2$ have been obtained by NIRS, at rest, and during isometric exercise by inducing an arterial occlusion.[13,14] However, this technique can cause discomfort to the subject and cannot be used repeatedly at short time intervals because of the reperfusion phenomenon that follows ischemia. $\dot{V}O_2$ and forearm blood flow (FBF) can be measured by inducing a venous occlusion.[15] This $\dot{V}O_2$ method has recently been validated[16] and the FBF method has also been confirmed by others.[17] We have been using both methods for routine FBF and $\dot{V}O_2$ measurements of patients in our intensive care unit.[18] The $\dot{V}O_2$ method based on ischemia, although more accurate, is more troublesome than the method based on venous occlusion. This paper compares forearm $\dot{V}O_2$ measurements obtained by the two different methods.

2 METHODS

2.1 SUBJECTS

Ten patients admitted to the intensive care unit were studied; 5 had acute respiratory distress syndrome, 4 had cardiocirculatory failure, and one patient was in a coma state from head trauma. All of them received a routine treatment for their conditions; in particular, they were subjected to dopamine infusion as the only inotropic drug. This study was carried out according to the principles of the Helsinki Declaration. Written informed consent was obtained from all the patients or their next of kin.

2.2 PROCEDURES

A 20-gauge Teflon catheter was inserted percutaneously in the radial artery of the right arm for continuous blood pressure monitoring. Arterial hemo-

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globin concentration was measured using a Co-oximeter (IL482, Laboratory Instrument, U.S.). Administration of sedative drugs and changes of the infusion rate of fluids were not allowed during NIRS measurements. No transfusion was performed in the 24 before the measurements.

2.3 NIRS INSTRUMENTATION

The measurements were obtained using an NIRO500 (Hamamatsu Photonics, Hamamatsu City, Japan), previously described in detail.[19] Four laser diodes generated light at 775, 825, 850, and 904 nm. A fiberoptic bundle with an emitting area of 2.5 mm diameter carried the light into the tissue. A second fiberoptic bundle of the same size collected the transmitted light for detection by a photomultiplier. The optical fibers (optodes) were firmly attached to the skin by a special support that allowed both the distance (3.5 cm) and the angle between the optodes to be maintained constant. The sampling time was 1 s. Data collected by NIRS were transferred on-line to a computer for storage and subsequent analysis. The optodes were placed over the brachioradial muscle of the right arm. The [Hb] and $[HbO_2]$ changes were quantified using a differential path-length factor value of 4.16 measured on adult forearm using a phase-modulation prototype.[12] Taking into account that the interoptode distance was 3.5 cm and subjects with subcutaneous adipose tissue thickness higher than 0.8 cm were avoided, the near-infrared light is estimated to have penetrated the muscle tissue at least deep enough to reach half the distance between the light source and the detector.[20]

2.4 PROTOCOL

The protocol was performed when the patient was clinically stable. A 15-min rest period followed the placement of the optic fibers on the forearm. The forearm was positioned with the wrist suspended 10 cm above the heart level to allow for a rapid venous drainage. A pneumatic cuff was placed around the arm above the elbow and inflated in less than 0.5 s to a pressure of 45 mm Hg to obtain a venous occlusion. The cuff was maintained inflated for 20 s and then released. This procedure was repeated three times consecutively with a 15-s interval between each measurement. Five minutes after the last venous occlusion, the cuff was inflated to a pressure of 240 mm Hg for 2 min in order to induce an arterial occlusion, then released.

Systemic and regional blood flows were modified by changing the dopamine dose. Three different conditions of measurement for each patient were obtained by changing the dopamine dose in the range of therapeutic treatment. The NIRS measurements were performed 20 min after each change in dopamine infusion rate.

2.5 FOREARM MEASUREMENTS

Measurements of FBF and $\dot{V}O_2$ were obtained by evaluating the rate of the $[HbO_2]$ and [Hb] increase following venous occlusion.[16] The rapid $[HbO_2]$ rise provoked by venous occlusion ($d[HbO_2]/dt$) was ascribed to the inflow of the arterial blood. The concomitant [Hb] increase ($d[Hb]/dt$) was ascribed to O_2 uptake into the tissue and to the rate of [Hb] coming from arterial blood. The sum of the $[HbO_2]$ and [Hb] changes expressed in grams was converted to milliliter of blood, taking into account the hemoglobin content value of each subject. The FBF was expressed as $ml \times 100\ g^{-1} \times min^{-1}$. Forearm $\dot{V}O_2$ was calculated by considering the [Hb] increment following venous occlusion extrapolated to 1 min. The resulting values were expressed as $\mu MO_2 \times 100\ g^{-1} \times min^{-1}$.

During the procedure of arterial occlusion, the difference between $[HbO_2]$ and [Hb] ([Hbdif]) was taken as an index of Hb oxygenation change when the sum of the $[HbO_2]$ and [Hb] ([Hbtot]) did not change. The decrease of [Hbdif] following arterial occlusion was considered to be related to the O_2 uptake from the tissue. $\dot{V}O_2$ was calculated by considering the first 60 s of linear decrement of [Hbdif] following arterial occlusion. Also, in this case, forearm $\dot{V}O_2$ value was expressed as $\mu MO_2 \times 100\ g^{-1} \times min^{-1}$.

2.6 STATISTICS

The differences among groups were statistically evaluated by using a nonparametric test for independent values, such as the Mann-Whitney U test. A two-tailed value of $P < 0.05$ was considered as significant. The relationship between the variables was studied using a multiple linear regression analysis. The square of the regression coefficient (r^2) was determined. In order to assess the agreement between the two methods of $\dot{V}O_2$ measurement, the Bland and Altman agreement test was used.[21]

3 RESULTS

Representative $[HbO_2]$ and [Hb] changes during forearm venous occlusions and ischemia are shown in Figure 1. In the upper panel, the venous occlusion, which decreases the pressure gradient along the capillary, reduces the arterial blood inflow in the forearm and consequently the hemoglobin deoxygenation rate by 10 to 20 s after the beginning of the occlusion. Therefore, the linear increment of [Hb] observed 10 to 20 s after the beginning of the occlusion was used to calculate $\dot{V}O_2$. The $\dot{V}O_2$ values obtained by each method for each subject are reported in Table 1 and Figure 2. The three values correspond to different dopamine infusion rates. One value could not be used because of technical problems during the measurement. $\dot{V}O_2$ values

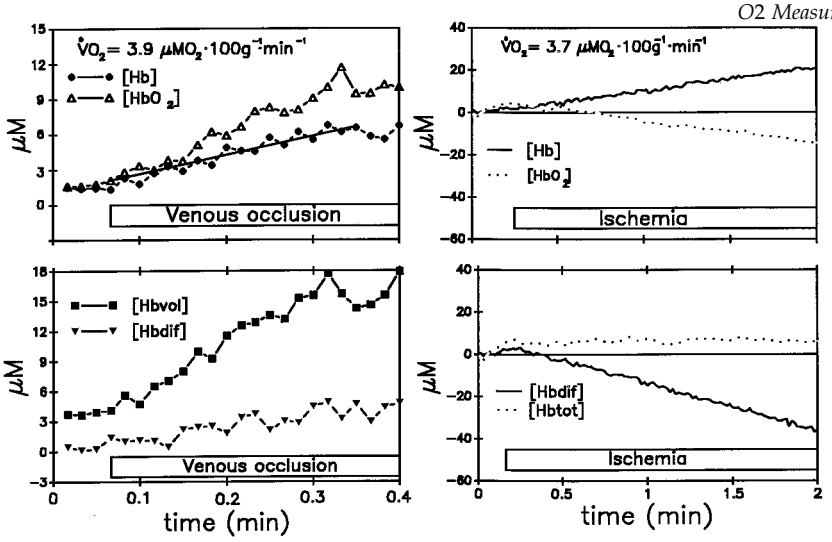

Fig. 1 Typical tracings of the [HbO_2] and [Hb] changes during forearm venous occlusion and ischemia (upper panels). The linear increment of [Hb] values following the occlusion was used to perform the regression analysis for $\dot{V}O_2$ calculation. The lower panels show the corresponding [Hbtot] and [Hbdif] tracings. The linear decrease of [Hbdif] was used for $\dot{V}O_2$ calculation. No variation of [Hbtot] was observed during ischemia.

measured during venous occlusion ranged from 1.7 to 7.4 $\mu MO_2 \times 100\ g^{-1} \times min^{-1}$ (3.3±1.1). $\dot{V}O_2$ values from arterial occlusion ranged from 1.4 to 5.1 (2.9 ±0.9). No difference was found between the two groups of values. The difference between the mean values was 0.4 $\mu MO_2 \times 100\ g^{-1} \times min^{-1}$. The individual differences observed in the $\dot{V}O_2$ measurement could be explained by the unstable metabolic status of patients, which was related to their pathological condition.

The 29 $\dot{V}O_2$ values of the 10 subjects determined during venous occlusion were regressed against the corresponding $\dot{V}O_2$ values obtained during arterial occlusion. The linear regression, the intercept, the mean SE of the predicted values, and 95% confidence interval are shown in Figure 3. The r^2 value was 0.66 with $p<0.01$. For the agreement test, the average of the $\dot{V}O_2$ obtained by the two methods was plotted against the difference between the two values (Figure 4). The mean of the differences (d) and 2 SD levels are also reported. All data lie well within the 95% confidence interval ($d \pm 2SD$).

4 DISCUSSION

The evaluation of the contribution of muscle $\dot{V}O_2$ to total body $\dot{V}O_2$ can be a very useful tool in the diagnosis of patients.[18] The $\dot{V}O_2$ measured on the whole body does not reflect the contribution of single organs or tissues. A simple and noninvasive technique for measuring muscle $\dot{V}O_2$ based on NIRS principles could find clinical applications, for example, in peripheral vascular diseases and shock.

The determinants of O_2 transport from the red cell to mitochondria are the partial pressure gradient of O_2 from capillary to myoglobin ($P_{Mb}O_2$) and the conductance.[22] It has been found that when blood flow is interrupted, as in the present protocol, then the Hb deoxygenation rate represents the driving force proportional to $\dot{V}O_2$. From a metabolic point of view, several combined NMR spectroscopy/NIRS studies have been performed during ischemia, and in a recent publication[23] it was demonstrated that no PCr changes occur in the first 5 min of forearm arterial occlusion. Therefore, no PCr changes are expected during venous occlusion either.

In the present study, forearm VO_2 was determined by two different methods. The results demonstrate a good correlation between $\dot{V}O_2$ values obtained with venous occlusion and those measured with arterial occlusion, thus indicating that skeletal muscle $\dot{V}O_2$ can be evaluated both in the presence and in the absence of blood flow. Although the Bland and Altman test showed a good agreement between the two methods (Figure 4), the distribution and the variability of the differences are very wide (Figure 2). Further information might contribute to our understanding of the variability of the data. The individual differences observed in the $\dot{V}O_2$ measurement may be explained by the different metabolic status of patients, which is related to their pathological condition.

The application of arterial occlusion can cause discomfort to the subject and does not favor consecutive measurements. The method of venous occlusion has the advantage of being a non-painful procedure that can be easily performed and repeated at the bedside. Furthermore, this procedure enables the simultaneous assessment of FBF and

Table 1 $\dot{V}O_2$ Measurement by two methods.

Patient No.	$\dot{V}O_2$ Venous occlusion $\mu MO_2 \times 100\ g^{-1} \times min^{-1}$	$\dot{V}O_2$ Ischemia $\mu MO_2 \times 100\ g^{-1} \times min^{-1}$
1	1.8	2.7
	2.1	1.4
	1.7	1.4
2	2.7	2.2
	2.1	2.3
	2.0	2.1
4	4.1	2.9
	4.0	3.6
	3.9	3.7
4	3.9	3.2
	3.4	3.0
	3.2	3.2
5	3.1	2.3
	2.8	2.5
	2.7	2.3
6	2.5	2.2
	2.3	2.0
	2.5	2.2
7	4.0	4.5
	3.3	4.4
	4.3	4.5
8	3.7	2.7
	4.1	3.2
9	2.3	1.8
	3.4	2.1
	2.8	2.8
10	3.2	2.8
	5.0	4.0
	7.4	5.1
Mean	3.3	2.9
±SD	1.1	0.9

$\dot{V}O_2$, allowing the correlation of these variables in different conditions.[18] $\dot{V}O_2$ data obtained by NIRS during venous occlusion were recently compared with those obtained by invasive methods.[16] A high correlation was found between the $\dot{V}O_2$ data and the $\dot{V}O_2$ values calculated as the product of arteriovenous O_2 difference and FBF, as measured by plethysmography. The venous occlusion method has been recently used[24] to measure tissue hemoglobin saturation in the forearm. Tissue saturation showed a strong correlation with saturation values measured in the venous blood.

The increase in blood volume during venous occlusion could in principle alter the optical properties of tissue by causing a change in the optical path length.[12] The change in path length that occurs during venous occlusion in the human forearm has, however, been studied separately by time-resolved spectroscopy.[11] Path length decreased about 4% after 3 min of venous occlusion. These changes are a negligible interference in the quantitation of [Hb] and [HbO_2].

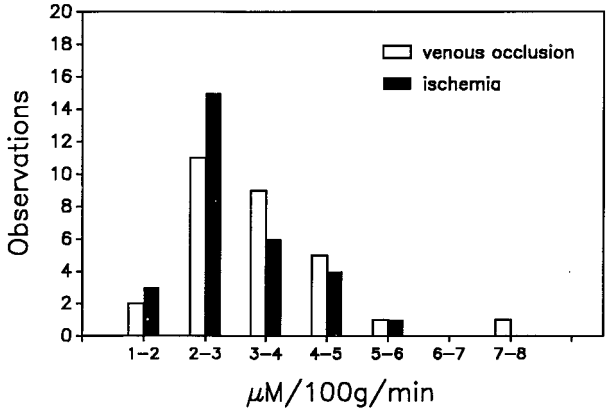

Fig. 2 $\dot{V}O_2$ values distribution measured by the two methods.

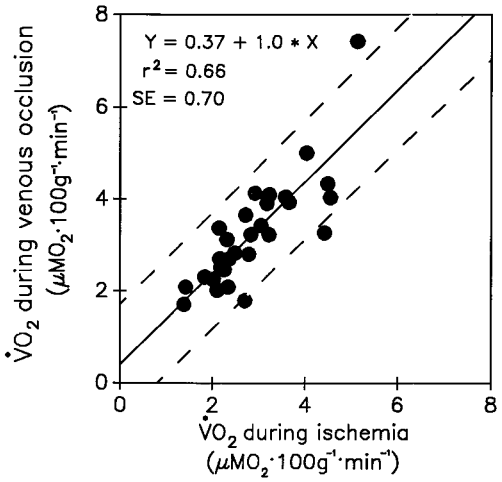

Fig. 3 Comparison between the $\dot{V}O_2$ values obtained with venous occlusion and those determined by ischemia. Solid line, first order regression that fits all data points ($n=29$). Dashed lines, 95% confidence intervals.

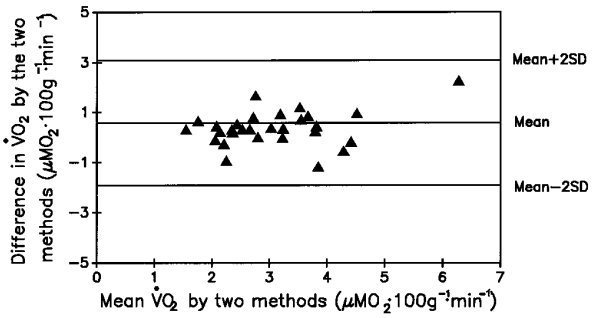

Fig. 4 Agreement test for $\dot{V}O_2$ values measured with NIRS by the two methods. The mean of the $\dot{V}O_2$ values obtained by both methods were plotted against their difference. All data are within the 95% confidence interval which represents double the standard deviation.

Acknowledgments

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