Mixed venous oxygen content estimated from oxygen saturation and heart rate measured for healthy students during a study tour in Colorado

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Abstract

Oxygen saturation (SpO₂) and heart rate (HR) were measured for 13 healthy third-grade students (4 males and 9 females ages 20 to 24) of the Physical Therapy Department of Yamagata Prefectural University of Health Sciences, who joined a study tour in Colorado from Sep. 19 to 27, 2012. Means and standard deviations of the SpO₂ values for the 13 students were 98 ± 0.95, 97 ± 1.4, 94 ± 1.9, 93 ± 1.7 and 87 ± 2.8 % at the Narita Airport (altitude 130 m), Denver City (1,609 m), Estes Park (2,499 m), Hidden Valley (2,816 m) and the Alpine Visitor Center (3,595 m), respectively. Averaged HR values simultaneously measured with SpO₂ at the each point were 75 ± 11.78 ± 5.8, 74 ± 7.4, 92 ± 11 and 85 ± 7.6 beats/min. These values except for those at the Narita Airport were measured within 6 hours on the fourth day for staying in Denver. Despite more than 10 % decrease in SpO₂ within 6 hours, no student felt unwell at the height of 3,595 m.

Based on the Fick principle, a correlation of SpO₂ in % with 1/HR in min/beats was described with a regression line that SpO₂ = 2650 (1/HR) + 60.6 with a coefficient of determination 0.600. With the standard oxygen content combined to hemoglobin in arterial blood 20.1 vol% by assuming the normal hemoglobin concentrations for each student, mixed venous oxygen content (CvO₂) was estimated from the intercept of the regression line as 12.2 vol%. The difference between arterial oxygen content (CaO₂) obtained from SpO₂ and the estimated CvO₂ (CaO₂ − CvO₂) was consistent with those reported by a venous catheter method or a rebreathing method. These results suggest that CvO₂ can be estimated from a noninvasive method to measure SpO₂ and HR.

Key words: mixed venous oxygen content, oxygen saturation, heart rate, high altitude, Colorado
third-grade students in our Nursing, Physical Therapy and Occupational Therapy Departments visit UC or CSU for 9 days in September, when they have no lecture in YPUHS. Table 1 shows the number of students who joined the fall visits by year and by the Departments. The numbers in parentheses are the ratio of the voluntary students to the whole students for each Department.

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| N: Nursing Dept. | PT: Physical Therapy Dept. | OT: Occupational Therapy Dept. |
| In 2007 study tour of PT Dept was not carried out because of the moving of the Physical Therapy Program of UC to the new campus. |

Thirteen physical therapy students (4 males, 9 females) joined the study tour in Colorado from Sep. 19 to 27, 2012. I went to Colorado with the students as one of the guiding faculty of the Physical Therapy Department. Using a portable pulse oximeter, oxygen saturation (SpO₂) and heart rate (HR) were measured for the 13 students with informed consents. Measuring points were the Narita Airport, Denver City and three points in the Rocky Mountain National Park, where the altitude was as high as 3,595 m. The Route 34 we passed on a chartered bus and the three points in the Rocky Mountain National Park where SpO₂ and HR were measured are shown in a map of Fig.1.

It is well accepted that SpO₂ decreases and HR increases at high altitudes compared with those at low altitudes. Inspired oxygen pressure decreases as the barometric pressure (Pₐ) is lowered at high altitudes. According to the alveolar gas equation, alveolar O₂ pressure (PₐO₂) can be calculated as:

\[
P_{\text{A}O_2} = 0.209 \left( P_{\text{B}} - 47 \right) - P_{\text{CO}_2}/\text{RER} + 0.209 P_{\text{CO}_2} \cdot (1 - \text{RER})/\text{RER},
\]

where PₐCO₂ and RER are arterial CO₂ pressure and respiratory exchange ratio, respectively, and 0.209 is the O₂ fraction in the air and 47 saturated water vapor pressure at 37 degrees Celsius. An equation to calculate Pₐ was shown by West.

\[
C_{\text{O}_2} = 1.39 \text{SpO}_2 \times \text{Hb}/100 + 0.00314 (P_{\text{A}O_2} - 5),
\]

where SpO₂ is in %, Hb hemoglobin concentration in g/dl, and 1.39 is O₂ quantity combined to hemoglobin.

![Alpine Visitor Center](image1.png)

Fig.1 The Alpine Visitor Center (3,595 m) and the other 2 points in the Rocky Mountain National Park where SpO₂ and HR were measured for the 13 students.
in ml/g and 0.00314 the solubility of O₂ in plasma in ml/dl/Torr. The first term in Eq.(2) is chemically combined O₂ to hemoglobin. The second term corresponds to physically dissolved O₂ in plasma with an assumption that alveolar-arterial O₂ gradient is 5 Torr for healthy subjects. Oxygen contents in arterial and mixed venous blood are fundamental parameters to combine cardiac output (Q) and O₂ uptake (VO₂) based on the Fick principle:

$$Q = HR \times SV = VO₂ / (CₐO₂ - CᵥO₂), \quad (3)$$

where SV is stroke volume. CₐO₂ cannot be estimated nor be measured easily. Wolfel et al. measured CₐO₂ at Pikes Peak in the Rocky Mountain National Park using a venous catheter. Although their research is worthy of special mention, such measurements using a venous catheter are invasive to subjects. In this study we introduce a new method to estimate CᵥO₂ from SpO₂ and HR, which can be measured noninvasively with a pulse oximeter.

2. Methods

The mean age of the 13 third-grade students (4 males, 9 females) were 21 (min.20, max.24) years old. The means and standard deviations for their height and body weight were 162.0 ± 9.5 cm and 58.0 ± 7.8 kg. They had no cardio-respiratory diseases. For the healthy 13 students SpO₂ and HR were measured during a study tour in Colorado using a pulse oximeter (PULSOX-2, KONICA MINOLTA) with their informed consents. They put their index or middle fingers into the oximeter for 1 or 2 seconds in a sitting position to measure SpO₂ and HR. The measuring points were the Narita Airport (altitude 130 m), Denver City (1,609 m), Estes Park (2,499 m), Hidden Valley (2,816 m) and at the Alpine Visitor Center (3,595 m). They did not show dyspnea, palpitation, dizziness or staggering.

Since the maximum O₂ volume combined with hemoglobin in arterial blood, which corresponds to CₐO₂ with SpO₂ at 100 % in Eq. (2) is 20.1 vol% (ml/dl) with a normal hemoglobin concentration, CₐO₂ can be approximated as

$$CₐO₂ = 0.201 \text{ SpO}_₂ + 0.00314 (PₐO₂ - 5). \quad (4)$$

Hemoglobin concentration increases at high altitudes after acclimation. In a short time stay at high altitudes as in this study, such changes in hemoglobin concentration can be excluded.

Combining Eq.(3) with Eq.(4), we have

$$Q = HR \times SV = 100 \text{ VO}_₂ / \{0.201 \text{ SpO}_₂ + 0.00314 (PₐO₂ - 5) - CᵥO₂\}, \quad (5)$$

with Q in ml/min, HR beats/min, SV ml, VO₂ ml/min, SpO₂ % and CᵥO₂ is in vol%. From this equation, SpO₂ is expressed as

$$\text{SpO}_₂ = (100/0.201) (\text{VO}_₂/\text{SV}) (1/HR) + \text{CᵥO₂}/0.201 - 0.00314 (PₐO₂ - 5)/0.201. \quad (6)$$

VO₂/SV and CᵥO₂ can be estimated from the slope and intercept of a regression line of SpO₂ on 1/HR, respectively.

3. Results

The averaged values for SpO₂ and HR for 13 students are shown in Table 2 with the altitudes of the 5 points where they were measured; Narita Airport, Denver City, Estes Park, Hidden Valley and the Alpine Visitor Center. SpO₂ was significantly reduced and HR increased with increasing altitude as in the earlier place.

<table>
<thead>
<tr>
<th>Place</th>
<th>Altitude (m)</th>
<th>Pₛ (Torr)</th>
<th>SpO₂ (%)</th>
<th>HR (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Narita Airport</td>
<td>130</td>
<td>749</td>
<td>98 ± 0.95</td>
<td>75 ± 11</td>
</tr>
<tr>
<td>(b) Denver City</td>
<td>1,609</td>
<td>633</td>
<td>97 ± 1.4</td>
<td>78 ± 5.8</td>
</tr>
<tr>
<td>(c) Estes Park</td>
<td>2,499</td>
<td>570</td>
<td>94 ± 1.9</td>
<td>74 ± 7.4</td>
</tr>
<tr>
<td>(d) Hidden Valley</td>
<td>2,816</td>
<td>549</td>
<td>93 ± 1.7</td>
<td>92 ± 11</td>
</tr>
<tr>
<td>(e) Alpine Visitor Center</td>
<td>3,595</td>
<td>500</td>
<td>87 ± 2.8</td>
<td>85 ± 7.6</td>
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</table>

Statistics p < 0.05  
(b) > (c)  
(a) < (e)  
(c) < (e)

Statistics p < 0.001  
(a) > (c)  
(a),(b) > (d)  
(a),(b),(c),(d) > (e)

Pₛ was calculated from Eq.(7).
literatures\textsuperscript{2-6}). The \( P_B \) values in Torr at each altitude were calculated from the following equation\textsuperscript{8, 9),}
\[ P_B = \exp (6.63268 \times 0.1112 h \times 0.00149 h^2), \quad (7) \]
with an altitude \( h \) in m.

In Table 3, \( P_aO_2 \) were calculated from Eq. (1) with the standard values of \( P_aCO_2 \) and RER as 40 Torr and 0.8, respectively, together with the calculated \( P_B \) values from Eq. (7) at each altitude. At extremely high altitudes like Mt. Everest\textsuperscript{14, 15),} or during a long stay at high altitudes like Mt Fuji\textsuperscript{16),} hyperventilation occurs and \( P_aCO_2 \) becomes less than 40 Torr. However, our students kept normal breathing during a short stay at 3,595 m and their \( P_aCO_2 \) were thought to remain at 40 Torr.

Correlation between \( SpO_2 \) in \% and \( 1/HR \) in min/ beats is shown in Fig. 2. The regression line was
\[ SpO_2 = 2650 \times (1/HR) + 60.6 \quad \text{(8)} \]

Table 3 Calculated parameters at the 5 points.
\[
\begin{array}{|l|c|c|c|c|c|}
\hline
\text{Place} & \text{\( P_aO_2 \) (Torr)} & \text{\( C_aO_2 \) (vol\%)} & \text{\( C_aO_2 - C_vO_2 \) (vol\%)} & \text{\( HR \times (C_aO_2 - C_vO_2)/100 \) \( \text{\( \times \) min}^{-1} \)} \\
\hline
\text{Narita Airport} & 96.8 & 20.0 & 7.8 & 5.9 \\
\text{Denver City} & 72.5 & 19.6 & 7.4 & 5.8 \\
\text{Estes Park} & 59.4 & 19.1 & 6.9 & 5.1 \\
\text{Hidden Valley} & 55.0 & 18.7 & 6.5 & 6.0 \\
\text{Alpine Visitor Center} & 44.7 & 17.5 & 5.3 & 4.5 \\
\hline
\end{array}
\]

\( P_aO_2 \) was calculated from Eq. (1). \( C_aO_2 \) was calculated from Eq. (4).

\textbf{Fig. 2} Correlation between the averaged values of \( SpO_2 \) and \( 1/HR \) measured for the 13 students at the 5 points. The regression line is shown by Eq. (8).

\( R^2 = 0.600 \). \( VO_2/SV \) was obtained as 5.32 from the slope and \( C_O_2 \) as 12.2 vol\% from the intercept of the regression line according to Eq. (6) using \( P_aO_2 \) in Table 3.

\( C_O_2 \) was calculated from Eq. (4) using the observed \( SpO_2 \). \( C_O_2 \) was estimated from the intercept of the regression line in Fig. 2 as 12.2 vol\% with the \( P_aO_2 \) values at each altitude. Then, arterio-venous \( O_2 \) content difference \( C_aO_2 - C_vO_2 \) was calculated as shown in Table 3. Thus obtained \( C_aO_2 - C_vO_2 \) was multiplied by \( HR \) in Table 2 for each altitude. \( HR \times (C_aO_2 - C_vO_2)/100 \) is equal to \( VO_2/SV \) according to Eq. (3).

\textbf{4. Discussion}

To assess the gas exchange in a lung \( C_O_2 \) is one of the most important factors connecting cardiac output and oxygen uptake. Unlike the other fundamental factor \( C_aO_2 \), \( C_vO_2 \) cannot be easily measured. Therefore, estimation of \( C_vO_2 \) is in high relevance to clinical medicine as well as to basic research. At fixed altitudes \( C_aO_2 \) slightly increases and \( C_vO_2 \) obviously decreases during exercise\textsuperscript{17),} which cause the extension of \( C_aO_2 - C_vO_2 \). The slight increase in \( C_aO_2 \) is due to the blood concentration by sweating during exercise. We observed \( C_aO_2 - C_vO_2 \) extension during exercise by a rebreathing method\textsuperscript{18).} The \( C_aO_2 - C_vO_2 \) at rest was 6.8 vol\% and that during exercise with \( VO_2 \) at 1,320 ml/min was 10.3 vol\%\textsuperscript{18).} The \( C_aO_2 - C_vO_2 \) value in Table 3 at low altitude (Narita Airport) corresponds to that from the rebreathing method at rest\textsuperscript{18).} Without exercise \( C_aO_2 \) and \( C_vO_2 \) remain constant at fixed altitudes.

If the altitude is varied, \( C_aO_2 \) will decrease with increasing altitude in accord with the decrease in \( P_aO_2 \). In this study without exercise, \( C_aO_2 \) decreased with increasing altitude as shown in Table 2, while \( C_vO_2 \) was estimated from the correlation between \( SpO_2 \) and \( 1/HR \) as 12.2 vol\%. Since \( C_aO_2 \) was obtained from the regression line across the data for the 5 points, thus
obtained \( C_{O_2} \) should be constant regardless of the altitudes. The observed fairly high correlation between \( SpO_2 \) and \( 1/HR \) suggests that resting \( C_{O_2} \) remained unchanged regardless of the altitudes. As shown in Table 3 the \( C_{O_2} - C_{O_2} \) value at 3,595 m was 5.2 vol\%, which was higher than that reported by Wolfel et al.\(^{12}\) 4.0 vol\% at Pikes Peak 4,300 m. This difference is probably due to the lower \( C_{O_2} \) at the higher altitude. A relation between \( C_{O_2} - C_{O_2} \) in vol\% and altitude \( h \) in m is shown in Fig. 3 with a regression line as

\[
C_{O_2} - C_{O_2} = -0.265 \times 10^7 h^2 + 0.289 \times 10^7 h + 7.74
\]

with a coefficient of determination \( R^2 = 0.992 \). At 4,300 m \( C_{O_2} - C_{O_2} \) is calculated from this regression line as 4.03 vol\%, which is nearly equal to the Wolfel’s value\(^{12}\), indicating that our estimated \( C_{O_2} \) is consistent with their observed value.

\( VO_2/SV \) was obtained as 5.32 from the slope of the regression line between \( SpO_2 \) and \( 1/HR \). The \( VO_2/SV \) value obtained from \( SpO_2 \) and \( HR \) with the data for across the 5 points also remained unchanged regardless of the altitudes. \( VO_2/SV \) can be written as

\[
HR (C_{O_2} - C_{O_2})/100 \text{ from Eq. (3)} \quad \text{with VO}_2 \text{ in ml/min.}, \text{SV ml and } C_{O_2} - C_{O_2} \text{ in vol\%.} \quad \text{HR} \quad (C_{O_2} - C_{O_2})/100 \text{ are shown in Table 3 at each altitude. The averaged HR} \quad (C_{O_2} - C_{O_2})/100 \text{ for the 5 points is 5.46 which is close to the VO}_2/SV \text{ value obtained from the slope of the regression line between SpO}_2 \quad \text{and} \quad 1/HR. \text{ This agreement suggests that VO}_2/SV \text{ remains constant regardless of the altitudes. In healthy Japanese young adults VO}_2 \text{ is around 200 mL and SV} \quad \text{is around 70 mL at rest}^{19}. \text{ Therefore, VO}_2/SV \text{ is expected to be nearly 3. The higher observed VO}_2/SV \text{ value than the expected value may be caused by higher VO}_2 \text{ or lower SV. Wolfel et al.}^{12} \text{ reported the increase in VO}_2 \text{ and the decrease in SV at rest from sea level to the summit of Pikes Peak at 4,300 m. Although we measured neither VO}_2 \text{ nor SV in this study, our higher VO}_2/SV \text{ value may be due to the increase in VO}_2 \text{ and the decrease in SV at high altitudes.}

The obtained \( C_{O_2} - C_{O_2} \) and \( VO_2/SV \) values were within normal ranges, indicating that respiratory and circulatory functions were well-matched despite the decrease in \( SpO_2 \) for our students by more than 10\% within 6 hours.

In conclusion, \( C_{O_2} \) and \( VO_2/SV \) can be estimated from the regression line between \( SpO_2 \) and \( 1/HR \) measured at different altitudes. At low altitudes \( SpO_2 \) in healthy subjects is hardly less than 90\% even with severe exercise, and in this sense the application of our noninvasive method to estimate \( C_{O_2} \) and \( VO_2/SV \) is limited. However, our method can be used by measuring \( SpO_2 \) and \( HR \) with inspired gases at various low \( O_2 \) concentrations which simulate high altitudes.

**Acknowledgements**

I am grateful to the thirteen students for the cooperation in the measurements of \( SpO_2 \) and \( HR \). I express my gratitude to all of the faculty and staffs of UC, CSU and YPUHS who participate in the sister-school relationships with my sincere wishes for the further development of the relationships. Thanks are also due to Mr. Sam Goodman for searching the altitudes in Colorado.

**References**

2) Noguchi I. \( SpO_2/pulse \) rate ratio and the prediction of the general condition —A study during the


抄録

2012年9月17日から26日にコロラド州での研修に参加した山形県立保健医療大学理学療法学科3年の13名の健常学生（男性4名、女性9名）について動脈血酸素飽和度（SpO₂）および心拍数（HR）が測定された。13名のSpO₂の平均値および標準偏差は、成田空港（標高130m）、デンバー市内（1,609m）、エステス・パーク（2,499m）、ヒイデン・バレー（2,816m）およびアルバイン・ビジター・センター（3,595m）で、それぞれ98 ± 0.95、97 ± 1.4、94 ± 1.9、93 ± 1.7および87 ± 2.8%であった。同時に測定されたHRの平均値は、それぞれ75 ± 11、78 ± 5.8、74 ± 7.4、92 ± 11および85 ± 7.6 beats/minであった。これらの値は、成田空港での値を除き、デンバー滞在4日目に6時間以内に測定されたものである。SpO₂が短時間に10%以上低下したにもかかわらず標高3,595mで気分が悪くなった学生はいなかった。

フィックの原理に基づいてSpO₂（%）と1/HR（min/beat）の相関を解析し、SpO₂ = 2650（1/HR）+ 60.6（決定係数0.600）の回帰直線を得た。学生たちのヘモグロビン濃度が正常であると仮定し、ヘモグロビンに結合する酸素含量の基準値20.1vol%を用いて回帰直線の切片から混合静脈血の酸素含量（C.O₂）が12.2vol%と得られた。SpO₂から得られた動脈血の酸素含量（C.O₂）との差C.O₂−C.O₂は、静脈カテーテル法あるいは再呼吸法で得られた文献値と矛盾していなかった。これらの結果は、C.O₂がSpO₂およびHRを測定するという非侵襲的方法で推定出来ることを示唆している。

キーワード：混合静脈血酸素含量、動脈血酸素飽和度、心拍数、高地、コロラド