PATHOPHYSIOLOGY AND NATURAL HISTORY
MYOCARDIAL INFARCTION

Oxygen delivery and consumption and \( P_{50} \) in patients with acute myocardial infarction

Seung Chul Yang, M.D., Vinod K. Puri, M.D., and Ramesh Raheja, M.D.

ABSTRACT  We investigated the relationship between oxygen delivery (DO\(_2\)) , oxygen consumption (VO\(_2\)), and influence of oxyhemoglobin dissociation (P\(_{50}\)) on VO\(_2\) in 40 patients with complicated myocardial infarction. A decrease in VO\(_2\) and an increase in P\(_{50}\) were observed as DO\(_2\) decreased due to pump failure. In a given range of DO\(_2\), VO\(_2\) was related to P\(_{50}\) in survivors (r values .472 to .647, \( p < .01 \)). Each millimeter of mercury increase in P\(_{50}\) was associated with a 5.2 to 6.5 ml/min-m\(^2\) increase in VO\(_2\) when DO\(_2\) was less than 450 ml/min-m\(^2\). No similar correlation was found for nonsurvivors. Lactate was higher in nonsurvivors despite the fact that DO\(_2\) and VO\(_2\) were similar in the two groups. The lack of compensatory increases in P\(_{50}\) may be pathologic in nonsurvivors. However, the value of VO\(_2\) as an indicator of tissue oxygenation or survival in patients with acute myocardial infarction is questionable.

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IN ADULTS with respiratory distress syndrome or in shock and in anesthetized patients, oxygen consumption (VO\(_2\)) has been demonstrated to be related to oxygen delivery (DO\(_2\)).\(^1\)–\(^4\) The cause of supply dependency of oxygen uptake under certain conditions and its pathophysiologic implications are uncertain.\(^5\) When DO\(_2\) is decreased, one of the compensatory mechanisms by which VO\(_2\) is maintained is a decrease in oxygen affinity for hemoglobin, i.e., an increase in oxyhemoglobin dissociation (P\(_{50}\)), to facilitate oxygen unloading and increased O\(_2\) extraction. Elevated P\(_{50}\) has been found in patients with anemia and low cardiac output and those living at high altitudes.\(^6\) In patients with acute myocardial infarction, elevated P\(_{50}\) is thought to improve VO\(_2\) when DO\(_2\) is decreased due to low cardiac output.\(^2\) Conversely, the clinical significance of VO\(_2\) has been questioned,\(^7\) even though some investigators have observed lower VO\(_2\) in nonsurvivors than survivors of septic shock.\(^8\) The purpose of our study was to evaluate the relationship of DO\(_2\), VO\(_2\), and \( P_{50} \) and the effect of \( P_{50} \) on VO\(_2\) after acute myocardial infarction.

Methods

Forty consecutive patients who required hemodynamic monitoring among 147 patients with acute myocardial infarction who were admitted to our institution between January 1983 and July 1984 were evaluated. Diagnosis of acute myocardial infarction was made by history, the electrocardiogram, and measurement of the creatine kinase–MB isoenzyme level. Hemodynamic monitoring was instituted for management of cardiogenic shock in 18 patients, pulmonary edema in 12, persistent chest pain in nine, and uncontrolled arrhythmia in one. A pulmonary arterial catheter was inserted through the internal jugular or subclavian vein and an arterial catheter was inserted in the radial artery of each patient. Cardiac output was measured by the thermodilution technique in triplicate, or until three measurements varied less than 5%. Simultaneous arterial and mixed venous blood were also drawn for analysis of pH, P\(_{O2}\), S\(_{O2}\), P\(_{CO2}\), hemoglobin, and arterial lactate. From these data, DO\(_2\) and VO\(_2\) were calculated with appropriate formulas.\(^9\) P\(_{50}\) was calculated from the mixed venous \( O_2 \) saturation with the method described by Aberman et al.\(^10\) The mean value of 27.9 ± 0.6(SEM) was obtained in 10 stable surgical patients who were electively monitored in the preoperative period. Arterial lactate was measured by an enzymatic method. The normal value for arterial lactate measured in our laboratory is 0.8 to 1.2 mmol/liter, but only values exceeding 2.4 mmol/liter are considered to indicate hypoperfusion. All of these measurements were repeated every 12 hr and whenever clinical conditions changed.

Patients were managed with vasoactive agents, fluids, and supportive care according to their hemodynamic status. A total of 349 measurements were obtained in 40 patients, including 23 survivors (group 1) and 17 nonsurvivors (group 2). DO\(_2\) ranged from 94 to 552 ml/min-m\(^2\) and the values were grouped into six ranges, as listed in table 1. The value range of 50 ml/min-m\(^2\) was chosen so that the relationship between \( P_{50} \) and VO\(_2\) could be examined independent of DO\(_2\). Although use of this narrow range resulted in fewer data points in each category, more than 40 observations were available for analysis. Correlations between \( P_{50} \) and VO\(_2\) were sought by linear regression analysis.
TABLE 1

<table>
<thead>
<tr>
<th>DO2 (ml/min-m²)</th>
<th>P50 (mm Hg)</th>
<th>VO2 (ml/min-m²)</th>
<th>r value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;250</td>
<td>30.5 ± 0.3</td>
<td>116 ± 2</td>
<td>.35&lt;</td>
</tr>
<tr>
<td>250-300</td>
<td>30.6 ± 0.4</td>
<td>134 ± 4</td>
<td>.416&lt;</td>
</tr>
<tr>
<td>300-350</td>
<td>30.2 ± 0.3</td>
<td>141 ± 3</td>
<td>.377&lt;</td>
</tr>
<tr>
<td>350-400</td>
<td>29.6 ± 0.4</td>
<td>161 ± 6</td>
<td>.396&lt;</td>
</tr>
<tr>
<td>400-450</td>
<td>29.5 ± 0.3</td>
<td>175 ± 6</td>
<td>.536&lt;</td>
</tr>
</tbody>
</table>

*p < .01.

Then, survivors and nonsurvivors were analyzed separately. The unpaired t test was used for comparisons between the two groups.

Results

As DO2 increased, a linear increase in VO2 and a decrease in P50 was observed (table 1). VO2 was significantly different (p < .05) at every range of DO2. For all patients as a group, the correlation between P50 and VO2 was significant, although weak. When group 1 and group 2 were compared, VO2 and P50 were similar at all ranges of DO2 (figure 1). In nonsurvivors, the correlation between P50 and VO2 was not significant at any range of DO2, while a moderate correlation between P50 and VO2 was found in survivors (table 2). In the patients with a DO2 of less than 450 ml/min-m², each millimeter of mercury increase in P50 was associated with a 5.2 to 6.5 ml/min-m² increase in VO2. Lactate, as shown in figure 1, was in the normal range in all survivors, even those with a DO2 of less than 250 ml/min-m² and a mean VO2 of less than 113 ml/min-m². In nonsurvivors, lactate was significantly higher when DO2 was less than 400 ml/min-m².

Discussion

In patients with low cardiac output due to cardiac disease a correlation between DO2 and VO2 has not been consistently observed. da Luz et al.2 noted reduced VO2 in patients with low DO2 due to cardiogenic shock. However, Chappell et al.11 reported no significant changes in VO2 when DO2 was increased with vasodilator therapy in patients with refractory left ventricular failure. In our studies the difference in VO2 at each range of DO2 was small, but over a wide range of DO2 values, a linear correlation between VO2 and DO2 was demonstrated (figure 1). With severe limitations of blood flow, such as those that were present in our patients as a result of pump failure, this relationship between DO2 and VO2 would be expected. A similar relationship between VO2 and DO2 has been observed to accompany, during volume loading, low cardiac output states associated with hypovolemic and septic shock.4 Shibutani et al.3 also demonstrated a critical level of DO2 below which VO2 was supply dependent. The unique situation in adult patients with respiratory distress syndrome, in whom VO2 continues to be supply dependent even at extremely high DO2 levels, perhaps represents disordered peripheral tissue metabolism.5 Although there may be several pathologic states in which the peripheral tissues lose their ability to

FIGURE 1. VO2, P50, and arterial lactate at different levels of DO2 in survivors (closed circles) and nonsurvivors (open circles). Lactate levels were significantly higher in nonsurvivors, despite VO2 and P50 similar to those in survivors.

TABLE 2

<table>
<thead>
<tr>
<th>DO2 (ml/min-m²)</th>
<th>r value</th>
<th>VO2/P50 (ml/min-m²/mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;250</td>
<td>.647&lt;</td>
<td>6.5</td>
</tr>
<tr>
<td>250-300</td>
<td>.564&lt;</td>
<td>5.9</td>
</tr>
<tr>
<td>300-350</td>
<td>.544&lt;</td>
<td>5.4</td>
</tr>
<tr>
<td>350-400</td>
<td>.472&lt;</td>
<td>5.2</td>
</tr>
<tr>
<td>400-450</td>
<td>.369</td>
<td>5.2</td>
</tr>
<tr>
<td>&gt;450</td>
<td>.608&lt;</td>
<td>12.9</td>
</tr>
</tbody>
</table>

*p < .01.
regulate VO₂, pump failure does not appear to be one of them.

The clinical significance of VO₂ remains unclear. The decrease in VO₂ with declining DO₂ is thought to cause inadequate tissue oxygenation, anaerobic metabolism, and lactic acidosis. In patients with septic shock, a correlation between reduced VO₂ and lactic acidosis has been suggested. Abraham et al. documented lower VO₂ in nonsurvivors than survivors with septic shock and concluded that impaired VO₂ adversely affects survival. However, it is possible that the differences in VO₂ in survivors and nonsurvivors simply reflect differences in DO₂, which are determined by cardiac output, arterial oxygenation, and hemoglobin. A significant decline in one or more of these variables reflects the severity of disease, which independently affects the outcome. In an extensive review of septic shock, Houtchens and Westenskow concluded that reduced VO₂ was neither a specific early indicator of sepsis nor a certain prognosticator of outcome.

In patients with acute myocardial infarction, no data are available regarding VO₂ and survival. Our data indicated that survivors and nonsurvivors had similar VO₂ values as long as values for DO₂ were similar. In survivors, marked decreases in DO₂ and VO₂ were not associated with lactic acidosis. A decreased VO₂ unassociated with lactic acidosis may be due to a reduction in oxygen demand or increased extraction of O₂. The compensatory mechanism of increased O₂ extraction, as revealed by widened arteriovenous O₂ differences in low flow states, was well maintained in both groups of patients. Bryan-Brown et al. have speculated that as P₅₀ increases, more consumable O₂ becomes available to the tissue. A correlation between "consumable" and "consumed" oxygen, however, has not been well demonstrated. da Luz et al. estimated the amount of available O₂ by the differences between actual VO₂ and that calculated based on normal P₅₀. According to these authors, an increase in VO₂ of 20 ml/min·m⁻² due to an increase in P₅₀ of 1.7 mm Hg was equivalent to a 19% increase in cardiac output. However, DO₂ in their patients varied from 135 to 734 ml/min·m⁻², which could directly affect VO₂. Since DO₂ cannot be kept constant in critically ill patients, we arbitrarily chose to group DO₂ values into 50 ml/min·m⁻² ranges to minimize the effect of DO₂ on the calculation of VO₂. In survivors, a moderate correlation between VO₂ and P₅₀ was found. The amount of increase in VO₂ per 1 mm Hg increase in P₅₀ was 5.2 to 6.5 ml/min·m⁻² in most of the ranges examined. Thus, the patient with a DO₂ between 300 and 350 ml/min·m⁻² and a normal P₅₀ of 27 mm Hg would have a VO₂ of 116 ml/min·m⁻² instead of 141 ml/min·m⁻², as was observed in patients with an increased P₅₀ (table 1). Our data indicate that in survivors more oxygen was consumed as more oxygen became available as a result of the rightward shift in the P₅₀ curve. The lack of a similar finding in the nonsurvivors is interesting. Although decreased DO₂, abnormal tissue metabolism, and lactic acidosis may serve as physiologic mechanisms for progressive shock after acute myocardial infarction, fatal outcome may be precipitated by arrhythmias or other clinical events. Also, we believe that the clinical significance of VO₂ as an indicator of tissue oxygenation or survival in patients with acute myocardial infarction remains questionable.

References
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