Oxygen Delivery in Critically Ill Patients*
Relationship to Blood Lactate and Survival
Mitchell C. Rashkin, M.D.; Carol Bosken, M.D.; and Robert P. Baughman, M.D.

Forty-four critically ill patients with or without adult respiratory distress syndrome (ARDS) were studied in an attempt to define critical levels of oxygen delivery. Blood lactate was used as the indicator of tissue hypoxia independent of cardiac output. Survival was good (55 percent) and blood lactate near normal for those with oxygen delivery more than 8 ml/kg/min. Below this level, survival was poor (14 percent) and blood lactate markedly increased. There were significant nonlinear correlations of lactate with O2 delivery (r = −.735, p < .001) and cardiac output (r = −.602, p < .001). Mixed venous oxygen was not a reliable index of blood lactate, survival, oxygen delivery, or oxygen consumption.

Normal cellular function depends upon a supply of oxygen adequate to meet metabolic needs. The supply of oxygen depends upon the cardiac output (Qt), hemoglobin (Hb), and the partial pressure of oxygen in arterial blood (PaO2). When a disease affects a single component of the oxygen delivery (O2D) system, clinical practice is guided by well-tested quantitative guidelines. When pneumonia causes hypoxemia, oxygen is delivered to raise the arterial oxygen to 55 to 60 mm Hg; when anemia is present, blood is transfused to bring the hematocrit to approximately 25 percent; when myocardial infarction causes shock, a volume infusion, inotropic drug or afterload reducing agent is given until the cardiac index is more than 2.2 L/min/M2. These guidelines assume normally functioning adaptive mechanisms in the remaining components of the system.

Acute respiratory failure is frequently associated with more than one abnormality of O2D. Several systems may need treatment simultaneously, and treatment of one component may adversely affect another. For example, when PEEP is used to treat hypoxemia, the cardiac output may fall. If more than one system is unstable or in a state of borderline compensation, the only way to determine the net effect of any therapeutic intervention is to calculate O2D.

The advent of pulmonary artery catheterization has made it possible to calculate O2D almost routinely. These numbers are helpful in determining the effect of various therapeutic maneuvers, but the lower limits compatible with recovery are not known. Is there a specific threshold that should be aimed for even at the cost of complications? One cannot make any assumptions about metabolic rate in these acutely ill patients.

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Methods
This study is a retrospective analysis of all patients admitted to the intensive care units of the University of Cincinnati and Veterans Administration Hospitals of Cincinnati from June 1981 through January 1983. Patients were eligible if they required cardiovascular monitoring with a triple lumen right heart catheter, and they had at least one set of simultaneously measured values for the following parameters: pulmonary artery systolic, diastolic, and mean pressures, pulmonary artery wedge pressure (PAW), arterial blood gases, mixed venous oxygen tension (PvO2) and hemoglobin (Hb). Charts were also reviewed for the course in the hospital until discharge or death. Patients were excluded if a primary cause for
lactic acidosis could be determined. Patients with mild-to-moderate liver disease were not excluded. Only one patient with a methanol overdose was thus excluded.

Patients were studied at one or more time points during their hospitalization. Each study included measurements of the pulmonary artery systolic, diastolic, and mean pressure and pulmonary capillary wedge pressure. Cardiac output was measured by the thermomilution technique using a cardiac output computer. Each cardiac output measurement was the mean of three determinations. Venous blood was collected from a free flowing vein and serum lactate and hemoglobin were determined. Arterial blood samples were obtained either by arterial puncture or from an indwelling arterial catheter. Mixed venous blood was sampled from the distal port of the pulmonary artery catheter. Arterial and mixed venous blood were collected anaerobically, heparinized, stored on ice, and subsequently analyzed within 30 minutes. Partial pressures of oxygen and carbon dioxide, as well as simultaneous pH, were determined with a blood gas analyzer. The mean arterial blood pressure was either read directly from a transducer attached to an indwelling arterial catheter or was calculated from cuff pressure. Oxygen content, oxygen delivery, and oxygen consumption were derived from the formulas shown in Table 1.¹

Statistical analysis was done with a general statistical program on a microcomputer. Analysis included Mann Whitney U test, chi square with Yates correction (x²), and linear correlation using the least squares technique as appropriate.¹ A p value of less than 0.05 was considered significant.

RESULTS

Table 2 provides a summary of the clinical diagnosis for all 44 patients who were identified as having adequate information to be included in the analysis. Twenty-one patients had ARDS, defined as respiratory distress associated with diffuse alveolar infiltrates on

| Table 2—Summary of Clinical Diagnoses |

<table>
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<th>Category</th>
<th>Diagnoses</th>
<th>Count</th>
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</thead>
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<tr>
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<td>Aspiration</td>
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<td></td>
<td>Shock</td>
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<td>Smoke inhalation</td>
<td>1</td>
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<tr>
<td></td>
<td>Drowning</td>
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<tr>
<td></td>
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<td></td>
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<td></td>
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**Table 1—Formula for Oxygen Content, Delivery and Consumption**

- Arterial oxygen content \((\text{CaO}_2) = \text{Hg} \times \% \text{ sat} \times 1.39\)
- Venous oxygen content \((\text{CVO}_2) = \text{Hg} \times \% \text{ sat} \times 1.39\)
- Arteriovenous oxygen difference \(= \text{CaO}_2 - \text{CVO}_2\)
- Oxygen delivery \((O,D) = Q_1 \times \text{CaO}_2\)
- Oxygen consumption \((V = O_2) = Q_1 \times (\text{CaO}_2 - \text{CVO}_2)\)

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**Figure 1.** Oxygen delivery \((O,D) vs blood lactate with power curve \((y = ax^2, a = 213.72, b = -1.58)\) demonstrated \(r = -0.735, p < .001\). Triangles indicate ARDS, circles, non-ARDS.

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**Figure 2.** Survival plotted against each patient's lowest \(O,D\). Median value for each group is shown. Mann Whitney U test showed all three groups to be significantly different from each other \(p<.02\). Closed circles indicate ARDS; open circles, non-ARDS.
Of the factors determining O\textsubscript{2}D (Qt, Hg, CaO\textsubscript{2}), only Qt had a significant correlation with blood lactate ($y = ax^b$, $a = 39.6$, $b = -1.18$, $r = -.602$, $p<.001$). Mean arterial blood pressure (MAP) had a less significant correlation to blood lactate ($r = -.413$, $p<.05$). Arterial-venous O\textsubscript{2} difference did not significantly correlate with blood lactate levels.

Patients were divided into three groups: those who died within 24 hours, those who lived longer than 48 hours but died in the hospital, and those who survived. In Figure 2, the lowest O\textsubscript{2}D is compared with survival. Patients were either monitored until they died, or until they improved and the monitoring was no longer clinically necessary. Of those who died after 48 hours, all recovered from their initial hypotensive crisis but subsequently died. There were significant differences in O\textsubscript{2}D between the long-term survivors, those who died later in the course, and those who died early. Patients with an O\textsubscript{2}D more than 8 ml/kg/min had a long-term survival of 55 percent, whereas those with an O\textsubscript{2}D less than or equal to 8 ml/kg/min had a long-term survival of 14 percent. Chi square analysis with Yates correction showed these two groups to be significantly different ($\chi^2 = 6.47$, $p<.025$).

Figure 3 shows the patients’ mixed venous oxygen tension (P\textsubscript{VO\textsubscript{2}}). Figure 3, top, illustrates P\textsubscript{VO\textsubscript{2}} vs blood lactate. There was no significant correlation. Similarly there was no correlation between mixed oxygen saturation (S\textsubscript{VO\textsubscript{2}}) and blood lactate. In Figure 3, bottom, P\textsubscript{VO\textsubscript{2}} is plotted against VO\textsubscript{2}. Only a poor correlation ($r = -.24$) was found. There was only a poor correlation ($r = .38$) with O\textsubscript{2}D. Compared to S\textsubscript{VO\textsubscript{2}}, VO\textsubscript{2} and O\textsubscript{2}D gave correspondingly poor correlation ($r = -.22$ and $r = 0.50$), respectively. In addition, P\textsubscript{VO\textsubscript{2}} obtained at the patients’ lowest O\textsubscript{2}D was a specific but not sensitive indicator of mortality. Using a P\textsubscript{VO\textsubscript{2}} of 28 mm Hg, as has been suggested,\textsuperscript{14} Chi square analysis with Yates' correction showed no significant difference between survivors and nonsurvivors.

**DISCUSSION**

Our selection criteria enabled us to look at patients with a broad spectrum of hemodynamic measurements. Patients being monitored prospectively for fluid balance were normal, whereas several patients were studied just hours prior to death. We found that patients who always had an O\textsubscript{2}D of more than 8 ml/kg/min had a good survival even if they were diagnosed as having ARDS. In addition, these patients with O\textsubscript{2}D greater than 8 ml/kg/min had lactic acid levels in or near the normal range.

Mixed venous oxygen tension has been described as a good predictor of O\textsubscript{2}D, mortality,\textsuperscript{14} and lactic acidosis.\textsuperscript{15} Recent reviews have suggested it is a good parameter to follow in treating ARDS,\textsuperscript{16} and a commercial catheter is now available for continuous monitoring of S\textsubscript{VO\textsubscript{2}}.\textsuperscript{17} We found this measurement either by direct measurement of P\textsubscript{VO\textsubscript{2}} or S\textsubscript{VO\textsubscript{2}} to be unhelpful in predicting the behavior of the group or in following the course of individual patients. Since measurement of P\textsubscript{VO\textsubscript{2}} requires invasive procedures, using one measurement for convenience instead of calculating O\textsubscript{2}D does not seem warranted. High P\textsubscript{VO\textsubscript{2}} levels are due to peripheral shunting,\textsuperscript{18} as in sepsis,\textsuperscript{19,20} or to other as yet undefined mechanisms. It can be seen by looking at Figure 3b, bottom, that some of our patients with ARDS had high P\textsubscript{VO\textsubscript{2}} despite very low VO\textsubscript{2}. In patients with a high O\textsubscript{2} demand (eg, fever), a low P\textsubscript{VO\textsubscript{2}} may be expected with a high O\textsubscript{2}D. In contrast, patients with a low or normal oxygen demand and low O\textsubscript{2}D (eg, heart failure), a low P\textsubscript{VO\textsubscript{2}} would be expected. The P\textsubscript{VO\textsubscript{2}} can not be expected then to be a good predictor of O\textsubscript{2}D in random patient populations or where multisystem disease is present. In select subpopulations, it may be of some value.

If O\textsubscript{2}D were low enough to limit VO\textsubscript{2}, then anaerobic metabolism should occur, indicated by a rise in blood lactate.\textsuperscript{18,21} It has been demonstrated that serum lactate levels correlate with severe anemia,\textsuperscript{22} and with the severity and prognosis of shock.\textsuperscript{23-25} Huckabee\textsuperscript{26} and Eldridge\textsuperscript{27} found that clinical hypoxemia will not lead to hyperlactatemia unless a systemic circulatory disor-
der was also present. In our study, lactic acidosis correlated with decreased O₂ delivery or decreased cardiac output but not with hypoxemia alone. This closely parallels the findings of Kashitz et al who found good correlation between cardiac output and blood lactate levels. There was not a significant correlation between hemoglobin and elevated serum lactate in those patients. The lowest hemoglobin in the population studied was 6.1 g/dl; Seibert and Ebaugh did not find a significant lactic acidosis until the hemoglobin was less than 6 g/dl.

Danek et al and Powers et al found that VO₂ was limited by O₂D over a wide range of O₂D in patients with ARDS. Until recently, the most common approach was to relate VO₂ to O₂D and designate an O₂D above which VO₂ would be stable. All of these studies have calculated VO₂ from the Fick relationship Qt (CaO₂-CvO₂) and compared this value to O₂D as calculated from Qt (CaO₂). The Qt is quantitatively important for both VO₂ and O₂D. It is, therefore, possible that relating these two parameters when both rely on the measurement of Qt by thermodilution may introduce an artificial positive correlation.

Our critical level of O₂D of 8 ml/min/kg is low by comparison with the data of Danek et al and Powers. Mohsenifar et al did find a leveling off of VO₂ and suggested that this did not occur until an O₂D of more than 20 ml/kg/min. We could find only two other studies of this problem using expired gas measurements instead of the Fick principle to estimate VO₂. In a clinical study of patients on extracorporeal membrane oxygenation for treatment of ARDS, Fallat and Eberhart measured VO₂ via expired gas measurements and related it to changes in O₂D. They found no decrease in VO₂ until O₂D was less than 7 ml/min/kg. In a review of several studies of patients in shock, Caldwell et al could demonstrate no decrease in VO₂ until O₂D was less than 250 ml/min/m². This level corresponds to 6.4 ml/kg/min. Shibutani et al showed in anesthetized patients undergoing cardiopulmonary bypass that VO₂ decreased and lactic acid rose when O₂D was less than a critical value of 8.2 ml/kg/min or 330 ml/min/m². In dogs, Cain found that below an O₂D of 9.8 ml/kg/min, oxygen demand exceeded supply.

Our data showed that below an O₂D of 8 ml/kg/min, lactic acid levels rise rapidly and mortality is high. Three patients died with O₂D less than 6 ml/kg/min but only mildly elevated levels of blood lactate. It is possible that in these three patients, circulation was so poor that lactic acid was not delivered to the sampling site. We did not find blood lactate levels a sensitive indicator of changes in O₂D in individual patients. Only in the aggregate was there a significant relationship between lactic acid and O₂D. However, a recent study by Vincent et al showed that if measured every 20 minutes, a decrease in lactate concentration over the first hour of shock therapy can be used as a prognostic indicator.

The group of patients who died late are of interest. At least seven of them died of complications arising from the original hypotensive episode, eg, renal failure or brain death. While poor O₂D was not the proximate cause of death, it was certainly an important contributing factor. One factor which we could not accurately quantify was the duration of the poor delivery. Of the three patients with O₂D less than 8 ml/kg/min who survived, two had rapidly reversible causes of hypotension (arrhythmias). It is possible that there is a range of relative oxygen lack in which duration is an important determinant of ultimate organ recovery.

In summary, we feel it is not necessary to pursue unduly high levels of O₂D to ensure survival in critically ill patients with or without ARDS. In lieu of accurate measures of metabolic rates in individual patients, we feel that an O₂D greater than 8 ml/min/kg is probably sufficient to sustain organ function. On the other hand, levels of less than 8 ml/min/kg were encountered fairly frequently and were associated with a high mortality. In these selected patients, heroic measurement to increase O₂D may be indicated. Measurement of PVO₂ was not a reliable indicator of either lactate, O₂D, VO₂, or survival.

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