Assessment of Cardiac Index in Anemic Patients*

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Study objectives: During isovolemic hemodilution, healthy individuals maintain oxygen consumption (VO₂) by identical increases in cardiac index (CI) and oxygen extraction ratio (O₂ER). In critically ill patients, the relationship between CI and O₂ER may be different. Patients with an altered cardiac function may have a decreased CI/O₂ER ratio, whereas patients with sepsis may have an increased CI/O₂ER ratio. We hypothesized that the analysis of the CI-O₂ER relationship could help us to assess the adequacy of cardiac function in critically ill patients with anemia.

Design: Prospective, observational study.

Setting: Thirty-one-bed medicosurgical ICU of a university hospital.

Patients: Sixty patients equipped with arterial and Swan-Ganz catheters presenting with anemia, which was defined as a hemoglobin level <10 g/dL in the absence of active bleeding. Patients were classified into those with compromised cardiac function (group 1; n = 40), and those with normal cardiac function (group 2; n = 20).

Measurements and results: In addition to the pertinent clinical data, initial hemodynamic measurements, including pulmonary artery occlusion pressure (PAOP), CI, and O₂ER, were collected in all patients at the onset of anemia. As anticipated, group 1 patients (n = 40) had lower CIs, higher O₂ER levels, and lower CI/O₂ER ratios than group 2 patients. However, there was no significant difference in PAOP values between the groups. The CI/O₂ER ratio was <10 in 27 of 40 group 1 patients but only in 4 of 20 group 2 patients. Of these latter four patients, three were found to be hypovolemic, and one patient with sepsis had severe myocardial depression. There was no statistically significant difference in PAOP in group 2 patients with or without hypovolemia ([mean ± SD] 12.3 ± 2.1 mm Hg vs 13.7 ± 4.3 mm Hg; p = 0.21). In group 1, survivors had a higher CI and CI/O₂ER ratio than nonsurvivors. In group 2, however, such a relationship did not reach statistical significance.

Conclusions: The relationship between CI and O₂ER level can help interpret the CI in anemic patients. In anemic patients with no cardiac history, a low CI/O₂ER ratio (<10) suggests hypovolemia even when CI is not depressed.

Key words: cardiac index; hemodynamics; hypovolemia; invasive monitoring; isovolemic hemodilution; oxygen extraction; sepsis

Abbreviations: CI = cardiac index; DO₂ = oxygen delivery; O₂ER = oxygen extraction ratio; PAOP = pulmonary artery occlusion pressure; SaO₂ = arterial oxygen saturation; SVO₂ = mixed venous oxygen saturation; VO₂ = oxygen consumption

Growing concerns about the potentially hazardous complications of blood transfusion, the limited supplies and escalating costs of procuring blood, and a lack of demonstrated benefits of transfusion, as well as a good tolerance to anemia in normovolemic patients, have made us rethink our transfusion strategies.¹⁻³ Good tolerance to anemia is due to increases in cardiac index (CI) and oxygen extraction ratio (O₂ER), which maintain oxygen consumption (VO₂). Although a high CI in an anemic patient may appear to be adequate, if analyzed in isolation, the cardiac response may still be inadequate for the degree of anemia. Indicators of peripheral vascular mechanisms involved in maintaining VO₂, mixed venous oxygen saturation (SVO₂) and O₂ER, may be useful in interpreting the CI under these conditions. Various studies have shown that during isovolemic hemodilution, healthy individuals increase their CIs and O₂ER levels to a similar extent to maintain VO₂.⁴⁻⁻⁵ Hence, the relationship between CI and

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O2ER could be used to interpret the adequacy of CI in anemic patients and can be visualized easily on a computer or even on a sheet of paper at the bedside.10 The CI/O2ER ratio, which is around 12 (3:0:25) in healthy humans, is relatively stable in healthy individuals with isovolemic hemodilution.4–8 In critically ill patients, the relationship between CI and O2ER may be different. In particular, patients with an altered cardiac function or with hypovolemia may have a decreased CI/O2ER ratio, whereas patients with sepsis may have an increased CI/O2ER ratio.11,12 We hypothesized that the analysis of the CI-O2ER relationship would help to assess the adequacy of the CI during anemia in critically ill patients.

**MATERIALS AND METHODS**

The initial measurements of hemodynamics and blood gas levels were collected from 60 patients presenting with anemia, defined as a hemoglobin level < 10 g/dL in the absence of active bleeding, who were equipped with arterial (femoral or radial) and pulmonary artery catheters (7.5F Swan-Ganz catheter; Baxter; Irvine, CA). Patients were classified into two groups depending on the presence or absence of a history of cardiac disease. Group 1 patients (n = 40) were those with any one of the following signs of compromised cardiac function: recent history of clinically significant arrhythmias; congestive heart failure; ECG signs of ischemic heart disease; echocardiographic signs of altered cardiac function (ejection fraction, < 50%); significant valvular disease; or coronary angiographic evidence of coronary artery disease. Group 2 patients (n = 20) were those with no history of compromised cardiac function. CI and O2ER data were not used to separate the patients into the two groups. Sepsis was defined as a clinically suspected or proven infection, with fever (temperature, > 38°C), hypothermia (temperature, < 36°C), or altered WBC count (ie, > 12,000/μL or < 4,000/μL). Hypovolemia was defined by clinical signs such as tachycardia, peripheral vasoconstriction, oliguria, fluid balance (as determined by the intake/output chart), hypotension, and response to fluid challenge with improvement in vital signs such as heart rate, BP, and CI.

The initial measurements of complete hemodynamic data at the onset of anemia with hemoglobin ≤ 10 g/dL were obtained by a physician using a standard procedure. After intravascular pressure measurements, the CI was determined by the thermodilution technique, using 10-mL injections of iced 5% dextrose in water via a closed system (CO-set; Baxter) and a cardiac output computer (SC 9000; Siemens; Danvers, MA). In patients receiving mechanical ventilation, the bolus injection was started at the end of the inspiratory phase. The CI was averaged from three to five injections, the values of which were within 5% of each other.13,14 Immediately after CI determination, arterial and mixed venous blood samples were simultaneously collected anerobically for the immediate measurement of arterial and mixed venous blood gas levels in an automatic analyzer providing rapid results (model ABL3; Radiometer; Copenhagen, Denmark). The arterial oxygen saturation (SaO2) and SvO2 were measured by a co-oximeter (Hemoximeter OSM3; Radiometer). O2ER was calculated as

\[
\text{O2ER} = \frac{(\text{CaO}_2 - \text{CVO}_2)}{\text{CaO}_2} = \frac{[(\text{Hb} \times C \times \text{SaO}_2) - (\text{Hb} \times C \times \text{SvO}_2)]}{\text{Hb} \times C \times \text{SaO}_2}
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\]

Results

Hemoglobin concentrations ranged between 6.5 and 9.9 g/dL and were similar in the two groups (Table 1). As anticipated, group 1 patients had a lower CI, a higher O2ER, and a lower CI/O2ER ratio than group 2 patients. However, there was no significant difference in pulmonary artery occlusion pressure (PAOP) between the two groups (Table 1).

In group 1, the CI/O2ER ratio was < 10 in the majority of patients (27 of 40), indicating that the VO2 was usually determined by a greater increase in O2ER than in CI (Fig 1). Of the 13 patients with a CI/O2ER ratio > 10, 12 had evidence of sepsis.

In group 2, the CI/O2ER ratio was > 10 in 16 of 20 patients, and 12 of the 16 patients had sepsis. Only 4 of 20 patients had a CI/O2ER ratio < 10 (Fig 2). Three of these patients were found to be hypovolemic, and one patient was suspected of having severe sepsis-related myocardial depression, which was proved on echocardiographic examination. Two of these four patients had a CI > 3 L/min/m². There was no significant difference in PAOP between patients with and without hypovolemia in this group (PAOP, 12.3 ± 2.1 mm Hg vs 13.7 ± 4.3 mm Hg, respectively; p = 0.21).

In group 1, survivors had a higher CI and CI/O2ER ratio (when expanded after ignoring the dissolved oxygen) where C is the amount of oxygen carried by 1 g hemoglobin

\[
\text{O2ER} = \frac{(\text{CaO}_2 - \text{CVO}_2)}{\text{CaO}_2} = \frac{[(\text{Hb} \times C \times \text{SaO}_2) - (\text{Hb} \times C \times \text{SvO}_2)]}{\text{Hb} \times C \times \text{SaO}_2}
\]

### Table 1—Comparison of CI, O2ER, CI/O2ER Ratio, Hemoglobin Concentration, and PAOP in the Two Groups of Patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI, L/min/m²</td>
<td>2.98 ± 1.02</td>
<td>3.89 ± 0.86</td>
<td>0.001</td>
</tr>
<tr>
<td>O2ER, %</td>
<td>35.3 ± 8.6</td>
<td>28.7 ± 7.6</td>
<td>0.002</td>
</tr>
<tr>
<td>CI/O2ER ratio</td>
<td>9.2 ± 4.3</td>
<td>14.7 ± 5.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>8.2 ± 1.0</td>
<td>8.6 ± 1.1</td>
<td>0.29</td>
</tr>
<tr>
<td>PAOP, mm Hg</td>
<td>14.3 ± 5.2</td>
<td>13.5 ± 4.0</td>
<td>0.26</td>
</tr>
</tbody>
</table>

*Values given as mean ± SD, unless otherwise indicated.*
O₂ER ratio than did nonsurvivors (Table 2). In group 2, however, such a relationship did not reach statistical significance.

**DISCUSSION**

The normal compensatory response to hemodilution, in relation to blood flow, is an increase in CI, a change in the regional distribution of blood flow toward vital organs like the brain and heart, and an increase in O₂ER.4–9 A shift of the oxyhemoglobin dissociation curve due to increased levels of 2,3-diphosphoglycerate and the increased oxygen tension at half saturation also may contribute to the response.15 An inability to exercise this compensatory mechanism uniformly through various systemic vascular beds may limit the patient’s tolerance to anemia.12,16–18

The magnitude of the physiologic response, and the mechanisms involved, depend on the species, state of awareness (awake or anesthetized), type of anesthesia, type of exchange solution, and condition of the heart prior to hemodilution.11,12,19–22 Various human studies of isovolemic hemodilution have shown an identical increase in CI and O₂ER to meet V̇O₂.4–9 Duke and Abelmann5 showed that when

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**FIGURE 1.** Relationship between CI and O₂ER in the patients with compromised cardiac function (group 1).

**FIGURE 2.** Relationship between CI and O₂ER in the patients with normal cardiac function (group 2).

* = three patients with concomitant hypovolemia; ▲ = one patient with severe myocardial depression due to sepsis.
patients with chronic anemia were treated with blood transfusions, their CIs and O₂ERs fell from 4.73 L/min/m² and 39.6%, to 3.44 L/min/m² and 29.4%, respectively, indicating a proportional contribution of the CI and O₂ER. Woodson et al. studied the effects of acute and established anemia on oxygen transport at rest, during submaximal work, and during maximal work in young healthy volunteers. During maximal exercise in patients with acute anemia, they observed a 233% increase in the CI from 4.5 L/min/m² at rest to 10.5 L/min/m², and a 300% increase in O₂ER from 23 to 32%. This response to anemia. However, the majority of patients with sepsis in this group still had a high CI/O₂ER ratio, as is typically observed in these circumstances. On the contrary, the majority of patients with normal cardiac function had a CI/O₂ER ratio > 10. In the presence of sepsis, most of these patients showed a greater cardiac response to anemia. Moreover, the CI-O₂ER relationship is obtained easily on any computer and can be viewed on a graph at the bedside, as is the case in our ICU. We selected a CI/O₂ER ratio of 10 to assess the adequacy of CI. Hence, in the presence of normovolemic anemia with normal cardiac function, a CI/O₂ER ratio of > 10 should suggest adequate cardiac compensation. However, if the CI response is inadequate, the O₂ will be maintained by a proportionately larger increase in O₂ER and the CI/O₂ER ratio will be < 10.

In our study, as anticipated, the majority of patients with compromised cardiac function had a CI/O₂ER ratio < 10 due to a blunted cardiac response to anemia. However, the majority of patients with sepsis in this group still had a high CI/O₂ER ratio, as is typically observed in these circumstances. On the contrary, the majority of patients with normal cardiac function had a CI/O₂ER ratio > 10. In the presence of sepsis, most of these patients showed a greater cardiac response than did patients with compromised cardiac function. Of the four patients with a normal cardiac

### Table 2—Comparison of CI, O₂ER, CI/O₂ER Ratio, and PAOP in Survivors and Nonsurvivors of Group 1 and Group 2

<table>
<thead>
<tr>
<th>Variables</th>
<th>CI, L/min/m²</th>
<th>O₂ER, %</th>
<th>CI/O₂ER Ratio</th>
<th>PAOP, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survivors</td>
<td>3.09 ± 1.07</td>
<td>34.6 ± 8.8</td>
<td>9.7 ± 4.5</td>
<td>13.7 ± 4.9</td>
</tr>
<tr>
<td>Nonsurvivors</td>
<td>2.48 ± 0.55</td>
<td>38.5 ± 7.2</td>
<td>6.5 ± 1.3</td>
<td>17.3 ± 5.8</td>
</tr>
<tr>
<td>p value</td>
<td>0.02</td>
<td>0.12</td>
<td>0.001</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Group 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survivors</td>
<td>3.91 ± 0.94</td>
<td>27.5 ± 6</td>
<td>15.1 ± 6.2</td>
<td>13.9 ± 4.2</td>
</tr>
<tr>
<td>Nonsurvivors</td>
<td>3.77 ± 0.59</td>
<td>31.9 ± 12.8</td>
<td>13.2 ± 5.0</td>
<td>12.7 ± 3.5</td>
</tr>
<tr>
<td>p value</td>
<td>0.36</td>
<td>0.29</td>
<td>0.28</td>
<td>0.33</td>
</tr>
</tbody>
</table>

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function but a low CI/O₂ER ratio, three were hypovolemic and one had severe myocardial depression. Hence, a CI/O₂ER ratio < 10 indicates an impaired cardiac response to anemia but obviously does not help to identify the cause. An inadequate CI is generally due to impaired myocardial contractility and/or to inadequate preload. Interestingly, PAOP was not a reliable guide to assess the adequacy of patient fluid status. PAOP, which is routinely used as a guideline of left ventricular end-diastolic pressure, may be altered by a number of factors related to lung function, pulmonary hemodynamics, respiratory condition, and cardiac factors. Moreover, there are other factors involved in the reliability of PAOP data even if great care is taken in its measurement. Differences in clinical environment due to the differences in nurse training and in the nurse/patient ratio also may account for significant differences in the frequency of technical problems. Therefore, a normal PAOP may not rule out hypovolemia, and reference to the CI/O₂ER ratio diagram may help to identify this problem and may be of help in practicing a goal-oriented therapeutic approach in critically ill patients, especially against a background of conflicting views on the concept of routine supranormal DO₂.

This diagram was particularly useful in the 41 patients with a CI between 2.5 and 5 L/min/m². In these patients, a CI/O₂ER ratio < 10 identified patients with an inadequate cardiac response to anemia, while a CI/O₂ER ratio > 12 in patients with a history of cardiac disease was suggestive of sepsis. The use of a CI/O₂ER ratio in the 10 to 12 range may be more difficult to use. It may correspond to a normal response as well as to an inadequate cardiac response associated with sepsis in a patient with preexisting cardiac disease, inadequate preload, or myocardial depression. An algorithm to interpret the CI/O₂ER ratio is proposed in Figure 3.

In conclusion, a low CI/O₂ER ratio suggests an inadequate CI response to anemia. In patients with anemia and normal cardiac function, a CI/O₂ER ratio < 10 should suggest an inadequate CI that is due either to hypovolemia or to altered myocardial function; if there is no evidence of altered cardiac function in these patients, it is likely that they are hypovolemic. Since the CI-O₂ER relationship can be obtained easily and viewed graphically at the bedside, we propose that the assessment of the CI-O₂ER relationship could be used to determine the adequacy of CI in anemic patients.

REFERENCES
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