INFLUENCE OF ARTERIAL DISSOLVED OXYGEN LEVEL ON VENOUS OXYGEN SATURATION: DON’T FORGET THE PAO2!

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ABSTRACT—Dissolved oxygen (i.e., unbound to hemoglobin) is often neglected as a determinant of central venous oxygen saturation (ScvO2) in review articles and textbooks. These statements may lead to potential misinterpretation of ScvO2 value across FiO2 changes. In this study, we aimed to explore the influence of PaO2 and FiO2 on ScvO2 in ventilated critically ill patients. This was a prospective observational study in two surgical intensive care units. Mechanically ventilated and sedated patients with cardiac output and ScvO2 monitoring and PaO2/FiO2 > 200 with inspiratory oxygen (FiO2 ≤ 0.5) were enrolled (cohort [ScvO2]). A second cohort of brain-injured patients with jugular venous oxygen saturation monitoring was studied to assess the application of the results to regional circulation (cohort [SjvO2]). Central venous oxygen saturation was measured at baseline FiO2 and at FiO2 = 1. We finally estimated the participation of the dissolved oxygen (PdissolvO2) to the ScvO2 variations. Twenty patients formed the cohort ScvO2 and eight formed the cohort SjvO2. Central venous oxygen saturation rose from 71% (69%–76%) to 84% (78%–88%) after increasing FiO2, whereas PaO2 rose from 100 (85–124) mmHg to 387 (360–449) mmHg. The rise of ScvO2 was mostly ascribable to the dissolved oxygen. The increase of ScvO2 was not explained by changes in cardiac output or hemoglobin levels. Jugular venous oxygen saturation rose from 76% (58%–78%) to 83% (78%–89%) after increasing FiO2. Arterial dissolved oxygen level can significantly influence the ScvO2 value. Therefore, PaO2 should not be overlooked while considering the ScvO2 value as a therapeutic goal. Interpretation of ScvO2 variations in response to a therapeutic challenge (i.e., fluid challenge, inotropic drug initiation) should be performed at constant FiO2.

KEYWORDS—Oxygen saturation, oxygen pressure, hemoglobin, cardiac output, shock, resuscitation

INTRODUCTION

One major goal of critically ill patient’s management is to ensure appropriate oxygen supply to the organs to avoid organ dysfunction (1). An adequate tissue oxygenation is obtained when the tissue oxygen consumption (VO2) is covered by sufficient oxygen delivery (DO2) associated with a normal range of oxygen (O2) extraction (2). Central venous oxygen saturation (ScvO2) measurement is considered a guide for hemodynamic optimization in circulatory failure conditions (3). Cardiac output (CO), plasma hemoglobin (Hb) concentration, arterial Hb oxygen saturation, and oxygen consumption are the most important factors influencing ScvO2. In textbooks and reviews, dissolved oxygen (i.e., unbound to Hb) is often neglected as a part of DO2 and consequently as a determinant of ScvO2. This is mostly caused by the very low oxygen solubility coefficient (i.e., 0.003). However, this statement may lead to a potential misinterpretation of ScvO2 values across FiO2 changes inducing large changes in PaO2. With this study, we aimed to study the influence of PaO2 and FiO2 on ScvO2 in ventilated critically ill patients. We hypothesized that dissolved oxygen (PdissolvO2) can significantly contribute to ScvO2 values when PaO2 increases.

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MATERIALS AND METHODS

The study population

This study was approved by our local ethics committee (Comité d’Évaluation de l’Ethique des projets de Recherche Biomédicale), and written informed consent was waived because of the noninterventional design of the study. Patients were eligible for inclusion if their blood arterial pressure was invasively monitored, if they were under sedation (with midazolam and fentanyl) with a Ramsay score of 5 to 6, mechanically ventilated with a PaO2/FiO2 > 200 with FiO2 ≤ 0.5, and with hemodynamic stability (i.e., no need for fluid loading or change of vasopressor infusion rate over the last 6 h). Patients had to have a central venous line and to be monitored for CO with a transesophageal Doppler (Deltex Medical, Chichester, UK). A second cohort of brain-injured patients with jugular vein oxygen saturation (SjvO2) monitoring was also included (cohort SjvO2) to assess whether the concept holds true when applied to regional circulation (4).

Measurements

As a standard of care in our unit, once daily, all patients monitored with ScvO2 had both arterial and venous blood gas analyses at the FiO2 that ensure a SaO2 greater than 95% (baseline FiO2) and PaO2 approximately 100 mmHg and at FiO2 = 1 to assess pulmonary shunting. The blood gas analysis was performed 15 min after changing the FiO2. Blood gases for analyses performed at both FiO2 were collected when patients were resting without any external stimulation. No changes in vasopressor infusion rate, fluid bolus, or other therapeutic intervention between the two measurements were required for data analysis. The following parameters were measured in cohort A: hemodynamic parameters (CO, blood arterial pressure) and blood gas analysis using a Rapidlab 1265 Series automat (Siemens, Camberley, UK) including arterial oxygen pressure (PaO2), venous oxygen pressure (PvO2), measured Hb arterial oxygen saturation (SaO2), Hb venous oxygen saturation measured on blood gas analysis (ScvO2) and Hb concentration. A chest x-ray confirmed the adequate position at entrance of the right atrium of the tip of the central venous catheter. In cohort B (SjvO2), cerebral oxygenation monitoring was performed using a retrograde internal jugular catheter. The correct placement of the catheter tip in the jugular bulb was confirmed with x-ray.

Calculation of oxygenation parameters

Formulae used for calculated oxygenation parameters are presented in Table 1. Formula 5 in Table 1 was used for predicting ScvO2 variation (Delta ScvO2) after change in FiO2 (=0.4 vs. 1), considering oxygen consumption...
was stable between the two measurements. Impact of dissolved oxygen content \( (C_{\text{dissolvO2}}) \) on ScvO2 was evaluated by subtracting the ScvO2 at FiO2 approximately 0.4 and 1 (Table 1). All were paired measures.

**Statistical analysis**

Values are reported as median (25–75 percentiles). Paired Wilcoxon test analysis was used for intragroup comparisons for ScvO2 and SjvO2 between FiO2 at approximately 0.4 and 1. A Wilcoxon test was used for paired comparisons. Value of \( P < 0.05 \) was considered statistically significant. Statistical analysis was performed with GraphPad Prism version 4.0 for Windows (GraphPad Software, San Diego, Calif). We estimated that we needed to include 16 patients to show an increase of ScvO2 of 9% (SD, 6%) after increasing PaO2 from 100 to 500 mmHg, assuming a median Hb level of 10 g/dL and median oxygen consumption of 200 mL/min, with an alpha risk of 5% and a power of 90%.

**RESULTS**

**Characteristics of patients**

Twenty patients formed the cohort ScvO2, aged 63 (46–80) years, Simplified Acute Physiology Score (SAPS2) score 54 (42–58), 5 women and 15 men. Eleven had sepsis, five were trauma/burn patients, two had hemorrhagic shock, and two had cardiogenic shock. Twelve patients were under norepinephrine 0.5 (0.35–0.95) \( \mu \)g/kg per min, three received epinephrine 0.41 (0.35–0.47) \( \mu \)g/kg per min, and two received dobutamine 10 (10–10) \( \mu \)g/kg per min. Serum lactate level was 3.2 (1.8–4.3) mmol/L, platelets 166 (85–352) \( \times 10^3 \) /L, serum bilirubin 14 (9–25) \( \mu \)mol/L, serum creatinine 125 (72–240) \( \mu \)mol/L. Eight patients formed the cohort SjvO2, aged 32 (20–54) years, SAPS2 score 46 (34–57), five had a traumatic brain injury, two had stroke, and one had subarachnoid hemorrhage.

**Oxygenation parameters**

We observed that increasing FiO2 from 0.4 (0.3–0.5) to 1 (1–1) leads to an increase of PaO2 from 100 (85–124) mmHg to 387 (360–449) mmHg and a significant increase of ScvO2 from 71% (69–76%) to 84% (78–88%) (Fig. 1). We found similar results with SjvO2 when increasing FiO2 in patients with brain injury (Fig. 1). The rise of ScvO2 was not explained by changes in CO or Hb levels (5 [3.9–6.1] L/min vs. 5 [3.9–6.2] L/min and 11.1 (9.8–12.8) vs. 10.9 (9.8–12.7) g/dL, respectively, ns). Hemoglobin arterial oxygen saturation slightly increased from 97% (96%–98%) to 99% (98%–100%) \( (P < 0.001) \). Dissolved oxygen arterial content \( (C_{\text{dissolvO2}}) \) rose significantly after increasing the FiO2 from 0.30 (0.26–0.37) to 1.16 (1.08–1.35) mL and from 0.32 (0.23–0.45) to 1.47 (1.20–1.72) mL in the ScvO2 group and the SjvO2 group, respectively (Table 2; Fig. 2). However, estimated participation of the dissolved oxygen component (based on formula 6 in Table 1) revealed that it largely accounted for the rise of ScvO2 (8.0% [5.9%–11.9%]) (Tables 1 and 2). Arterial carbon dioxide partial pressure (PaCO2), venous carbon dioxide partial pressure (PvCO2), arterial pH, and venous pH were not different between FiO2 approximately 0.4 and 1. Fourteen patients had a third time point available, performed at FiO2 0.5 or 0.6, allowing to plot ScvO2 values against PvO2 values and showing a sigmoidal relationship (Fig. 3).

**DISCUSSION**

Our study shows that dissolved oxygen can significantly influence the ScvO2 value. Similar results were observed using
SjvO₂ in brain-injured patients, suggesting that it can also be applied at a regional circulation level. Our study highlights a well-known basic physiological principle, which has been overlooked in most reviews and textbooks that may lead to misinterpretation of ScvO₂. These misinterpretations of the determinant of ScvO₂ might arise from the oversimplification of the determinants of ScvO₂ with PaO₂ omission (leaving CO, SaO₂, and Hb level as sole determinants). We therefore believe that the results of our study can reach an important educational target in providing evidence for careful reading of the determinant of ScvO₂: PaO₂ should not be neglected when interpreting the ScvO₂ value.

The ScvO₂ has been widely included in goal-directed therapy algorithms both in critically ill patients and patients undergoing major surgery. These algorithms propose to optimize systemic hemodynamics to reach ScvO₂ greater than 70% and improve oxygen delivery (5). Because most textbooks and reviews proposed to neglect dissolved oxygen as part of O₂ content, PaO₂ is not included in most formulae showing the main determinants of ScvO₂ [i.e., ScvO₂ = SaO₂ − [VO₂ / (CO × Hb × 1.34)]] (2,6). Likewise, most observational studies did not mention the PaO₂ level in their results. For example, an observational study from Hernandez et al. showed a ScvO₂ increase from 61.8% ± 12.6% to 68.9% ± 12.2% when in critically ill patients were intubated and mechanically ventilated (7). The authors did not find any correlation between increase of ScvO₂ and changes in SaO₂, although blood gas were obtained 15 min after mechanical ventilation with FiO₂ = 1, a situation where high PaO₂ values might have accounted for the rise of ScvO₂. Because PaO₂ was not reported, it became difficult to conclude on this point. This is true for many studies testing and measuring ScvO₂ as an algorithm target (1, 8–10).

The range of ScvO₂ changes associated with the increase in FiO₂ (~9%–10%) can be seen modest when compared with those associated with CO or SaO₂ level. Indeed, because of the sigmoid shape of the oxygen-Hb dissociation curve, modest changes in PvO₂ can induce significant changes in ScvO₂. However, this range of ScvO₂ variation appears relevant in the light of current recommendation for resuscitation of patients with severe sepsis (i.e., to reach ScvO₂ >70%) (5). Furthermore, it is reasonable to expect a more pronounced effect of dissolved O₂ content when CO and Hb level are low (11).

The aim of the study was not to evaluate the potential benefit of increasing PaO₂ for improving tissue oxygenation but to appreciate the influence of variations in PaO₂ on ScvO₂ to raise awareness of intensivists while using the ScvO₂ as a hemodynamic target. However, different studies have used high inspiratory fraction of O₂ and dissolved O₂ as factors to improve

### Table 2. Oxygenation parameters between FiO₂ 40% and FiO₂ 100% in the cohort ScvO₂

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>FiO₂ 40% (30% – 50%)</th>
<th>FiO₂ 100%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO, L/min</td>
<td>5 (3.9–6.1)</td>
<td>5 (3.9–6.2)</td>
<td>0.76</td>
</tr>
<tr>
<td>Hb, g/dL</td>
<td>11.1 (9.8–12.8)</td>
<td>10.9 (9.8–12.7)</td>
<td>0.91</td>
</tr>
<tr>
<td>SaO₂, %</td>
<td>0.97 (0.96–0.98)</td>
<td>0.99 (0.98–1.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PaO₂, mmHg</td>
<td>100 (85–124)</td>
<td>387 (360–449)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DO₂, mL O₂/min</td>
<td>712 (557–890)</td>
<td>761 (589–976)</td>
<td>0.44</td>
</tr>
<tr>
<td>CaO₂, mL O₂/mL</td>
<td>14.8 (13.0–14.8)</td>
<td>15.7 (14.3–18.2)</td>
<td>0.12</td>
</tr>
<tr>
<td>CaO₂assO₂O₂, mL O₂/mL</td>
<td>0.30 (0.26–0.37)</td>
<td>1.16 (1.08–1.35)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CvO₂, %</td>
<td>39 (36–44)</td>
<td>50 (45–57)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ScvO₂, %</td>
<td>11.0 (9.1–12.5)</td>
<td>12.0 (11.0–14.4)</td>
<td>0.05</td>
</tr>
<tr>
<td>PaO₂, mmHg</td>
<td>71 (69–76)</td>
<td>84 (78–88)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Delta ScvO₂, %</td>
<td>—</td>
<td>9.3 (8.3–14.5)</td>
<td>—</td>
</tr>
<tr>
<td>Delta ScvO₂assO₂O₂, %</td>
<td>—</td>
<td>8.0 (5.9–11.9)</td>
<td>—</td>
</tr>
</tbody>
</table>

PaO₂, arterial PO₂; DO₂, oxygen delivery; VO₂, oxygen consumption; CaO₂, arterial oxygen content; CaO₂assO₂O₂, arterial dissolved oxygen content; PvO₂, venous PO₂; CvO₂, venous oxygen content; ScvO₂, central venous oxygen saturation; Delta ScvO₂, variation of ScvO₂; Delta ScvO₂assO₂O₂, estimated variation of dissolved oxygen to the ScvO₂.

![Fig. 2. Evolution of the dissolved fraction of oxygen after increasing FiO₂ from 0.4 to 1 in the ScvO₂ cohort (A) and the SjvO₂ cohort (B). Data presented in box and whisper plots (min-max).](http://journals.lww.com/shockjournal)
tissue oxygen tension, illustrating that the amount of dissolved O2 content may participate in tissue oxygenation. Yu et al. (12) observed a significant increase of tissue PO2 (PtO2) in critically ill patients after an oxygen challenge test (i.e., increase FiO2 to 100%), illustrating the better oxygen delivery to tissue after increasing FiO2. Likewise, Dyson et al. (13) observed a significant rise of PtO2 in animal breathing at FiO2 = 1 compared with room air. Although this study was not designed to assess the role of high FiO2 to increase DO2, this question merits to be prospectively addressed.

Our study has several limitations. The cohort size is small. The sizing was, however, fitting well with the sample size calculation, and the results are sustained by a strong physiological basis. It is unlikely that increasing the sample size would modify the results. Second, VO2 was not measured. However, our patients were considered stable, nonstimulated, and under sedation, making a significant change in VO2 between measurements unlikely.

Our study has direct clinical implications. In addition to CO and Hb levels as key determinant of ScvO2 or organ SvO2, our study shows that PaO2, when varying significantly, is also to be taken into account when interpreting changes in ScvO2. It can therefore be recommended to assess the impact of each therapeutic intervention (e.g. fluid loading, inotropes or vaso-pressors infusion, blood transfusion) at a constant FiO2 and avoid significant variations in PaO2.

In conclusion, our study shows that increasing dissolved oxygen content can notably influence ScvO2 and SjvO2 values in intensive care unit patients.

REFERENCES