Changes in arterial-mixed venous oxygen content difference 
\( (C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}}) \) and the effect on shunt calculations in critically ill patients

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Summary

Many commonly used indices of pulmonary oxygen transfer assume that \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) is constant. We studied changes in \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) in critically ill patients to determine the effect on calculated shunt of assuming a fixed \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \). Two hundred pairs of arterial and mixed venous blood gas measurements were obtained retrospectively from 43 patients, each providing four or five pairs from a period of 48 h. \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) ranged from 13 to 74 ml l\(^{-1}\). The mean within-patients \( \text{SD} \) was 6.8 ml l\(^{-1}\) and the overall between-patient \( \text{SD} \) was 10.9 ml l\(^{-1}\). Our results show that assuming a fixed \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) leads to errors in quantifying pulmonary oxygen transfer. (Br. J. Anaesth. 1998; 80: 829–831)

Keywords: intensive care; oxygen transfer pulmonary; oxygenation indices

Shunt fraction \((Q/Q_s)\) is the most accurate index commonly available to quantify impairment of pulmonary oxygen transfer. The value of \( Q/Q_s \) is calculated using the equation:

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Q/Q_s = \frac{(C_{c,\text{O}_2} - C_{a,\text{O}_2})}{(C_{c,\text{O}_2} - C_{\text{v,\text{O}_2}})}
\]

where \( C_{c,\text{O}_2} \), \( C_{a,\text{O}_2} \) and \( C_{\text{v,\text{O}_2}} \) are the oxygen content of end-capillary, arterial and mixed venous blood respectively. When mixed venous blood is not sampled, methods using a fixed \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) are considered possible surrogates. “Virtual shunt” and “iso-shunt charts” are two such methods where \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) is given a fixed value of 50 ml l\(^{-1}\). If \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) should vary, this can cause changes in “virtual shunt” that, if large, could become clinically misleading. This is particularly relevant in patients in whom serial measurements of shunt are used to determine changes in oxygen content.

Mean \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) is approximately 35 ml l\(^{-1}\) in critically ill patients, but changes in \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) are more important than absolute values when assuming \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) to quantify oxygenation defects. These changes have not been studied previously and the present study was undertaken to determine variations in \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) and to evaluate the effect of such changes on shunt calculations.

Methods and results

We collected 200 pairs of arterial and mixed venous blood gas measurements retrospectively from 43 patients who were treated in an ICU over a period of 10 months. All patients with four or more shunt measurements during any 48 h of their stay were included in the study and four or five readings were obtained from each patient. \( P_{\text{a,\text{O}_2}} \) had been set according to clinical need (range 0.35–1.0). The position of the pulmonary artery catheter was confirmed radiologically in all patients. The ICU where the study was carried out takes part in a National Quality Assurance Programme, requiring regular automated calibration of the blood gas machine and co-oximeter (BGE and IL-282-Instrumentation Laboratory, Italy). Externally referenced samples are analysed regularly to confirm the accuracy of the system as part of this programme. The measuring range for \( P_{\text{a,\text{O}_2}} \) was 0–106 kPa with a resolution of 0.1 kPa (coefficient of variation not greater than 1.3%). The system measures oxygen tension, oxygen saturation and haemoglobin concentration and calculates oxygen content and shunt fraction, as outlined in the operator’s manual.

We found that \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) ranged from 13 ml l\(^{-1}\) to 74 ml l\(^{-1}\) (mean 35.6 ml l\(^{-1}\)). The mean within-patient \( \text{SD} \) was 6.8 ml l\(^{-1}\) and the overall between-patient \( \text{SD} \) 10.9 ml l\(^{-1}\).

The effect of assuming a fixed \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \) for shunt calculations in the presence of the above variability was then studied using an iso-shunt chart described by Benatar and colleagues. There were 188 readings (from 40 patients) within the specified range for iso-shunt charts for comparison. Each measured shunt fraction was compared with the corresponding shunt values interpolated from the charts, using the method of Bland and Altman and two-way analysis of variance for repeated measurements.

The correlation coefficient between measured shunt and estimated shunt was 0.62. The chart underestimated shunt fraction with a mean bias of 6.5% (confidence interval 1.1%) with wide limits of agreement (2 SD 16%) (fig. 1). The difference was statistically significant (\( P < 0.001 \) for F ratio).

In 23 patients there was no change in estimated shunt with changes in measured \( Q/Q_s \) <10% and in 11 the changes in estimated and measured values were in the opposite direction at least once. In one patient, a change in \( Q/Q_s \) >10% was not detected by the chart as it was masked by concurrent changes in \( C_{a,\text{O}_2} - C_{\text{v,\text{O}_2}} \).
Comment

We corroborate the findings of Harrison and colleagues that the mean $\text{CaO}_2-\text{CVO}_2$ in critically ill patients is approximately 35 ml l$^{-1}$. The assumption of a constant $\text{CaO}_2-\text{CVO}_2$ is common to many estimates of oxygen transfer, but changes in $\text{CaO}_2-\text{CVO}_2$ are frequent and can occur within relatively short periods. Lawler and colleagues found a 20% change in $\text{CaO}_2-\text{CVO}_2$ within approximately 2 h, in a patient who seemed clinically stable. Changes in clinical condition and in therapy such as ventilation, fluid administration and vasoactive drugs may change oxygen delivery, consumption or both and thereby could alter $\text{CaO}_2-\text{CVO}_2$. We have quantified this variability and have shown that assuming a fixed $\text{CaO}_2-\text{CVO}_2$ will hamper interpretation of changes in oxygen transfer. Using sampled values of $\text{PAO}_2$, $\text{PVO}_2$ arterial blood and mixed venous blood our model shows how a measured change in $\text{CaO}_2-\text{CVO}_2$ of more than 27 ml l$^{-1}$ could mask an actual change in shunt of more than 10%. Assuming a $\text{CaO}_2-\text{CVO}_2$ of 35 ml l$^{-1}$ will minimize the bias between measured and estimated shunt (bias 0.23, $P > 0.05$ for F ratio). Similar observations were made by Cane and colleagues but the limits of agreement are unchanged, so the accuracy of such estimates remain poor. The modification of iso-shunt charts proposed by Petros and colleagues was not used, as all patients received an $\text{FiO}_2 > 0.35$. Shunt calculations are inaccurate at high $\text{FiO}_2$ because of errors in measuring high $\text{PaO}_2$; however, the $\text{PaO}_2$ range in our patients (7.9 kPa–76 kPa) was well within the measuring range of the blood gas machine. Potential errors in measurement should therefore have minimal influence on our findings.

Interest in use of the $\text{PaO}_2/\text{FiO}_2$ ratio to assess defects of oxygen transfer was renewed by the work of Gowda and colleagues. They showed that $\text{PaO}_2/\text{FiO}_2$ ratio, unlike measured shunt, was relatively independent of changes in $\text{FiO}_2$ in patients with adult respiratory distress syndrome (ARDS), in the presence of ventilation/perfusion abnormalities and severe hypoxaemia (shunt fraction > 30% and $\text{PaO}_2 < 13.3$ kPa). However they assumed that $\text{CaO}_2-\text{CVO}_2$ was constant or altered minimally. Patients with severe ARDS often have multiple organ failure requiring treatment that could alter $\text{CaO}_2-\text{CVO}_2$. In a hypothetical patient with a 35% shunt receiving an $\text{FiO}_2$ of 0.7 and a mean $\text{CaO}_2-\text{CVO}_2$ of 35.6 ml l$^{-1}$, a variation of 13.6 ml l$^{-1}$ (2 sd of the within-patient variation) would alter the $\text{PaO}_2/\text{FiO}_2$ ratio between 91 and 195. Such a variation could be misleading in the management of such patients. The correlation between measured shunt fraction and $\text{PaO}_2/\text{FiO}_2$ ratio in our patients on $\text{FiO}_2 > 0.5$ (n = 32) was similar to the correlation between measured shunt and that estimated by the iso-shunt chart ($r = -0.56$).

The indices referred to above are used to quantify oxygen transfer. They do not necessarily reflect the severity of the underlying lung injury or the patient’s illness, and by and large do not predict clinical outcome satisfactorily. The dynamic changes induced by altering oxygen administration are an integral part of the processes that influence oxygenation. Therefore in spite of being altered by $\text{FiO}_2$, measured shunt fraction remains the best measure of oxygen transfer taking into consideration factors such as the underlying lung injury, effect of $\text{FiO}_2$ changes and the mode of respiratory support.

We conclude that the changes in $\text{CaO}_2-\text{CVO}_2$ seen in critically ill patients preclude the assumption of a fixed $\text{CaO}_2-\text{CVO}_2$ value in quantifying oxygen transfer. There is no substitute for measured shunt fraction, and it is important to re-evaluate published work where indices of oxygen transfer that assume a fixed $\text{CaO}_2-\text{CVO}_2$ have been used to evaluate outcome.

Acknowledgement

We thank Dr M Columb, FRCA, for critical advice.
References