Estimating venous admixture using a physiological simulator

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Venous admixture (expressed as a fraction of cardiac output) is the pulmonary shunt fraction, in addition to ideal ventilation:perfusion matching, required to account for an observed degree of hypoxaemia. Knowledge of venous admixture allows objective assessment of the efficacy of interventions, objective monitoring of the patient’s progress and calculation of the inspired oxygen requirements for optimal arterial oxygenation.¹ It may be derived directly by calculations using data obtained with a pulmonary artery catheter, although such invasive monitoring is not easily justified for measurement of venous admixture alone. Alternatively, an iso-shunt-type calculation may be performed using assumed values for haemoglobin concentration (Hb), arterial carbon dioxide partial pressure (Paco₂), temperature, plasma pH and arteriovenous oxygen content difference (CaO₂ – CvO₂). This calculation forms the basis of the iso-shunt diagram described by Benatar, Hewlett and Nunn.² Hope and colleagues described an alternative to this, where the traditional shunt equation is used with estimates for the required data based on non-invasive measures such as end-tidal carbon dioxide concentration and pulse oximetry.³ We have compared the accuracy of a new method of venous admixture estimation using the Nottingham physiology simulator and data commonly available in the intensive therapy unit (ITU) with an iso-shunt-style calculation using assumed values for the physiological variables.

Patients and methods

The Nottingham physiology simulator (NPS) is a comprehensive, validated computer simulation of original, multi-compartmental physiological models. It has been described in detail elsewhere.⁴

Patients were not selected or excluded from the study on the basis of pathology. Reasons for admission included septic shock, cardiogenic failure, head injury and drug overdose. Formal discussion with the Local Ethics Committee concluded that acquisition of informed consent was neither required nor desirable, as it could cause further distress to relatives and because the study was entirely observational rather than interventional. Venous admixture was measured indirectly 35 times in 19 patients who had pulmonary artery catheters in situ. The formula used for calculation of venous admixture is given in the appendix. Subsequently, each venous admixture was recalculated with an iso-shunt-type calculation. This calculation uses the same formula, using measured values for the patient’s inspired oxygen fraction (FI O₂) and the patient’s arterial oxygen tension (PA O₂), but assumes the following values⁴:
Estimating shunt using a physiology simulator

- **PaCO$_2$**: 4.3 kPa (corresponding to the middle of the described range 3.3–5.3 kPa)
- **Extracellular base excess (BE$_{ecf}$)**: 0 mmol litre$^{-1}$
- **Haemoglobin concentration**: 120 g litre$^{-1}$
- **Core temperature**: 37°C
- **Arteriovenous oxygen content difference (CaO$_2$–CV$_O2$)**: 50 ml litre$^{-1}$

Venous admixture was next calculated with the NPS using the following data:
- **PaCO$_2$**: (measured using a regularly calibrated 278 Blood-Gas System, Ciba-Corning)
- **BE$_{ecf}$**: (calculated manually from measured PaCO$_2$ and pH (described in the appendix))
- **Haemoglobin concentration**: (measured daily)
- **Core temperature**: measured via the pulmonary artery catheter
- **Arteriovenous oxygen content difference (CaO$_2$–CV$_O2$)** was assumed to be 50 ml litre$^{-1}$.

Venous admixture values were also calculated using a value of 40 ml litre$^{-1}$ for CaO$_2$–CV$_O2$ as this was a more appropriate value for the patients under consideration.

**Statistical methods**

The accuracies of the iso-shunt-style calculation and the NPS calculation were compared by calculating the 95% limits of agreement (LA$_{95\%}$) between each method and the indirectly measured value. Bias in estimating virtual shunt fraction was calculated as the mean of the estimated minus the measured venous admixture. LA$_{95\%}$ values were calculated as 95% confidence intervals of the bias$^6$; 95% confidence intervals (CI$_{95\%}$) were calculated as mean$\pm$1.96×sd. Bland–Altman plots were constructed relating the errors in estimating venous admixture to the mean of the measured and estimated values.$^6$ Correlation coefficients were calculated from these plots$^7$ to investigate the possibility of errors being related in size to the magnitude of either the measured or estimated venous admixture. The correlation coefficient between the magnitude of the venous admixture and CaO$_2$–CV$_O2$ was calculated. All data recording, charting and data analyses were performed using Microsoft Excel (version: Office 97).

**Results**

When CaO$_2$–CV$_O2$ was assumed to be 50 ml litre$^{-1}$, the iso-shunt calculated LA$_{95\%}$ values were $-6.4\pm10.6\%$, while values calculated using the NPS were $-3.9\pm8.5\%$. CI$_{95\%}$ for CaO$_2$–CV$_O2$ in this patient group were $41.1\pm9.6$ ml litre$^{-1}$. When CaO$_2$–CV$_O2$ was assumed to be 40 ml litre$^{-1}$, the LA$_{95\%}$ of the iso-shunt calculated values were $-2.1\pm10.1\%$, while those for NPS were $0.5\pm8.2\%$. Figures 1 and 2 show Bland–Altman plots of the NPS and iso-shunt calculated data assuming a CaO$_2$–CV$_O2$ value of 40 ml litre$^{-1}$. Correlation coefficients between the error in estimating venous admixture and the mean of the estimated and measured values were not significant at the 5% level in either group calculated by the NPS (where CaO$_2$–CV$_O2$=40 ml litre$^{-1}$, r$=-0.17$; where CaO$_2$–CV$_O2$=50 ml litre$^{-1}$, r$=-0.3$). There was a statistically significant correlation between the error in estimating venous admixture and the mean of the measured value and that predicted using the iso-shunt calculation (where CaO$_2$–CV$_O2$=40 ml litre$^{-1}$, r$=-0.43$, P<0.01; where CaO$_2$–CV$_O2$=50 ml litre$^{-1}$, r$=-0.53$, P<0.01). There was a statistically significant correlation between measured venous admixture and CaO$_2$–CV$_O2$ (r$=-0.54$, P<0.01, venous admixture=$-0.006\times$CaO$_2$–CV$_O2$+0.53). Data describing the values assumed for the iso-shunt calculation and those seen in this patient sample are described in Table 1.
Discussion

Knowledge of venous admixture is clinically useful. The NPS is capable of estimating venous admixture. The accuracy (bias) and reliability (LA95%) of estimation of venous admixture is only marginally improved by including data that are otherwise assumed in an iso-shunt-type calculation. This technique will probably improve the existing technique, although adding to its complexity. Hope and colleagues’ method\(^3\) allows estimation of venous admixture from entirely non-invasive means with reasonable accuracy (LA95% 0±16% venous admixture) although a correction factor derived from within their study group was used to remove bias by eliminating the trend of increasing inaccuracy with increasing values for venous admixture. Comparison of the accuracy of the NPS method with that of Benatar, Hewlett and Nunn is not useful as they made no direct measurement of venous admixture in their patients, and all measurements were performed in only four patients.\(^2\)

Bland–Altman plots were used to describe the distribution of errors in predicting venous admixture by each method. These plots display trends in errors related to the magnitude of either measured or estimated venous admixture. Previous workers have used variants on this plot, such as using only the measured value on the horizontal axis.\(^3\) This indicates trends in errors related purely to the ‘true’ size of venous admixture, but ignores errors related to the size of the estimated venous admixture. Regression analysis within these plots allows statistical isolation of a linear relationship between the error size and the size of venous admixture (measured or estimated). Such a relationship was found to exist when the iso-shunt-type calculation was performed, assuming fixed values of Hb, \(P_a\text{CO}_2\), temperature, plasma pH and \(C_a\text{O}_2–C_v\text{O}_2\). This is probably caused by the increasing importance of these incorrect assumptions when venous admixture is greater. For example, a patient whose haemoglobin concentration is 50 g litre\(^{-1}\) will deviate further from the venous admixture calculated in the iso-shunt manner during large venous admixture because the venous desaturation caused by anaemia has greater impact during larger venous admixture.

Accuracy and reliability (i.e. bias and limits of agreement) were improved for both methods by using a value of 40 ml litre\(^{-1}\) for \(C_a\text{O}_2–C_v\text{O}_2\) (this value more closely matched the actual \(C_a\text{O}_2–C_v\text{O}_2\) value of 41.1 ml litre\(^{-1}\) in this patient sample). Use of 40 ml litre\(^{-1}\) as the assumed \(C_a\text{O}_2–C_v\text{O}_2\) during calculation of venous admixture is within the range of values found by previous workers in the critically ill. Hope and colleagues suggested that \(C_a\text{O}_2–C_v\text{O}_2\) depends on the magnitude of venous admixture.\(^3\) This is supported by the data presented here, where there was a statistically significant correlation between measured venous admixture and \(C_a\text{O}_2–C_v\text{O}_2\) \((r=-0.54, P<0.01)\). This may explain the discrepancy between the findings of Benatar, Hewlett and Nunn of a \(C_a\text{O}_2–C_v\text{O}_2\) value of 50 ml litre\(^{-1}\) in healthy adults and the findings of recent workers of lower values in critically ill patients who have greater venous admixture.\(^2\,8–10\) For most purposes, 40 ml litre\(^{-1}\) is a reasonable assumed value for \(C_a\text{O}_2–C_v\text{O}_2\) in calculating venous admixture.

In summary, this method of estimating venous admixture uses data commonly available for ITU patients and provides a slight improvement in accuracy and reliability over previously described methods. The NPS may prove to be a useful tool in the management of critically ill patients.

Appendix

Venous admixture (\(\dot{Q}_s:\dot{Q}_t\)) was calculated as follows\(^{10–12}\):

\[
\dot{Q}_s:\dot{Q}_t = \frac{(C_a\text{O}_2–C_v\text{O}_2)}{(C_a\text{O}_2–C_v\text{O}_2)}
\]

where \(C_a\text{O}_2\) = blood oxygen content at the end of the pulmonary capillary; \(C_a\text{O}_2\) = arterial oxygen content; and \(C_v\text{O}_2\) = mixed venous (pulmonary arterial) oxygen content. \(C_a\text{O}_2\), \(C_a\text{O}_2\) and \(C_v\text{O}_2\) were calculated as follows from the following example:

\[
C_a\text{O}_2\text{O}_2 \text{ ml litre}^{-1} = h \times \text{Hb} \times S_C\text{O}_2 + 0.225 \times P_{c\text{O}_2}/k
\]

where \(h\) = oxygen carrying capacity of haemoglobin. A value of 1.36 ml g\(^{-1}\) was used for \(h\), lying below the theoretical, maximal value of 1.39 ml g\(^{-1}\) (Hüfner’s constant), taking account of haemoglobin impurities such as methaemoglobin.\(^3\) \(C_a\text{O}_2\) = haemoglobin concentration (g litre\(^{-1}\)); \(S_C\text{O}_2\) = end-pulmonary capillary oxyhaemoglobin saturation; \(P_{c\text{O}_2}\) = end-pulmonary capillary oxygen tension; \(k\) = temperature correction for oxygen solubility,\(^{13}\) \(k = 1 + \log(\text{temperature}/37)+0.00012 \times (\text{temperature}–37)^2\).

\(P_{c\text{O}_2}\) is assumed to equal alveolar oxygen tension (\(P_{A\text{O}_2}\)), which was calculated as follows:

\[
P_{A\text{O}_2} = F_{I\text{O}_2} \times (P_h–SVP_{H_2O}) + (P_{a\text{CO}_2} / R) + (P_{a\text{CO}_2} \times F_{I\text{O}_2} 	imes (1–R)/R)
\]

where \(P_h\) = barometric pressure (assumed to be 101.3 kPa); \(SVP_{H_2O}\) = saturated vapour pressure of water, adjusted for core temperature; and \(R\) = respiratory exchange ratio, assumed to be 0.8.

Extracellular base excess was calculated as follows\(^{14}\):

\[
\text{BE}_{ext} = [\text{HCO}_3^-]–11.6 \times \log(7.4–\text{pH})–24
\]

where \([\text{HCO}_3^-]\) = bicarbonate concentration calculated using the Henderson–Hasselbalch equation from \(P_{c\text{O}_2}\) at 37°C.

References

12 Riley RL, Lilienthal JL, Proemmell DD, Franke RE. On the determination of the physiologically effective pressures of oxygen and carbon dioxide in alveolar air. Am J Physiol 1946; 147: 191