RESEARCH PAPER

Comparison of different methods to calculate venous admixture in anaesthetized horses

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Abstract

Objective The aim of this study was to compare different methods to determine venous admixture ($\dot{Q}_s/\dot{Q}_t$) in anaesthetized horses. The first objective was to estimate $\dot{Q}_s/\dot{Q}_t$ using jugular venous blood oxygen content ($\dot{Q}_s/\dot{Q}_{t\ jugular}$), and a fixed value for the oxygen extraction (F-shunt). The second objective was to assess the influence of blood pressure and positioning on oxygen extraction. The third objective was to perform regression analysis between jugular and mixed venous blood oxygen tensions.

Study design Prospective, experimental trial.

Animals The study was performed with seven warmblood horses that were anaesthetized with detomidine, butorphanol, ketamine, diazepam and isoflurane in oxygen.

Methods Multiple simultaneous arterial, jugular venous and pulmonary arterial blood samples were taken under normotensive and hypotensive conditions in lateral and dorsal recumbency. Arterial, mixed venous, and end-capillary oxygen content were calculated.

Results A significant correlation between $\dot{Q}_s/\dot{Q}_t$ and $\dot{Q}_s/\dot{Q}_{t\ jugular}$ was found [intraclass correlation coefficient (ICC) = 0.68, $p < 0.001$], and Bland–Altman analysis showed a bias of −11.5% and wide limits of agreement (−27.7% to 4.6%). F-shunt significantly correlated with $\dot{Q}_s/\dot{Q}_t$ (ICC = 0.88, $p < 0.001$), and Bland–Altman analysis showed a lower bias (−1.97) and narrower limits of agreement (−13.8% to 9.9%). Positioning and blood pressure significantly influenced oxygen extraction. The regression formula was $Y = 0.80X + 2.61$ (where Y is the calculated mixed venous oxygen tension and X is the jugular venous oxygen tension) when outliers were excluded (ICC=0.82, $p < 0.001$).

Conclusions and clinical relevance This study shows that F-shunt provides reasonable estimates of $\dot{Q}_s/\dot{Q}_t$ but can possibly be improved by using simple algorithms without the need for pulmonary arterial catheterization. These algorithms use blood pressure- and positioning-dependent oxygen extraction and regression analysis between jugular venous and pulmonary arterial oxygen tension. Although promising, the validity of these algorithms needs to be determined in future studies.

Keywords anaesthesia, equine, oxygen content, $\dot{Q}_s/\dot{Q}_t$, venous admixture.

Introduction

Anaesthetized horses are at risk of developing hypoxaemia as a result of ventilation − perfusion ($\dot{V}/\dot{Q}$) mismatch, leading to venous admixture (Nyman et al. 1990). Furthermore, oxygen delivery to the peripheral tissues may be compromised as a result of decreases in cardiac output and arterial blood pressure during general anaesthesia (Steffey 2002; De Vries et al. 2009). The combination of hypoxaemia and decreases in cardiac output likely increases equine anaesthesia-related risk significantly (Hubbell and Muir 2015).

The gold standard for determining venous admixture ($\dot{Q}_s/\dot{Q}_t$) is calculation using the Berggren 'shunt equation':

$$\dot{Q}_s/\dot{Q}_t = \frac{\text{end capillary oxygen content } (Cc'O2) - \text{arterial oxygen content } (CaO2)}{Cc'O2 - \text{mxedvenous oxygen content } (CmvO2)}$$

(Berggren 1942). This 'shunt equation' requires pulmonary arterial (mixed venous) as well as peripheral arterial blood sampling, whereas pulmonary end-capillary blood oxygen content is calculated from inspiratory oxygen fraction (FIO_2) and arterial carbon dioxide tension ($PaCO_2$) using the alveolar gas equation. In experimental studies, this approach is feasible and is used to obtain the most accurate calculation of venous admixture in anaesthetized horses (Mosing et al. 2016). However, pulmonary artery catheterization is a more invasive procedure that requires more sophisticated equipment. In critically ill human patients, central venous blood samples have been used as a surrogate for mixed venous blood samples (Rivers et al. 2001). However, in human patients (Martin et al. 1992) and in canine experimental studies (Martin et al. 1985), central venous oxygen saturation may be similar to mixed venous oxygen saturation, but the correlation is not consistently high enough to allow simple substitution for mixed venous oxygen values.

An alternative method to determine venous admixture is to assume a fixed arterial to mixed venous oxygen content difference [$C(a-v)O_2$] of 3.5 mL dL^{-1}, thus negating the need for a pulmonary artery catheter. This estimate has become known as 'F-shunt' and has shown reasonable to good agreement with venous admixture calculations based on mixed venous blood samples in humans (Wandrup 1995), anaesthetized sheep (Araos et al. 2012) and horses (Briganti et al. 2015). However, the assumption of a fixed oxygen extraction ignores the possibility of changes in oxygen extraction as a result of changes in tissue perfusion and the state of cellular metabolism. If oxygen delivery decreases, oxygen extraction may increase in order to maintain aerobic conditions in the peripheral tissues (McLellan & Walsh 2004). In human patients with septic shock, oxygen extraction may be very low because of the inability of the tissues to extract and/or utilize oxygen. Therefore, during tissue hypoperfusion and/or in critically ill patients, assuming a fixed arterial to mixed venous oxygen content difference to calculate venous admixture may produce inaccurate results (Park et al. 2015).

The aim of this study was to improve the estimation of $\dot{Q}_s/\dot{Q}_t$ in anaesthetized horses, without the need for mixed venous blood sampling. The first objective was to compare the correlation between venous admixture ($\dot{Q}_s/\dot{Q}_t$) with venous admixture estimated from jugular venous blood oxygen content values ($\dot{Q}_s/\dot{Q}_{t\,jugular}$), and with venous admixture estimated from a fixed value for the arterio-venous oxygen content difference (F-shunt). The second objective was to calculate arterio-venous oxygen content differences during states of arterial normo- and hypotension and during lateral and dorsal recumbency. The third objective was to calculate regression formulas describing the relationship between jugular venous oxygen tension ($PjvO_2$) and pulmonary arterial mixed venous oxygen tension ($P\bar{v}O_2$). These new algorithms should then be tested in a new data set to determine their accuracy to estimate $\dot{Q}_s/\dot{Q}_t$.

Materials and methods

Study design

The study was designed as a prospective experimental trial and was performed with seven healthy (American Society of Anesthesiologists status I) warmblood horses (Table 1) anaesthetized for an unrelated nonrecovery procedure. The study was approved by the institutional ethics committee on animal experimentation, in accordance with Dutch national legislation on experimental animal use (2013. III.01.012).

Anaesthesia

Horses were premedicated with detomidine intravenous (IV) 0.01 mg kg^{-1} (Domosedan; Orion Pharma, Finland) and butorphanol IV 0.02 mg/kg (Dolorex; MSD Animal Health, The Netherlands). The jugular vein was catheterized with an IV catheter (Intraflon; Vygon, France; 12 gauge, 80 mm). General anaesthesia was induced with ketamine 2.2 mg kg^{-1} IV (Narketan; Vetoquinol, The Netherlands) and diazepam 0.05 mg kg^{-1} IV (Diazepam; Centrafarm, The Netherlands), and the trachea was intubated with a cuffed endotracheal tube (internal diameter 26 mm). Horses were connected to a large animal circle (BDO Medipass, The Netherlands) and mechanically ventilated (Smith; BDO Medipass). Anaesthesia was maintained with an end-tidal isoflurane ($F_E'Iso$) concentration of 1.2−1.4% (Isoflo; AST Farma, The Netherlands) in oxygen supplemented with a detomidine constant rate infusion (CRI; 0.01 mg kg^{-1} $hour^{-1}$). During anaesthesia, normotension was maintained by a crystalloid infusion (Ringer; Fresenius, Germany; 5−10 mL kg^{-1} $hour^{-1}$) and a dobutamine CRI (Dobutamine; Hameln Pharma, Germany; 1−5 μg kg^{-1} $minute^{-1}$ to effect) to maintain mean arterial pressure (MAP) above 70 mmHg.

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Table 1 Demographics and details of blood sampling in horses anaesthetized with detomidine, butorphanol, ketamine, midazolam and isoflurane in oxygen in lateral and dorsal recumbency during normotensive (mean arterial pressure >70 mmHg) and hypotensive (mean arterial pressure <70 mmHg) anaesthesia. Data are reported as number (*n*) or as mean ± standard deviation

Variable	
Warmblood horses (*n*)	7
Mares (*n*)	5
Geldings (*n*)	1
Stallions (*n*)	1
Age (years)	10.7 ± 4.8
Weight (kg)	547.1 ± 83.7
Blood samples (*n*)	56
Duration of anaesthesia (minutes)	189 ± 41
Haemoglobin concentration at beginning of procedure (g dL^{-1})	11.0 ± 1.7
Haemoglobin concentration at end of procedure (g dL^{-1})	12.8 ± 2.3

Hypotension was induced by increasing isoflurane concentration towards 2−2.4% F_E'Iso and cessation of dobutamine CRI. Monitoring of anaesthesia consisted of electrocardiography, pulse oximetry, capnography, invasive blood pressure measurement, rectal temperature and clinical parameters (eyelid reflex, position of the eyeball, muscle tension, swallowing reflex). A balloon-tipped arterial pressure monitoring catheter (7F, 110 cm; Biosensors International, The Netherlands) was advanced using an introducer from the left jugular vein towards the pulmonary artery. Correct positioning was assessed by direct observation of typical pressure waveforms. The pulmonary artery catheter was used to sample mixed venous blood. The left transverse facial artery was percutaneously catheterized using an 18 gauge butterfly needle for arterial blood sampling and blood pressure monitoring. Peripheral venous blood was sampled from the jugular venous catheter. Oxygen tension (PO_2), carbon dioxide tension (PCO_2), and pH were measured from heparinized blood samples directly after collection, and barometric pressure (Pb) was measured using the blood gas analyser (Rapidlab; Siemens, The Netherlands). Haemoglobin concentrations were measured in ethylenediaminetetraacetic acid (EDTA)-collected blood samples taken from the pulmonary artery catheter using a haematology analyser validated for equine blood (Scil Vetabc; Hariba, The Netherlands).

Study protocol

After induction of general anaesthesia, horses were placed in right lateral recumbency and the animals were instrumented with all monitoring equipment and venous and arterial catheters. The order of conditions that were evaluated was as follows: lateral recumbency with normotension (MAP >70 mmHg), lateral recumbency with hypotension (MAP < 70 mmHg), dorsal recumbency with normotension (MAP >70 mmHg), and dorsal recumbency with hypotension (MAP <70 mmHg). Each condition was maintained for 20 minutes before blood collection was started. At each sampling time, arterial blood samples were taken anaerobically from the transverse facial artery, mixed venous blood samples were taken from the pulmonary artery catheter, and peripheral venous blood was taken from the jugular venous catheter simultaneously, and relevant monitoring parameters were recorded. Oxygen saturation (SaO_2) was calculated from oxygen partial pressures (PaO_2) via algorithms described by Smale et al. (1994) for equine haemoglobin, correcting for pH and arterial carbon dioxide tension ($PaCO_2$). Alveolar oxygen tension (P_AO_2), blood oxygen content, $\dot{Q}_s/\dot{Q}_t$, and F-shunt were calculated using the formulas provided in Table 2. Mean oxygen extraction was calculated for each condition for all horses (lateral recumbency with normo- and hypotension, dorsal recumbency with normo- and hypotension), and the relation between jugular venous ($PjvO_2$) and mixed venous ($P\bar{v}O_2$) oxygen tensions was determined via linear regression analysis.

Statistical analysis

Data were tested for normality using the Shapiro−Wilk test. All data are expressed as mean ± standard deviation (SD). Changes in arterio-venous oxygen content difference (oxygen extraction) between lateral and dorsal recumbency with normo- and hypotension were analysed using a linear mixed model with Tukey *post hoc* tests. Difference in haemoglobin concentration between the beginning and end of the procedure was tested with a paired samples *t*-test.

Intraclass correlation coefficient (ICC) analysis was used to calculate the correlation between venous admixture as determined from arterial and mixed venous blood samples ($\dot{Q}_s/\dot{Q}_t$), and venous admixture as calculated using either jugular blood samples ($\dot{Q}_s/\dot{Q}_{t\ jugular}$) or an assumed fixed arterial-venous oxygen content difference (F-shunt).

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Table 2 Formulas and equations, used in horses anaesthetized with detomidine, butorphanol, ketamine, midazolam and isoflurane in oxygen in lateral and dorsal recumbency during normotensive (mean arterial pressure >70 mmHg) and hypotensive (mean arterial pressure <70 mmHg) anaesthesia

P_AO_2	$P_AO_2 = F_IO_2 \times (Pb - P_{H2O}) - (PaCO_2/RQ)$
CaO_2 (g dL^{-1})	$CaO_2 = (1.34 \times SaO_2 \times Hb) + (0.003 \times PaO_2)$
$\dot{Q}_s/\dot{Q}_t$	$\dot{Q}_s/\dot{Q}_t = (Cc'O_2 - CaO_2)/(Cc'O_2 - C\bar{v}O_2)$
Oxygen extraction (OE) (mL O_2 dL^{-1})	$OE = CaO_2 - C\bar{v}O_2$
F-shunt: calculation of shunt fraction with fixed arterio-venous oxygen content difference	F-shunt $= (Cc'O_2 - CaO_2)/[Cc'O_2 - (CaO_2 - 3.5)]$

P_AO_2, alveolar oxygen tension; F_IO_2, inspiratory oxygen fraction; Pb, barometric pressure; P_{H_2O}, water vapour pressure; $PaCO_2$, arterial carbon dioxide tension; RQ, respiratory quotient; CaO_2, arterial oxygen content; SaO_2, arterial oxygen saturation; Hb, haemoglobin; $\dot{Q}_s/\dot{Q}_t$, venous admixture; $Cc'O_2$, end-capillary oxygen content; $C\bar{v}O_2$, mixed venous oxygen content. P_{H2O} and $PaCO_2$ in mmHg, Hb in g dL^{-1}.
Similar equations to that used for CaO_2 were used for $C\bar{v}O_2$ and $Cc'O_2$, with $P\bar{v}O_2$ used to calculate $C\bar{v}O_2$ and alveolar O_2 tension (P_AO_2) for $Cc'O_2$.

For both arterial normo- and hypotension in different body positions, oxygen extraction was calculated. The correlation between $PjvO_2$ and $P\bar{v}O_2$ was determined via linear regression analysis ($y = ax + b$), where x is $PjvO_2$ and y is $P\bar{v}O_2$. The analysis was repeated after exclusion of the outliers.

Bland–Altman analysis was used to assess the agreement between $\dot{Q}_s/\dot{Q}_t$ and the two alternative measures of venous admixture ($\dot{Q}_s/\dot{Q}_{t\ jugular}$ and F-shunt). The difference between $\dot{Q}_s/\dot{Q}_t$ and the alternative measure of venous admixture for each sample was plotted against their mean value. The upper and lower limits of agreement were calculated as the mean difference (bias) ± 1.96 times the SD. Bias ± 10% was deemed acceptable for valid clinical application of the estimates of $\dot{Q}_s/\dot{Q}_t$. Statistical analysis was performed with SPSS (version 22; IBM, NY, USA). Statistical significance was accepted at $p < 0.05$.

Results

The haemoglobin concentration did not increase over time from the beginning to the end of the procedure ($p = 0.11$, Table 1). Table 3 shows various parameters obtained under normotensive and hypotensive conditions. Linear mixed model analysis showed a significant interaction between body position and blood pressure ($p < 0.05$), with significantly higher oxygen extraction in the hypotensive state in dorsal recumbency (3.97 ± 1.35 mL O_2/100 mL blood), compared with both lateral (3.09 ± 0.61 mL O_2/100 mL blood) and dorsal recumbency during normotension (2.82 ± 0.68 mL O_2/100 mL blood) (mean ± SD) ($p < 0.05$). For lateral recumbency during hypotension, oxygen extraction was 3.25 (±0.99) mL O_2/100 mL blood. (Fig. 1).

The correlation analysis showed a significant positive correlation between $PjvO_2$ and $P\bar{v}O_2$

Table 3 Normotensive (mean arterial pressure > 70 mmHg) and hypotensive (mean arterial pressure < 70 mmHg) conditions in horses anaesthetized with detomidine, butorphanol, ketamine, midazolam and isoflurane in oxygen in lateral and dorsal recumbency. Data are reported as number (n) or as mean ± standard deviation

Variable	Normotension	Hypotension
Blood samples (n)	28	28
MAP (mmHg)	78.9 ± 7.4	43.6 ± 9.1
PaO_2 (mmHg) [kPa]	117.8 ± 66.8 [15.7 ± 8.9]	94.7 ± 66.6 [12.6 ± 1.2]
$PaCO_2$ (mmHg) [kPa]	54.2 ± 8.3 [7.2 ± 1.1]	51.1 ± 6.7 [6.8 ± 0.9]
PjvO2 (mmHg) [kPa]	52.4 ± 16.0 [7.0 ± 2.1]	42.6 ± 9.8 [5.7 ± 1.3]
$P\bar{v}O_2$ (mmHg) [kPa]	42.4 ± 9.0 [5.7 ± 1.2]	36.0 ± 7.7 [4.8 ± 1.0]

MAP, mean arterial pressure; PaO_2, arterial oxygen tension; $PaCO_2$, arterial carbon dioxide tension; $PjvO_2$, jugular venous oxygen tension; $P\bar{v}O_2$, pulmonary arterial mixed venous oxygen tension.

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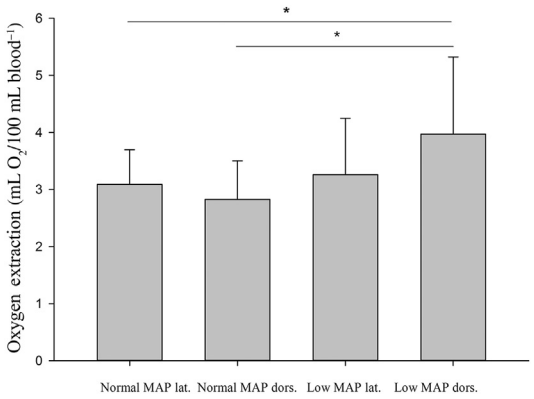

Figure 1 Oxygen extraction (mL O_2/100 mL blood^{-1}) in anaesthetized horses during different positions and blood pressure conditions. Normal mean arterial pressure (MAP), MAP > 70 mmHg; Low MAP, MAP < 70 mmHg, lat., lateral recumbency; dors., dorsal recumbency. *$p < 0.05$.

(ICC = 0.83, $p < 0.001$) (Fig. 2a). When outliers were excluded, an ICC of 0.82 ($p < 0.001$) was found (Fig. 2b). Regression formulas explaining the relationship between $PjvO_2$ and $P\bar{v}O_2$ are $Y = 0.68X + 8.2$ (where Y is the calculated $P\bar{v}O_2$ and X is $PjvO_2$) for all data (Fig. 2a) and $Y = 0.80X + 2.61$ (where Y is the calculated $P\bar{v}O_2$ and X is $PjvO_2$) when outliers were excluded (Fig. 2b).

A significant moderate correlation between $\dot{Q}_s/\dot{Q}_t$ and $\dot{Q}_s/\dot{Q}_{t\ jugular}$ was found (ICC = 0.68, $p < 0.001$) (Fig. 3a). However, bias was −11.52, with wide limits of agreement of −27.65 to 4.61 (Fig. 3b). Using a fixed value for the arterio-venous oxygen content difference (3.5 mL dL^{-1}) for calculation of $\dot{Q}_s/\dot{Q}_t$ (F-shunt), an ICC of 0.88 was found, indicating stronger correlation (Fig. 3c), with a bias of −1.97 and limits of agreement of −13.8 to 9.85 (Fig. 3d).

Discussion

In the present study, the use of $PjvO_2$ proved unreliable to estimate $\dot{Q}_s/\dot{Q}_t$. The F-shunt showed much better accuracy to estimate $\dot{Q}_s/\dot{Q}_t$, with a low bias and lower limits of agreement in Bland–Altman analysis. However, because of the dependency of the oxygen extraction on perfusion state, the use of a variable oxygen extraction formula to estimate $\dot{Q}_s/\dot{Q}_t$ could further improve the accuracy of the estimate of $\dot{Q}_s/\dot{Q}_t$. The relation between $PjvO_2$ and $P\bar{v}O_2$ was also assessed and showed significant linear regression. This regression formula could be used in an algorithm to estimate $\dot{Q}_s/\dot{Q}_t$ from $PjvO_2$ as well.

The use of a fixed oxygen extraction (of 3.5 mL dL^{-1}) to calculate $\dot{Q}_s/\dot{Q}_t$ has been called F-shunt in literature previously. The original F-shunt equation was derived from studies in humans (Harrison et al. 1975) and is strictly dependent on the assumption of stable cardiovascular conditions. However, in clinical practice cardiovascular conditions will be different in different animals and might also be changing during an anaesthetic procedure. Therefore, it might be interesting to assess the influence of cardiovascular conditions on the oxygen extraction. In the study by Briganti et al. (2015), the oxygen extraction was 4.5 (±1.0) mL O_2/100 mL blood under baseline conditions and decreased to 1.9 (±0.3) at higher infusion rates of dobutamine (7.5 μg kg^{-1} minute^{-1}). We also found increased oxygen extraction at lower blood pressure states (representing lower perfusion states of the peripheral tissues).

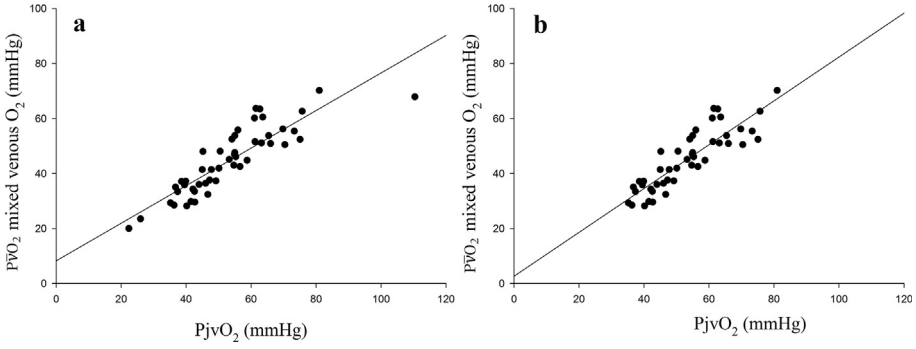

Figure 2 Relationship between jugular venous ($PjvO_2$) and mixed venous pulmonary arterial ($P\bar{v}O_2$) oxygen tension [(a) intraclass correlation coefficient (ICC) = 0.83, $p < 0.001$]. (b) Shows same results when outliers are excluded [(b) ICC = 0.82, $p < 0.001$]. Regression formulas explaining the relationship between $PjvO_2$ and $P\bar{v}O_2$ are $Y = 0.68X + 8.2$ (where Y is the calculated $P\bar{v}O_2$ and X denotes $PjvO_2$) for all data (a) and $Y = 0.80X + 2.61$ (where Y is the calculated $P\bar{v}O_2$ and X denotes $PjvO_2$) when outliers were excluded (b).

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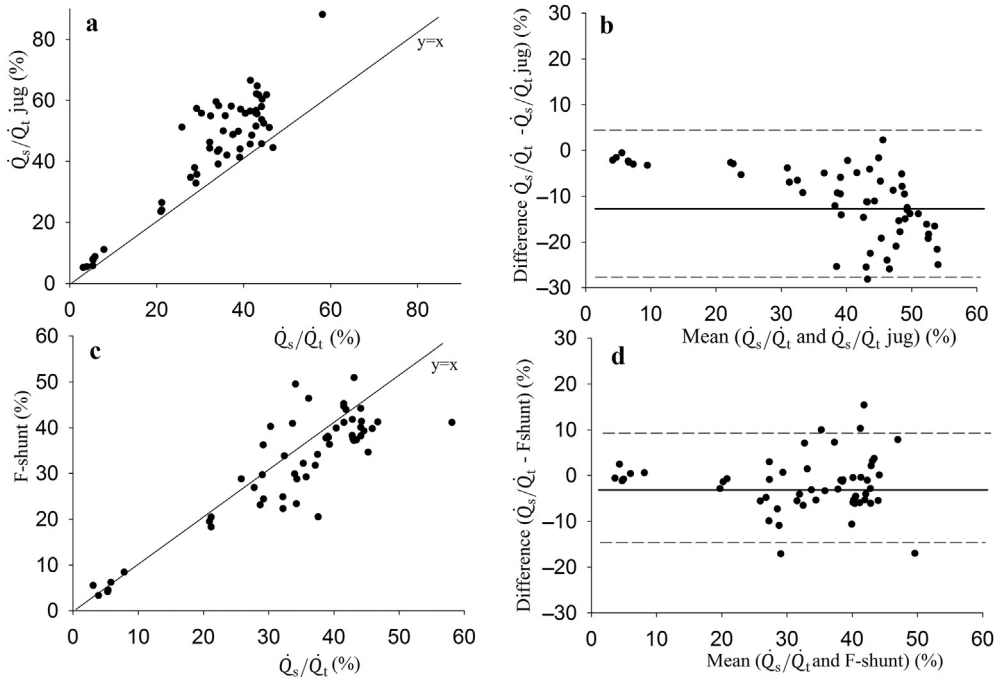

Figure 3 Relationship between venous admixture ($\dot{Q}_s/\dot{Q}_t$) and calculated $\dot{Q}_s/\dot{Q}_t$ (a, b) Scatter plot and Bland–Altman plot with $\dot{Q}_s/\dot{Q}_t$, based on jugular venous oxygen tension ($PjvO_2$) ($\dot{Q}_s/\dot{Q}_{t\,jug}$). Intraclass correlation coefficient (ICC) = 0.68 ($p < 0.001$), bias = −11.5, limits of agreement = −27.7 to 4.6. (c, d) Scatter plot and Bland–Altman plot with $\dot{Q}_s/\dot{Q}_t$, based on fixed oxygen extraction of 3.5 mL O_2 dL^{-1} (F-shunt) ICC = 0.88 ($p < 0.001$), bias = −1.97, limits of agreement = −13.8 to 9.85.

When dobutamine was used to increase blood pressure and cardiac output (the latter not being measured in our study), oxygen extraction decreased. These corresponding findings of Briganti et al. (2015) and our findings led us to believe that using an estimate of $\dot{Q}_s/\dot{Q}_t$ that is based on a variable and blood pressure dependent oxygen extraction and therefore taking the cardiovascular status of the patient better into account, instead of the fixed oxygen extraction in the F-shunt, would possibly be more accurate in estimating $\dot{Q}_s/\dot{Q}_t$. In a follow-up study with new horses, $\dot{Q}_s/\dot{Q}_t$ will be calculated with this adjusted F-shunt with the variable oxygen extraction difference and can be compared with the original F-shunt.

We assessed the correlation between $\dot{Q}_s/\dot{Q}_t$ and F-shunt by means of ICC analysis. Briganti et al. (2015) assessed this correlation by means of the coefficient of determination (r^2) that was found to be 0.73. This correlation was much better compared with the other indices that were described in this study. The correlation was lower at the higher dobutamine rates that were used by Briganti et al. (2015). These higher rates likely created a hyperdynamic circulatory state reducing the time available for equilibration at the alveolar–capillary interface for oxygen diffusion. This may have led to decreased correlation between $\dot{Q}_s/\dot{Q}_t$ and F-shunt at the highest levels of cardiac output (Briganti et al. 2015). In the study by Araos et al. (2012), the F-shunt was assessed in anaesthetized sheep and showed strong correlation ($R^2 > 0.9$) with $\dot{Q}_s/\dot{Q}_t$ over a range of FIO_2 from 0.21 to 1.00. In that study, circulation was stable with assumed normotension during all conditions.

However, correlation between $\dot{Q}_s/\dot{Q}_t$ and F-shunt might not be reflecting validity of the F-shunt to the best extent. Therefore, Bland–Altman analysis was also included in both the studies of Briganti et al. (2015) and our study. With this technique, the bias and limits of agreement can be determined. When using jugular venous oxygen content to estimate $\dot{Q}_s/\dot{Q}_t$, correlation was moderate (ICC = 0.68), but there was a large bias and wide limits of agreement. Using the F-shunt, the bias was relatively low and the limits of agreement were within 15%. Since anatomical shunt flow is 4–5%, and clinically significant venous admixture in horses can likely be well over 20% up to 30–40% (Hubbell and Muir 2015), the observed limits of agreement between $\dot{Q}_s/\dot{Q}_t$ and the F-shunt of less than 10–15% may be deemed acceptable to allow the use of this formula for

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estimation of venous admixture in clinical patients during normo- or hypotension in lateral or dorsal recumbency. Briganti et al. (2015) described comparable bias and limits of agreement (0.3% and −9.4% to +10.1%, respectively) in anaesthetized horses compared with our data. A total of 81.3% of their data were within ±5% of the difference of $\dot{Q}_s/\dot{Q}_t$ and F-shunt. In our study, we found 73.2% of the data to be within ±5% of the difference of $\dot{Q}_s/\dot{Q}_t$ and F-shunt. In the study by Araos et al. (2012), limits of agreement between $\dot{Q}_s/\dot{Q}_t$ and F-shunt in anaesthetized sheep were between −8.3% and 15.1% in the Bland–Altman analysis. These findings are also comparable with our findings.

We hypothesize that using a variable oxygen extraction value in the F-shunt (F-shunt$_{variable}$) to estimate $\dot{Q}_s/\dot{Q}_t$, based on the findings of our study, might lead to further improved validity of the $\dot{Q}_s/\dot{Q}_t$ estimates obtained with lower limits of agreement and a more accurate estimation of $\dot{Q}_s/\dot{Q}_t$. In previous studies (Mosing et al. 2012; van Oostrom et al. 2017), a fixed oxygen extraction of 3.5 mL dL^{-1} has been used to assess venous admixture under varying conditions. The accuracy of such calculations, particularly for the purpose of scientific studies, could be further improved if mean oxygen extraction values established for various blood pressure states (and body positions) or regression formulas for calculation of $P\bar{v}O_2$ from $PjvO_2$ developed in the current study were used.

Not surprisingly, our results show weak validity of the $PjvO_2$ and jugular venous oxygen content to estimate $\dot{Q}_s/\dot{Q}_t$. However, the correlation between $PjvO_2$ and $P\bar{v}O_2$ was good with a linear relationship and the regression formulas between these two could theoretically provide another means of valid estimation of the mixed venous oxygen content and thereby $\dot{Q}_s/\dot{Q}_t$. The validity of this approach would need to be assessed in a future study with new horses as well, providing a new data set of simultaneously obtained PaO_2, $PjvO_2$ and $P\bar{v}O_2$. In human literature, the relationship between central venous (caval vein) oxygen content and mixed venous oxygen content has been described (Faber 1995; Walley 2011). Although central venous oxygen content could not replace mixed venous oxygen content in all types of cardiovascular procedures (Lorentzen et al. 2008), the use of less invasive venous oxygen indices could be useful to monitor patients (Walley 2011).

The current study has some limitations that should be noted. We did not perform cardiac output measurements, which could have provided further insight in global perfusion and oxygen delivery. This did not, however, interfere with measurement of oxygen extraction, since this parameter can be calculated independently of cardiac output. Furthermore, blood samples were taken simultaneously and therefore at very similar cardiac output levels. We used an anaesthetic protocol that consisted of isoflurane with a CRI of detomidine for maintenance. This led to a balanced situation in terms of vasodilative effects of isoflurane and vasoconstrictive effects of detomidine. To influence the mean arterial blood pressure, we either increased F_E'Iso (to induce hypotension) or increased the dobutamine CRI (to maintain normotension). We used low blood pressure conditions as a model for low tissue perfusion states, without knowledge of prevailing cardiac output. However, hypotensive conditions were created by discontinuation of inotropic agent (dobutamine) and increasing F_E'Iso, which is known to decrease both cardiac output and peripheral vessel tone dose-dependently (de Vries et al. 2009; Hopster et al. 2015). The use of blood pressure states to determine different degrees of oxygen extraction does reflect the clinical situation, where cardiac output measurements are not performed routinely in equine patients. The assessment of effects of different body positions and blood pressure states was performed in a fixed rather than a randomized order as this was dictated by the experimental surgical procedure the horses were undergoing. Finally, the correlations between $\dot{Q}_s/\dot{Q}_t$ and calculated $\dot{Q}_s/\dot{Q}_t$ and the regression formulas we obtained for calculation of $P\bar{v}O_2$ from $PjvO_2$ are unlikely to hold true for animals suffering from septicaemia or circulatory shock, because under these circumstances extremely low blood pressures or hyperdynamic circulation as well as cytotoxic changes might lead to altered oxygen extraction ratios (Park et al. 2015).

Conclusions

Using a fixed oxygen extraction to calculate $\dot{Q}_s/\dot{Q}_t$, also called F-shunt, provides acceptable accuracy for routine clinical use, but agreement with pulmonary artery-based $\dot{Q}_s/\dot{Q}_t$ calculations could possibly be further improved using different estimates of oxygen extraction depending on prevailing conditions of arterial blood pressure and positioning, and by use of corresponding regression formulas for calculation of $P\bar{v}O_2$ from $PjvO_2$. This means that $\dot{Q}_s/\dot{Q}_t$ and global oxygen extraction could more reliably be calculated

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in clinical patients, which may lead to improved monitoring of the cardiovascular and respiratory systems during general anaesthesia.

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Authors' contributions

JPAMvL: study design, data collection, statistical analysis and preparation of manuscript. JCdG: study design, data collection, data management and statistical analysis, and preparation of manuscript. HvO: study design, data collection, data management, and preparation of manuscript.

Conflict of interest statement

The authors declare no conflict of interest.

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